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Kernel density estimation applications in vessel extraction for MRA images

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Abstract

Vascular-related diseases have become increasingly significant as public health concerns. The analysis of blood vessels plays an important role in detecting and treating diseases. Extraction of vessels is a very important technique in vascular analysis. Magnetic Resonance Angiography (MRA) is a medical imaging technique used to visualize the blood vessels and vascular system in three-dimensional images. These images provide detailed information about the size and shape of the vessels, any narrowing or stenosis, as well as blood supply and circulation in the body. Tracing vessels from medical images is an essential step in the diagnosis and treatment of vascular-related diseases. Many different techniques and algorithms have been proposed for vessel extraction. In this paper, we present a vessel extraction method based on the Kernel density estimation (KDE). Numerical experiments on real 2D MRA images demonstrate that the presented method is very efficient. The effectiveness of the proposed method has been proven through comparative analysis with validated existing methods.

Keywords. Vessel extraction, Kernel density estimation, MRA images, Bandwidth selection. 1991 Mathematics Subject Classification.

1. INTRODUCTION

Vascular disease is one of the most important causes of death worldwide, especially in industrialized countries. In the U.S.A., heart and cerebrovascular diseases were the leading and third leading causes of death in 2006, respectively [16, 17]. Malignant tumors, which heavily rely on vessel recruitment and angiogenesis, ranked second as the cause of death [15]. Additionally, vascular diseases are a major contributor to mortality and disability in individuals with diabetes [8]. These compelling facts emphasize the need for research efforts to enhance our understanding of the vascular system's structure, associated processes, and diseases. Such endeavors can ultimately lead to advancements in diagnostic and intervention procedures. It's worth noting that the vessel structure of the blood circulatory system is exceptionally intricate, being one of the most complex structures within the body [16].

Blood vessel delineation on medical images is crucial for various practical applications like diagnosing vessel conditions (e.g., stenosis or malformations) and aligning patient images taken at different times [20]. Vessel segmentation algorithms play a vital role in automated radiological diagnostic systems. These segmentation methods vary based on imaging modality, application field, automation level, and other specific factors [23]. There's no one-size-fits-all segmentation method that works for every medical imaging modality. While some methods rely on intensity-based pattern recognition techniques such as thresholding followed by connected component analysis [13, 28], others utilize explicit vessel models to extract vessel contours [1–3]. Depending on image quality and artifacts like noise, certain segmentation methods may require preprocessing before applying the algorithm [9, 40]. Additionally, some methods employ post-processing techniques to address issues related to over-segmentation [20].

Medical imaging is a technique used to create images of the human body for use in clinical studies or medical science. There are several different types of imaging as X-ray imaging, Computed tomography (CT), Mammography, Nuclear medicine and molecular imaging, Magnetic Resonance Imaging (MRI), Magnetic Resonance Angiography (MRA),

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Radiography and Fluoroscopy to diagnose this disease. Among which X-ray angiography is known as the standard method for diagnosis [20, 32]. MRA is a type of MRI that looks specifically at the body's blood vessels. These images mainly have low quality and contrast and high noise, and the difference between the vessel and the background is small in many cases [6, 20].

In the present day, numerous medical imaging modalities and protocols have been developed specifically for visualizing vessels, typically referred to as angiography. Among them are techniques that involve administering a contrast agent specific to the modality, which enhances the visibility of blood vessels [32].

Magnetic Resonance Angiography is a non-invasive medical imaging technique used to visualize the blood vessels in the human body. Initial advancements in MRA imaging were made in the 1980s, which allowed for the creation of digital angiographic images[19]. This technique is utilized in the diagnosis of vascular diseases and disorders such as vessel narrowing, abnormal vessel formation, and vessel obstructions [16, 19]. In 1980, a version of the MRA technique called TOF-MRA was developed. This field induces blood flow in the vessels, which is captured in the imaging. This technique provides higher quality images than classical angiography and does not require surgery [14, 19].

Several researches have been done to extract vessels in MRA images and various methods have been used. The history of extracting vessels in MRA images dates back to the 1970s. Initially, this technique was used during open surgeries with the use of classical angiography. In this method, a contrast agent was injected into the vessels, and then images of the vessels were captured using film in angiography. However, this method was invasive and required surgery to refresh the injection from the bone in the chest and face. Currently, there is no universally applicable method that achieves good results for every type of image. Therefore, it is necessary to quantify the effectiveness of an edge detection method by comparing the results obtained with a ground truth model [22, 29, 38]. However, finding a measure that accurately evaluates the obtained boundaries poses a complex problem [39].

In the 1990s, newer methods for vessel extraction in MRA images were introduced. New techniques such as the use of magnetic resonance imaging (MRI), dynamic contrast agent utilization, and phase-contrast imaging have brought significant improvements in the accuracy and diagnostic precision of these images [26].

The Probability Density Function (PDF) plays a vital role in blood vessel extraction and image processing. The PDF is a tool for obtaining information about the features and structure of blood vessels, enabling their separation from the image background [24, 36]. By fitting a statistical model using the probability density function, specific features such as pixel intensity can be accurately analyzed within the domain occupied by the blood vessels. This capability illuminates and distinguishes between blood vessels and the image background, aiding in the identification of patterns and disease-related features [5].

The most general method of estimating the density function in the non-parametric state is the estimation of the density function using the kernel method [21]. The concept of the kernel estimate of the KDE density function was first introduced by the German mathematician Walter Rosenblatt in 1956 [30]. However its modern and generalized form can be attributed to the work of Edward Parzen, who independently developed this technique in 1962 [10]. In this method, it is assumed that we have no information about the probability distribution of the data. Apart from the fact that the data has a probability density function, we do not consider any other assumptions about the probability distribution of the data. To apply the KDE, one needs to specify the kernel function K(.) as well as the bandwidth parameter h controlling the smoothness of \hat{f} . It is recognized the choice of h is more signicantly related to the accuracy of the density estimation than the choice of kernel function K [4, 34].

Over the years, the vessel extraction methods using kernel density estimation have been refined to enhance accuracy and reduce false positives and false negatives. Researchers have incorporated additional techniques such as edge detection, vessel tracking, and multi-scale analysis to improve the performance of these algorithms [4]. More recently, kernel density estimation-based vessel extraction methods have been combined with machine learning techniques such as deep learning and convolutional neural networks [4, 20, 23]. This integration has allowed for even more accurate and efficient vessel extraction, opening new avenues for clinical diagnosis and treatment planning.

2. Kernel density estimation

Probability density function is a basic concept in statistics. Consider a quantitative variable that has a probability density function f. The determination of the function f gives a natural description of the distribution. Now suppose



we have a set of observed data, which we assume is a sample of an unknown probability density function. Density estimation is making an estimate of the density function from a number of observed data. Density estimation can provide us with useful explanations about the shape of the data, such as their skewness and multimodality.

The kernel density estimation (KDE) is a non-parametric method that is commonly used for density estimation and data smoothing. The KDE can be used to estimate the probability density function (PDF) of image data and then use this information to perform segmentation based on density thresholds. The KDE estimates the underlying PDF of the image data by considering each pixel as a data point. A kernel function (e.g., Gaussian) is used to compute the density at each point, which is a weighted average of neighboring points. The bandwidth of the kernel determines the size of the neighborhood.

Kernel density estimation is a technique for estimation of probability density function that is a must-have enabling the user to better analyse the studied probability distribution than when using a traditional histogram. Unlike the histogram, the kernel technique produces a smooth estimate of the pdf, uses all sample point locations and more convincingly suggests multimodality. Unlike histograms, even with a small number of samples, kernel density estimation leads to a smooth, continuous, and differentiability density estimate. Since kernel density estimation does not assume any specic underlying distribution and the estimate can converge to any density shape with enough samples, this approach is suitable for modeling the color distribution of regions with patterns and mixture of colors.

Let the series $\{x_1, x_2, \ldots, x_n\}$ be an independent and identically distributed (i.i.d) sample of n observations taken from a population X with an unknown probability distribution function f(x). Kernel estimate $\hat{f}(x)$ of original f(x)assigns each *i*-th sample data point x_i a function $K(x_i, t)$ called a kernel function in the following way [21]:

$$\hat{f}(x) = \frac{1}{nh} \sum_{i=1}^{n} K\left(\frac{x - X_i}{h}\right),$$
(2.1)

K(x) is nonnegative and bounded for all real x and $\int_{-\infty}^{\infty} K(x) dx = 1$.

The kernel estimator $\hat{f}(x)$ defined in (2.1) constructed from any general nonnegative bounded kernel function k(.) that satisfies

$$(i) \int k(v) \, \mathrm{d} \, v = 1,$$

$$(ii) \, k(v) = k(-v),$$

$$(iii) \int v^2 k(v) \, \mathrm{d} \, v = \kappa_2 > 0,$$

(2.2)

is a consistent estimator of f(x). Note that the symmetry condition (ii) implies that $\int vk(v) dv = 0$. By consistency, we mean that $\hat{f}(x) \to f(x)$ in probability [21].

Note that k(.) dened in (2.2) is a (symmetric) PDF. For recent work on kernel methods with asymmetric kernels, see Abadir and Lawford (2004). In general, we refer to k(.) as a kernel function and to h as a smoothing parameter (or, alternatively, a bandwidth or window width). In fact one might use many other possible choices for the kernel function k(.) in this context. For example, one could use a standard normal kernel given by

$$k(v) = \frac{1}{\sqrt{2\pi}} e^{-\frac{1}{2}v^2}, \qquad -\infty < v < \infty.$$
(2.3)

This class of estimators can be found in the first published paper on kernel density estimation by Rosenblatt (1956), while Parzen (1962) established a number of properties associated with this class of estimators and relaxed the nonnegativity assumption in order to obtain estimators which are more efficient.

The KDE with automatic bandwidth selection [33] is used to estimate the density function of pixel intensities. Gaussian kernel functions are used for the KDE for each spot as Eq. (2.4).

$$\hat{f}(y_j) = \frac{1}{n} \sum_{i=1}^n \frac{1}{\sqrt{2\pi h}} \exp\left(-0.5 \cdot \left(\frac{y_j - x_i}{h}\right)^2\right),\tag{2.4}$$

where x_i is the *i*-th sample in a spot, y_j is the *j*-th spot, h is a bandwidth used in the Gaussian kernel to estimate a spot probability density function (pdf), n is the sample size of pixels in a spot.

3. BANDWIDTH SELECTION

The performance of kernel density estimators, however, is highly dependent on the choice of "bandwidth". Although it is not possible to determine a single best selection method in bandwidth selection, the population structure in which the data to be estimated for density is observed has great importance [11, 25]. Unfortunately, there is no universal bandwidth selector that fits all the situations.

A poorly chosen bandwidth value may lead to undesired transformations of the density plot. A small bandwidth leads to undersmoothing and a huge bandwidth leads to oversmoothing. In both cases, the true picture is hidden from us. So, we need an algorithm that chooses the optimal bandwidth value and avoids oversmoothing and undersmoothing. Many methods have been proposed to find the optimal bandwidth. The most famous and simplest of these methods are Scott's rule and Silvermans rule [35, 37]. If you want know more about nonparametric bandwidth selectors, you can find nice overviews in [12, 27, 31].

MSE is a common criterion used to measure the accuracy or goodness of t of a statistical estimation or prediction, including the KDE. In the context of the KDE, the MSE is used to evaluate how well the estimated PDF matches the true underlying distribution. The MSE of KDE can be written as follows [11]:

$$MSE\left(\hat{f}(x)\right) = E\left\{\left[\hat{f}(x) - f(x)\right]^{2}\right\}$$
$$= \operatorname{var}\left(\hat{f}(x)\right) + \left[E\,\hat{f}(x) - f(x)\right]^{2}$$
$$\equiv \operatorname{var}\left(\hat{f}(x)\right) + \left[\operatorname{bias}\left(\hat{f}(x)\right)\right]^{2}.$$

Theorem 3.1. Let X_1, \ldots, X_n denote *i.i.d.* observations having a three-times differentiable PDF f(x), and let $f^{(s)}(x)$ denote the s-th order derivative of f(x)(s = 1, 2, 3). Let x be an interior point in the support of X, and let f(x) be that defined in (1.8). Assume that the kernel function k(.) is bounded and satisfies (2.2). Also, as $n \to \infty, h \to 0$ and $nh \to \infty$, then

$$MSE\left(\hat{f}(x)\right) = \frac{h^4}{4} \left[\kappa_2 f^{(2)}(x)\right]^2 + \frac{\kappa f(x)}{nh} + o(h^4 + (nh)^{-1}) \\ = O(h^4 + (nh)^{-1}),$$
(3.1)

where $\kappa_2 = \int v^2 k(v) \, \mathrm{d} v$ and $\kappa = \int k^2(v) \, \mathrm{d} v$.

Proof. in [26].

However, MISE is preferred over the MSE in the KDE because it is better suited for assessing the accuracy of PDF estimates across the entire data space. It considers the global behavior of the estimator and incorporates the trade-off between bias and variance, making it a more appropriate criterion for evaluating the KDE performance, and it can be written as follows [21, 25]:

IMSE
$$(\hat{f}) \stackrel{\text{def}}{=} \int E\left[\hat{f}(x) - f(x)\right]^2 dx = \frac{1}{4}h^4\kappa_2^2 \int \left[f^{(2)}(x)\right]^2 dx + \frac{\kappa}{nh} + o(h^4 + (nh)^{-1}).$$
(3.2)

AMISE stands for Asymptotic MISE and AMISE are expressed as follows [30]

IMSE
$$\left(\tilde{f}_{n,h}(\cdot)\right) = (nh)^{-1}R(K) + \frac{1}{4}h^4\mu_2(K)^2\Psi_4,$$
(3.3)

where $\Psi_4 = \int_{-\infty}^{\infty} f^{(4)}(x) f(x) dx$ or more general

$$\Psi_r = \int_{-\infty}^{+\infty} f^{(r)}(x) f(x) \, \mathrm{d}\, x = \mathcal{E}(f^r(X)), \quad \text{and} \quad R(K) = \int K(x)^2 \, \mathrm{d}\, x, \mu_2(K) = \int x^2 K(x) \, \mathrm{d}\, x.$$

Hence, the optimum bandwidth value that minimizes the MISE or AMISE must be found. To minimize $MSE(\hat{f}(x))$, one should balance the squared bias and the variance terms. The optimal choice of h (in the sense that $MSE(\hat{f}(x))$ is minimized) should satisfy $d MSE(\hat{f}(x))/dh = 0$. By using (3.1), it is easy to show that the optimal h that minimizes the leading term of $MSE(\hat{f}(x))$ is given by

$$h_{\rm opt} = c(x)n^{-1/5},\tag{3.4}$$

where $c(x) = {\kappa f(x)/[\kappa_2 f^{(2)}(x)]^2}^{1/5}$. Suppose that we are interested not in tailoring the bandwidth to the pointwise estimation of f(x) but instead in tailoring the bandwidth globally for all points x, that is, for all x in the support of $f(\cdot)$ (the support of x is defined as the set of points of x for which f(x) > 0, i.e., $\{x : f(x) > 0\}$). In this case we can choose h optimally by minimizing the "integrated MSE" (IMSE) of $\hat{f}(x)$. letting h_{opt} denote the optimal smoothing parameter that minimizes the leading terms of (3.2), we use simple calculus to get

$$h_{\rm opt} = c_0 n^{-1/5},\tag{3.5}$$

where $c_0 = \kappa_2^{-2/5} \kappa^{1/5} \left\{ \int \left[f^{(2)}(x) \right]^2 \mathrm{d}x \right\}^{-1/5} > 0$ is a positive constant.

One popular way of choosing the initial h, suggested by Silverman (1986), is to assume that f(x) belongs to a parametric family of distributions, and then to compute h using (3.5). For example, if f(x) is a normal PDF with variance σ^2 , then $\int [f^{(2)}(x)]^2 dx = 3/[8\pi^{1/2}\sigma^5]$. If a standard normal kernel is used, using (3.5), we get the pilot estimate

$$h_{\rm pilot} = (4\pi)^{-1/10} \left[(3/8)\pi^{-1/2} \right]^{-1/5} \sigma n^{-1/5} \approx 1.06\sigma n^{-1/5}.$$
(3.6)

In practice, σ is replaced by the sample standard deviation of $\{X_i\}$ in = 1, while Silverman (1986, p. 47) advocates using a more robust measure of spread which replaces σ with A that given by

$$A = \min\left(\hat{\sigma}, \frac{R}{1.34}\right),\tag{3.7}$$

$$h_{\rm opt} = 0.9An^{-1/5}.$$
(3.8)

Although they are simple and easy to compute, they have limitations. The first one requires the data from the normal distribution. Should the underlying distribution be "close" to a normal distribution, then this will provide good results and for exploratory purposes, it is certainly computationally attractive. By choosing the normal kernel, our concern in this regard has been resolved. Our approach for vessel extraction, which it is named "vessel extraction by Density" (VED) (see Algorithm 1), it is based on the estimation of density function in the central pixel of the mask, where the results of the convolution are stored into a new image. The obtained density image has values of pixels that belong to the interval [0, 1].

Vessel extraction method using kernel density estimation for MRA images can be summarized as the following algorithm:

- (1) Improve the quality of the image with any necessary image enhancement or denoising technique if needed.
- (2) Convert the MRA image to grayscale, if it is not already
- (3) Apply a Hessian-based vesselness filter to enhance the vessel-like structures in the image. This filter computes the eigenvalues of the Hessian matrix to identify regions with high curvatures, indicating the presence of vessels.
- (4) Threshold the vesselness image to obtain a binary image, where 1 represents vessel pixels and 0 corresponds to non-vessel pixels. The threshold value can be determined using techniques like Otsu's method or another



way by calculating the histogram of the density image and find around the associated density value of the biggest value of frequency in the histogram.

- (5) Compute the kernel density estimation (KDE) using nearby vessel pixels. The KDE generates a smooth probability map that represents the likelihood of a pixel being part of a vessel.
- (6) Label as vessel all pixels with the lower density values than threshold u
- (7) We construct the mask M as follows:

$$M_{ij} = \begin{cases} 1, & \text{if the pixel } ij \text{ is a vessel pixel,} \\ 0, & \text{otherwise,} \end{cases}$$

where M_{ij} denotes the *ij*-th value of mask M.

- (8) Do VEDs mask on f and set in f_{VED} .
- (9) Output: binary image

This algorithm serves as a general guideline, and various variations and optimizations may exist depending on specific requirements and the implementation approach chosen. As an explanation, we may have to Normalize the vessel probability map to ensure values are between 0 and 1 or Apply any additional post-processing steps to refine the vessel extraction, such as connected component analysis to remove small isolated regions, or region growing to include nearby vessel pixels.

Algorithm 1 Vessel extraction by KDE.

- 1: Input given image
- 2: Calculate the data-driven bandwidth for the KDE as Eq. (2.3).
- 3: Calculate the KDE using Eq. (2.4).

Initialize: R = 0;for i = 1, 2, ..., m do for j = 1, 2, ..., m do $R(i, j) = \hat{f}(p(i, j));$ function (2). Determine the sumi-

- $R(i,j) = \hat{f}(p(i,j))$; where p is the pixel in the Image 1 at position i, j and \hat{f} is the kernel density estimation function (2).
- 4: Determine the u using techniques like Otsu's method or the first local minimum of the KDE; that u = threshold(R) and R = |R| < u;
- 5: Compute VEDs mask by Eq. (3.9).
- 6: Do VEDs mask on f and set in f_{VED} . End.

(3.9)





FIGURE 1. Results of extraction for Example 4.1.

4. Numerical Example

In this section, we test the presented method on three different TOF-MRA Circle of Willis Inverted MIP images. The tests have been performed on a laptop with core i7, 2GHz processor and 4GB RAM. We compare our results with K-means clustering method [7], expectation maximization segmentation (EMS), the dual-tree complex wavelet tight frame algorithm [2] (TFA) and Wilson method [39].

The blood vessels contain regions with high and low intensities, containing some thin vessels with intensities as low as the intensity of the background. Intersections of partial structures even increase the difficulty of the segmentation [2]. A qualitative comparison among different approaches can only be done by direct observation of figures.

Example 4.1. Consider a 512×512 TOF-MRA Circle of Willis of carotid vascular system. Figure 1(a) shows such an image obtained by http://www.mrtip.com. The Figures 1(b)-1(f) show the results of vessel extraction by K-means, EMS, TFA algorithms, Wilson and presented methods.

results demonstrate that EMS algorithm, TFA algorithm, Wilson method and Presented method could provide better visibility of small vessels and yield better segmentation results. Comparisons of these results reveal that our presented method could be useful to improve the continuity of the extracted vessels. it is important to track vessels with small calibre in order to determine if there are pathological lesions around them. When comparing the segmented result, we see that these fine vessels could be detected when the kernel density estimation employed. The our method approach is indeed helpful in finding the edges of vascular with low contrast.







(c) EMS algorithm.







(e) Wilson method.

(f) Presented method.

FIGURE 2. results of extraction for Example 4.2.

Example 4.2. Consider a 512×512 TOF-MRA Circle of Willis coronal of carotid vascular system. Figure 2(a) shows such an image obtained by http://www.mrtip.com. The Figures 2(b)-2(f) show the results of vessel extraction by K-means, EMS, TFA algorithms, Wilson and presented methods.

The results clearly show that Presented method can get more features out from the image. We see that K-means clustering and TFA algorithm methods cannot detect many pixels that should be on the boundary of the vessels, especially those on the tips of the thin vessels. They are unable to recover the small occlusions along the coherence direction, while EMS algorithm, Wilson method and presented methods performed well. In contrast, EMS algorithm, Wilson method detects much more details of the thin vessels and with higher accuracy. EMS algorithm and Wilson methods have similar results.

To compare Wilson method and presented method more closely, we enlarge the rectangular boxes in Figure 2 we notice that our method is able to extract smoother boundaries than Wilson method and, in particular, it avoids some artifactsnear the boundary.

Example 4.3. Consider a 512×512 TOF-MRA Circle of Willis coronal of carotid vascular system. Figure 3(a) shows such an image obtained by http://www.mrtip.com. The Figures 3(b)-3(f) show the results of vessel extraction by K-means, EMS, TFA algorithms, Wilson and presented methods.





FIGURE 3. Results of extraction for Example 4.3.

The visual comparison between corresponding viewpoints highlights that K-means clustering method and TFA algorithm fails to detect most of the thin vessels which are, instead, well captured by EMS algorithm and Wilson method and presented method. The differences between the results of EMS algorithm and Wilson method and presented method is quite evident. Our presented method present a considerable number of thin vessels distributed around the thick vessels, and they are very hard to detect because of the weak contrast and the underlying noise. Our presented method is able to capture almost all the thin vessels correctly with much more details on them.



5. Conclusions

In this paper, we introduced a new vessel extraction method based on kernel density estimation. We presented new model for brain vessel data. In this model, kernel density estimation is used. The test of the algorithm on real MRA images demonstrate the ability of our method in vessel extraction. The method can be implemented fast and gives very accurate, smooth boundaries, and avoids artifacts. The results clearly show that presented method can get more features out from the image.

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