Brain vascular image enhancement based on gradient adjust with split bregman

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ABSTRACT

Light Sheet Microscopy (LSM) is a high-resolution fluorescence microscopic technique which enables to observe the mouse brain vascular network clearly with immunostaining. However, micro-vessels are stained with few fluorescence antibodies and their signals are much weaker than large vessels, which make micro-vessels unclear in LSM images. In this work, we developed a vascular image enhancement method to enhance micro-vessel details which should be useful for vessel statistics analysis. Since gradient describes the edge information of the vessel, the main idea of our method is to increase the gradient values of the enhanced image to make the micro-vessels contrast. Meanwhile, an optimum problem whose solution was the final enhanced image with increased gradient values was formulated by designing an energy function. Our method contained two steps: 1) calculate the gradient image of LSM image, and then amplify high gradient values of the original image to enhance the vessel edge and suppress low gradient values to remove noises. Then we formulated a new L1-norm regularization optimization problem to find an image with the expected gradient while keeping the main structure information of the original image. 2) The split bregman iteration method was used to deal with the L1-norm regularization problem and generate the final enhanced image. The main advantage of the split bregman method is that it has both fast convergence and low memory cost. In order to verify the effectiveness of our method, we applied our method to a series of mouse brain vascular images acquired from a commercial LSM system in our lab. The experimental results showed that our method could greatly enhance micro-vessel edges which were unclear in the original images.

Keywords: brain vascular image enhancement, Light Sheet Microscopy, split bregman algorithm, gradient image adjust, L1-regularization.

1. INTRODUCTION

Light Sheet Microscope is a powerful tool for volumetric fluorescence imaging with high temporal and spatial resolution [1][2]. It has been widely used in research on transparent samples such as zebra fish, drosophila, nematode as well as vitro organs with optical clearing [3][4][5][6]. Nicolas Renier etc developed an effective method called iDISCO to immunolabel large tissue samples for LSM imaging [7]. Due to such immunolabeling method, LSM is used to observe the mouse brain vascular network and most of the vessels are clearly visible. However, micro-vessels in the brain are unclear due to the weak fluorescent signal. Therefore, it is in great demand to enhance the micro-vessel signals when observing whole brain vascular network with LSM.

To circumvent this problem, many vessel image enhancement methods have been proposed including filtering in spatial domain or transform domain [8][9][10]. In this work, we have developed an effective brain vascular image enhancement method. Since gradient describes the edge information of the vessel, the main idea of our method is to increase the gradient values of the micro-vessels and make their edges sharp. We adjust the gradient image of original vascular image by amplifying high gradient values while suppressing low gradient. The high gradient regions were the most likely vascular structures. Then, we generate the final enhanced image from the revised gradient image. To achieve this goal,

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we design an energy minimization problem by using of L1-regularization on the gradient item. L1-regularization provide sparse solution and it is widely used in image processing and compressed sensing techniques due to its high reconstruction performance and few data demand [11][12]. The L1-regularized optimization problem can be well solved with split bregman method [13]. Therefore, the split bregman method is used in our method to generate the enhanced image. The experimental result on mouse brain vascular image shows that our method dramatically improves the vascular image quality by enhancing the micro-vessels signals.

2. METHOD

2.1 Expected gradient image calculation

Gradient reflects vessel edge information of mouse brain in vascular network image. High gradient value indicates sharp vessel edge and good visual effect. Therefore, in order to enhance vessel signal, a feasible way is to increase its gradient. In our method, very low gradient value is regarded as noise and greatly suppressed. A fix threshold T value is used to differentiate vascular vessel and noise on gradient image. If the gradient value of a pixel is greater than T, it is treated as vessel and meanwhile enhanced. On the contrary, gradient value lower than T will be suppressed. The gradient update strategy is formulated as:

$$w(x,y)=\begin{cases}1+\lambda/(1+\exp(a(\nabla u_0(x,y)-T)), & \nabla u_0(x,y)\geq T\\ 0, & \nabla u_0(x,y)<T\end{cases} \tag{1}$$

$$g_x(x,y)=w(x,y)*\nabla_x u_0(x,y),\ \ g_y(x,y)=w(x,y)*\nabla_y u_0(x,y)$$

, in which ∇ is a derivative operator, ∇u_0 is the gradient image of the original image u_0, g_x and g_y are the expected horizontal and vertical gradient image, λ limits the maximum amplification weight, T is the amplification threshold, and a is the coefficient of exponential function. Since the gradient values of micro-vessel are relatively low, high weight is allocated to the low gradient value greater than T. Therefore, the micro-vessels are enhanced rather than the noises. Note that, the original vascular image is smoothed by Gaussian filtering before the calculation of the gradient image to reduce the influence of noise.

2.2 Inverse problem formulation

In this step, the problem is converted to that knowing expected gradient image g how to get the enhanced image. We designed the following optimum problem:

$$\min_u \quad \|\nabla_x u-g_x\|_1+\|\nabla_y u-g_y\|_1+\frac{\mu}{2}\|u-u_0\|_2^2 \tag{2}$$

in which L1-regularization and L2-regularization are used. The item L1-regularization of gradient image makes sure that the final enhanced image has an expected gradient image. The item L2-regularization keeps the enhanced image with most of the vessel structure information in original LSM image. The parameter μ dynamically adjusts the weights between the enhanced image and original images to improve the vessel signals, especially for the signals of micro-vessel.

2.3 Optimization algorithm

Split bregman iteration method is an effective tool to solve L1-regularized optimization problem [13]. This method converges fast with low memory requirement and high parallelized performance. To solve the problem in formula (2), split bregman method further converts it to a constrained problem:

$$\min_u \quad \|d_x\|_1+\|d_y\|_1+\frac{\mu}{2}\|u-u_0\|_2^2 \quad s.t.\ d_x=\nabla_x u-g_x, d_y=\nabla_y u-g_y \tag{3}$$

Then we add L2 penalty function terms and strictly enforce the constraints by using of the Bregman iteration, yielding a new unconstrained problem:

$$\min_{d_x, d_y, u} \quad \|d_x\|_1 + \|d_y\|_1 + \frac{\mu}{2}\|u - u_0\|_2^2 + \frac{\lambda}{2}\|d_x - \nabla_x u + g_x - b_x^k\|_2^2 + \frac{\lambda}{2}\|d_y - \nabla_y u + g_y - b_y^k\|_2^2 \tag{4}$$

, where the proper values b_x^k and b_y^k are calculated by Bregman iteration. Then, formula (4) is split into three separate subproblems by decoupling u, d_x, and d_y.

u^{k+1} is calculated through the following subproblem:

$$u^{k+1} = \min_u \quad \frac{\mu}{2}\|u - u_0\|_2^2 + \frac{\lambda}{2}\|d_x^k - \nabla_x u + g_x - b_x^k\|_2^2 + \frac{\lambda}{2}\|d_y^k - \nabla_y u + g_y - b_y^k\|_2^2 \tag{5}$$

, which is differentiable. It has an optimality condition:

$$(\mu I - \lambda\nabla)u^{k+1} = \mu u_0 + \lambda\nabla_x^T(d_x^k + g_x - b_x^k) + \lambda\nabla_y^T(d_y^k + g_y - b_y^k) \tag{6}$$

In view of the strictly diagonally dominant of the system, Gauss-Seidel method, which is an effective iterative algorithm, is used to get approximate solutions [13].

The subproblems of d_x and d_y have similar form with u:

$$\begin{cases} d_x^{k+1} = & \min_{d_x} \|d_x\|_1 + \frac{\lambda}{2}\|d_x - \nabla_x u^k + g_x - b_x^k\|_2^2 \\ d_y^{k+1} = & \min_{d_y} \|d_y\|_1 + \frac{\lambda}{2}\|d_y - \nabla_y u^k + g_y - b_y^k\|_2^2 \end{cases} \tag{7}$$

, which can be solved using a generalized shrinkage formula

$$\begin{cases} d_x^{k+1} = & shrink(\nabla_x u^k - g_x + b_x^k, 1/\lambda) \\ d_y^{k+1} = & shrink(\nabla_y u^k - g_y + b_y^k, 1/\lambda) \end{cases} \tag{8}$$

where

$$shrink(r, \xi) = \frac{r}{|r|} * \max(r - \xi, 0) \tag{9}$$

Overall, the detailed steps of solving the minimization problem in formula (2) with split bregman iteration method are described as follows.

Initialize: $u^0 = u_0, d_x^0 = 0, d_y^0 = 0, b_x^0 = 0, b_y^0 = 0$

while $\|u^k - u^{k+1}\| > tol$ *and* $k < MaxSteps$

update u^{k+1} *by* (6)

update d_x^{k+1}, d_y^{k+1} *by* (8)

$b_x^{k+1} = b_x^k + (\nabla_x u^{k+1} - g_x - d_x^{k+1})$

$b_y^{k+1} = b_y^k + (\nabla_y u^{k+1} - g_y - d_y^{k+1})$

end while. *output enhance image* u^{k+1}

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3. APPLYING TO MOUSE BRAIN VASCULAR IMAGES

In order to test our method, a brain was obtained from a 5-day old C57BL/6J mouse. Mouse brain vessels were stained with Alexa Fluor-488 fluorescence antibody to CD31 by using of the iDISCO method. Then, the mouse brain was imaged with a commercial LSM system (UltraMicroscope, LaVision BioTec GmbH) and our method was applied to the brain vascular images. As shown in Figure 1(a), the large vascular vessel is clear but the micro-vessels are blurring in original LSM image. Figure 1(b) shows the enhanced image with a fix amplification threshold T (0.5σ). σ is the standard deviation of gradient magnitude image of the original image. The micro-vessels are greatly enhanced in Figure 1(b). The difference image between original image and enhanced images demonstrates that only the vessel edges are enhanced (shown in Figure 1(c)). Figure 1(d)-(f) show the zoom images of Figure 1(a)-(c). The red arrows in Figure 1(d) indicate three micro-vessels which are significantly enhanced. The experimental results show that our method is effective to enhance the micro-vessel in LSM images.

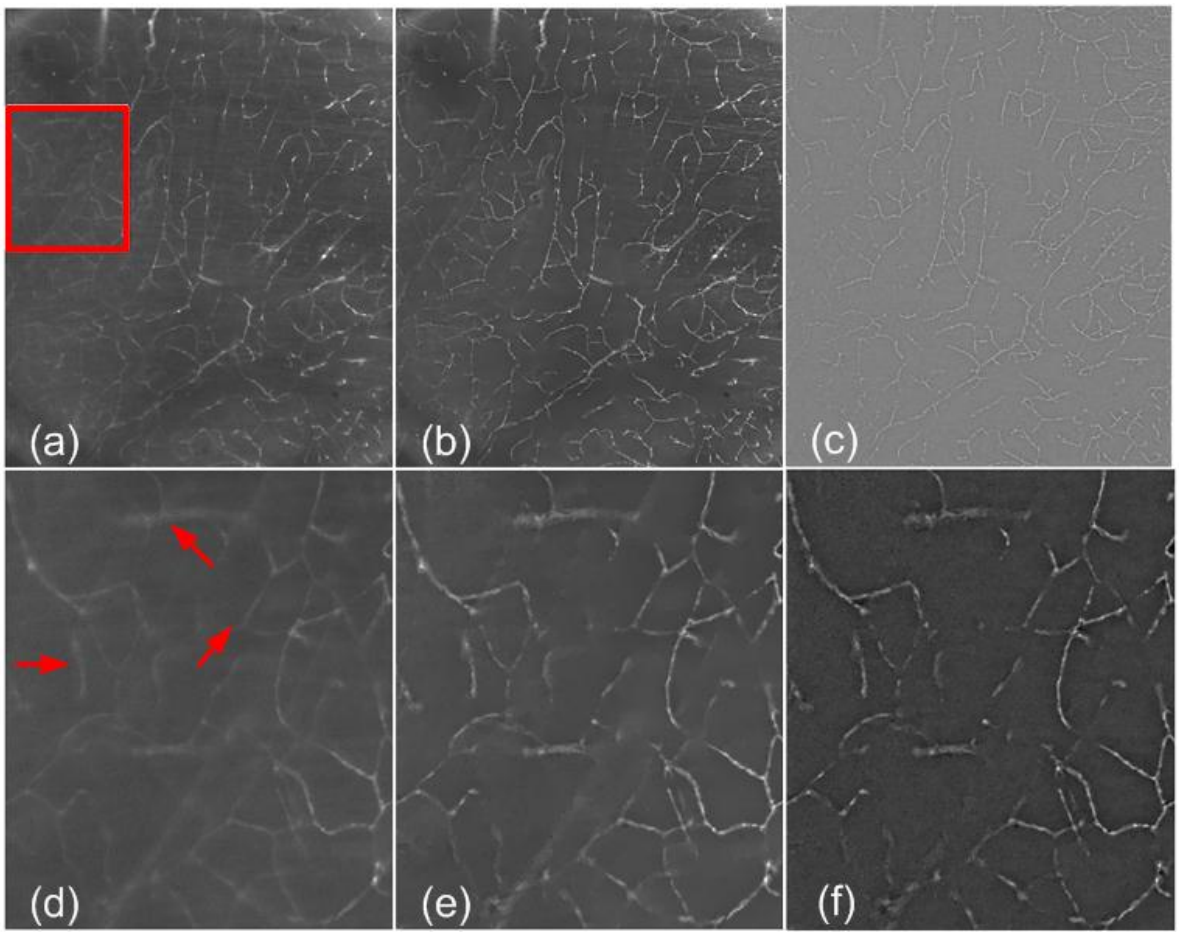

Figure 1. Image enhancement experiments of mouse brain vascular. (a) Original LSM vascular image. (b) Enhanced image of (a). (c) Different image between (b) and (a). (d) Zoomed image of rectangle region in (a). (e) Enhanced image of (d). (f) Different image between (e) and (d).

4. DISCUSSION AND CONCLUSION

In this paper we have proposed a vascular image enhance method mainly by adjusting the gradient image. The basic idea of our method is to amplify the low vessel gradient and improve micro-vessels' contrast. In our method, an L1 regularization optimum problem was designed and solved by split bregman algorithm. Furthermore, we applied our method to mouse brain vascular images. The experimental results demonstrated that the proposed method dramatically

improved vascular image quality through enhancing both large vessels and micro-vessels. It should be note that, the amplification threshold is very important in our method. Too low threshold will lead to an enhance for both vessels and noises like the stripe noises [14][15]. On the contrary, too high threshold will diminish the enhancement effect of the vessels. Therefore, it should be careful to choose a right threshold in our method for the best enhancement. In this work, the threshold value is fixed manually. In the future, we will develop automated threshold calculation method according to the evaluation of the enhanced image.

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