Adaptive window-based tracking for the detection of membrane structures in kidney electron micrographs

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Abstract. An algorithm for the detection and measurement of the glomerular basement membrane in kidney electron micrographs by image analysis techniques is described. Starting from a user-specified point, local features within a small window are computed to give a feature score. Feature scores for adjacent neighbourhoods are also determined, and windows that satisfy similarity criteria are linked to produce the centerline of the membrane. A region-growing process completes the segmentation procedure. The adaptive and local nature of the algorithm ensures successful segmentation despite the complex and variable characteristics of the micrograph image.

Medical image processing – Image segmentation – Adaptive segmentation – Region growing

1 Introduction

The application of image-analysis techniques to tissue sections (Abmayr et al. 1987; O’Gorman 1985; Yamada 1988) has had limited success because of the inherent complexity of histological images, variability in specimen preparation, non-negligible thickness of the specimen sections resulting in focal planes that are not sharply defined, and poorly contrasted and vague structures obtained with the staining protocols. Conventional techniques that have been successfully applied to images of single cells (Liedtke 1987; Ong and Nickolls 1986) will generally not work here without extensive modification, and there is no library of standard algorithms that can be applied to all types of histological images.

One area that has been neglected in the past is the application of computer vision techniques to the analysis of kidney electron micrographs. An example of a digitized electron micrograph as viewed on a video monitor is shown in Fig. 1. Morphometric analysis of kidney cellular structures is of interest to the renal pathologist, who often has to resort to manual methods to obtain the necessary data. One example is measurements of the glomerular basement membrane (GBM), which appears as a narrow, meandering light-gray strip of fairly uniform texture. This membrane is responsible for the prevention of loss of protein and red blood cells, and its quantification is important because changes in GBM structure and thickness indicate possible pathological conditions. Since glomeruli are three-dimensional objects, measurements of GBM widths from tissue sections can only provide an estimate of actual GBM thickness; notwithstanding this caveat, automated measurements would greatly assist the pathologist in diagnosis and research.

Fig. 1. A digitized electron micrograph viewed on a video monitor

The frequency distribution of GBM thickness has been used in investigations of different kidney diseases (Autio-Haromainen and Rapola 1983; Basta-Jovanovic et al. 1990; Coleman et al. 1986; Saxena et al. 1990; Tiebosch et al. 1989). In these studies, the measurements were done manually, with and without the aid of a computer. A popular method employs a sampling grid superimposed on the micrograph (Basta-Jovanovic et al. 1990; Marion and Carlson 1989; Saxena et al. 1990). Perpendicular intercepts of the GBM are measured at points of intersection with the grid. A fundamental objection to these measurements is the sub-
jective nature of determining the direction along which the width is to be measured. The unevenness of the boundary also raises doubts as to whether these point measurements reflect the actual GBM thickness. Another method (Coleman et al. 1986) measures the average thickness of the GBM from the area and length of GBM segments obtained from manual outlining with the assistance of a digitizing tablet and a computer. All such manual measurement methods, besides being slow and laborious, are prone to subjectivity and human error.

The image-analysis problem in this case is basically one of segmenting a relatively narrow structure in a complex scene. As will be explained in greater detail in the next section, the GBM does not exhibit distinctive features that can be employed for segmentation using standard algorithms. A somewhat similar problem is present in the tracking of coronary arteries in angiogram images for the purpose of arterial-width measurement (Eichel et al. 1988). Several sophisticated approaches have been explored, including the use of adaptive matched filtering (Sun 1989), gradient profiles (Colchester et al. 1990), and an intensity-based look-ahead technique for centerline tracing (van Cuyck et al. 1988). Though these methods are successful to some degree, they are not applicable to the segmentation of GBM structures because of the vast difference in image characteristics — angiogram images contain well-defined structures against a relatively uniform background and are very much simpler compared to kidney-tissue sections.

Based on visual characteristics and disease type, GBMs can be generally divided into two distinct categories. Type A GBM has a relatively regular internal texture while type B GBM contains additional structures (deposits) within the membrane. This paper describes a computer-based method of measuring type A GBM thickness. The basic technique, with appropriate modification, can also be employed in segmentation of similar objects in other applications, both medical as well as non-medical.

The objective was to develop a robust algorithm that would function with high accuracy despite variations and imperfections in sample preparation, staining and image acquisition. Since some user interaction is necessary and desirable (for example, the pathologist’s marking out segments of interest or discarding segments that are obliquely sectioned), it was not the aim to develop a fully automated system. The membrane centerline is first tracked using an adaptive window-based technique that measures local features within the membrane. Given an initial search point, the surrounding area is inspected, and regions with similar characteristics are progressively linked. A region-growing procedure extracts the GBM from the tracked centerline. The detected GBM is divided into short sections and the average width of each section is obtained. Compared to manual methods, the advantages are objectivity, consistency, and improvements in speed and accuracy.

2 Characteristics of the GBM

A typical type A GBM exhibits relatively regular texture with small intensity variation, as can be seen in Fig. 1. The internal region of the GBM is called the lamina densa. The outer boundary is frequently adjacent to darker regions while the inner boundary is contiguous with regions of lighter intensity. However, the actual boundaries are often not well defined and the GBM may merge gradually into the surrounding tissue. The GBM thickness and characteristics vary for different patients and diseases with the GBM sometimes appearing irregular in texture.

Global processing techniques were used to investigate the image characteristics of the GBM. An intensity-based analysis reveals that intensity information alone cannot provide any clear bimodal or multimodal distribution for automatic thresholding. This is caused by the presence of complex and variable structures resulting in unpredictable intensity distribution, the relatively small area taken up by the GBM, and the absence of distinctive gray levels characterizing the membrane. The GBM boundary, which is already poorly defined, is rendered even more indistinct by noise, the similar intensities of the surrounding tissues, and texture irregularities. Edge operations on the image thus fail to highlight the GBM boundaries; instead the result is discontinuous edge elements of generally low magnitudes. A texture-based approach for membrane characterization and segmentation is not suitable since the GBM width is too small for proper texture description. Another disadvantage of texture analysis is the expensive computational requirements.

In summary, the GBM does not possess unique characteristics that would allow a global segmentation method. The GBM, while generally uniform in texture, is irregularly textured at several points and is not of constant intensity. The boundaries are often indistinct and broken. The image characteristics of the surrounding regions vary and may even appear similar to those of the GBM. Inconsistent preparation of the tissue sections and electron micrographs compound the problem of accurate GBM detection.

3 Image acquisition

The host computer is a Silicon Graphics Iris 4D/70GT workstation on which the algorithms were developed and images stored. The image digitizer is a Pulnix TM-560 monochrome camera with a 500 (H) x 582 (V) CCD array sensor. An Androx frame-grabber card serves as the interface between the computer and the camera. The desired spatial resolution necessarily depends on the structures and features that have to be extracted. The magnification of the imaging optics has to be chosen in conjunction with the magnification of the micrographs so that the GBM appears sufficiently wide for analysis. Excessive enlargement, which would result in extra computation without concomitant gain in performance, should be avoided. It was determined that a membrane width of the order of 10–30 pixels was adequate for characterization and detection.