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Image Analysis and Processing with Applications in Proteomics and Medicine

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Abstract

This thesis introduces unsupervised image analysis algorithms for the segmentation of several types of images, with an emphasis on proteomics and medical images. Segmentation is a challenging task in computer vision with essential applications in biomedical engineering, remote sensing, robotics and automation. Typically, the target region is separated from the rest of image regions utilizing defining features including intensity, texture, color or motion cues. In this light, multiple segments are generated and the selection of the most significant segments becomes a controversial decision as it highly hinges on heuristic considerations. Moreover, the separation of the target regions is impeded by several daunting factors such as: background clutter, the presence of noise and artifacts as well as occlusions on multiple target regions. This thesis focuses on image segmentation using deformable models and specifically region-based Active Contours (ACs) because of their strong mathematical foundation and their appealing properties.

ACs are formulated according to an energy functional defined so as to be minimized when approximating target boundaries. The argument of the energy functional is typically a curve or surface, which evolves and defines the partitioning of the image based on external forces that hinge on image features such as intensity and/or texture. Additionally, internal constraints generate tension and stiffness, which preserve the smoothness and continuity of the model by preventing the formation of sharp corners. The corresponding Euler-Lagrange equation constitutes a Partial Differential Equation (PDE), i.e. an iterative gradient descent algorithm, which guides the evolution towards the minimum. The numerical implementation of the evolution is performed by the level set method, which endows the model with topological adaptability, i.e. splitting or merging, appearing or disappearing during the surface evolution. In this thesis, two different objectives are pursued. The first is the core issue of unsupervised parameterization in image segmentation, whereas the second is the formulation of a complete model for the segmentation of proteomics images, which is the first to exploit the appealing attributes of ACs.

The first major contribution of this thesis is a novel framework for the automated adjustment of region-based AC regularization and data fidelity parameters based on local image geometry information. Very often, AC parameters are empirically adjusted on a trial and error basis, a process which is laborious and time-consuming, based on subjectivity. On one hand, non-expert users such as Medical Doctors (MDs) and biologists require technical support since they are not familiar with the algorithmic inner mechanisms. On the other hand, parameter configurations empirically determined by image analysis experts are usually suboptimal and applicable to

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specific datasets. The presented framework aims to endow segmentation results with objectivity and robustness as well as to set domain users free from the cumbersome and time-consuming process of empirical parameter adjustment. It is applicable on various medical imaging modalities and remains insensitive on alterations in the settings of the acquisition devices. Starting from the observation that the AC parameters and the eigenvalues of structure tensors are associated with the same orthogonal directions, local image geometry is encoded by the orientation coherence in edge regions. The latter can be mined by means of Orientation Entropy (OE), a measure which is an increasing function of the variability in edge orientation, obtaining low values in structured regions containing edges of similar orientations and high values in unstructured regions containing edges of multiple orientations. Structured edge regions are associated with the actual region boundaries, whereas unstructured edge regions are associated with noise and artifacts. OE is calculated on directional subbands in each scale of the Contourlet Transform (CTr), which apart from intensity also represents textural information. CTr provides an inherent multi-directional filtering mechanism, capable of filtering out randomly oriented edges associated with noise, artifacts and/or background clutter and is directly implemented in the discrete domain. As a result, data fidelity forces that guide contour away from randomly oriented, high-entropy edge regions are appropriately amplified in the early stages of evolution and iterations dedicated to misleading local minima are avoided, speeding up contour convergence towards target edge regions. On the other hand, forces imposed within the proximity of structured edges, naturally related to target edge regions, are reduced, enhancing segmentation accuracy. The aim is to guide the contour directly to target edge regions, already from the beginning and to prevent any erroneous behavior during evolution by constantly reminding where the target edge regions lie.

The presented framework has been embedded into four region-based AC models consisting of regularization and data fidelity energy terms, in order to evaluate the segmentation performance of automated versus empirical parameterization. Additionally, it has been integrated into two image restoration models, so as to test its effectiveness on alternative inverse problems irrespective of the application. The results of the original, empirically parameterized algorithms were compared to those obtained by the automated versions. Experiments were conducted on large benchmark datasets of natural and medical images. All medical images used were investigated by MDs who provided ground truth images, whereas contour initialization was the same for both the presented framework and the empirically fine-tuned version, in order to facilitate fair comparisons. The experimental results demonstrate that the presented framework achieves comparable segmentation quality to the one obtained by the empirically fine-tuned version in an automated fashion.

The second major contribution of this thesis is a novel analysis method for the detection and segmentation of protein spots in 2D-Gel Electrophoresis (2D-GE) images. This is the first complete analysis model exploiting the appealing properties of the AC formulation in order to cope with crucial issues in 2D-GE image analysis, including the presence of noise, streaks, multiplets and faint spots. In addition, it is unsupervised, providing an alternative to the laborious, error-prone process of manual editing, which is still required in state-of-the-art 2D-GE image analysis software packages. The detection technique utilizes the dilation image operator, which embeds a disk-shaped Structuring Element (SE), adjusted to the dominant roundish shape of protein spots. The disk-shaped SE limits the falsely detected streaks. SE size is set considering that a certain radius value minimizes the detection of false negatives, whereas it allows the detection of local maxima associated with small spots, even in cases where they overlap with larger spots in complex regions. The accompanying segmentation scheme comprises four main processes, namely: (a) a detection process capable of identifying boundaries of spot overlap in regions occupied by multiplets, based on the observation that such boundaries are associated with local intensity minima, (b) histogram adaptation and morphological reconstruction so as to avoid unwanted amplifications of noise and streaks, as well as to facilitate the identification of faint spots, (c) a contour initialization process aiming to form a level set surface initializing the subsequent level set evolution, based on the observation that protein spots are associated with regional intensity maxima and, (d) a level set evolution process guided by region-based energy terms determined by image intensity as well as by information derived from the previous processes. Considering the separation of multiplets, the original 2D-GE image is scanned with parallel straight-line segments of variable lengths and multiple directions, so as to facilitate

the detection of local intensity minima, associated with each particular direction. Local intensity minima are identified for each parallel straight-line segment. Furthermore, a popular histogram equalization variant called Contrast-Limited Adaptive Histogram Equalization (CLAHE) is utilized to enhance the segmentation performance of the presented scheme with respect to the presence of faint spots in 2D-GE images. The enhanced image is binarized according to a threshold value and the flood-fill morphological operation is applied so as to eliminate holes as a result of intensity inhomogeneity. The level set function is initialized so that the associated zero levels approximate the actual protein spots. Starting from the observation that regional intensity maxima of a 2D-GE image are associated with protein spots, the presented initialization process constructs a level set surface of multiple cones centered at maxima positions. This surface can serve as a spot-targeted initialization of the level set function. Aiming to enhance segmentation performance, contour evolution is initialized by the spot-targeted level set surface generated by the previous initialization process.

The experimental evaluation of the presented segmentation scheme has been conducted on real and synthetic digital grayscale 2D-GE images, so as to facilitate qualitative and quantitative comparisons with state-of-the-art 2D-GE image analysis software packages. The experimental results demonstrate that the presented model endows detection and segmentation results with objectivity and reproducibility by automatically initializing the level set function based on regional intensity maxima associated with actual spots. Moreover, it outperforms 2D-GE image analysis software packages in terms of detection and segmentation quantity metrics and provides an alternate to the laborious, error-prone and time-consuming process of manual editing, which is required by gel analysis experts in state-of-the-art 2D-GE software packages.

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