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# Adaptive multi-level conditional random fields for detection and segmentation of small enhanced pathology in medical images

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ABSTRACT

Detection and segmentation of large structures in an image or within a region of interest have received great attention in the medical image processing domains. However, the problem of small pathology detection and segmentation still remains an unresolved challenge due to the small size of these pathologies, their low contrast and variable position, shape and texture. In many contexts, early detection of these pathologies is critical in diagnosis and assessing the outcome of treatment. In this paper, we propose a probabilistic Adaptive Multi-level Conditional Random Fields (AMCRF) with the incorporation of higher order cliques for detecting and segmenting such pathologies. In the first level of our graphical model, a voxel-based CRF is used to identify candidate lesions. In the second level, in order to further remove falsely detected regions, a new CRF is developed that incorporates higher order textural features, which are invariant to rotation and local intensity distortions. At this level, higher order textures are considered together with the voxel-wise cliques to refine boundaries and is therefore adaptive. The proposed algorithm is tested in the context of detecting enhancing Multiple Sclerosis (MS) lesions in brain MRI, where the problem is further complicated as many of the enhancing voxels are associated with normal structures (i.e. blood vessels) or noise in the MRI. The algorithm is trained and tested on large multi-center clinical trials from Relapsing-Remitting MS patients. The effect of several different parameter learning and inference techniques is further investigated. When tested on 120 cases, the proposed method reaches a lesion detection rate of 90%, with very few false positive lesion counts on average, ranging from 0.17 for very small (3–5 voxels) to 0 for very large (50+ voxels) regions. The proposed model is further tested on a very large clinical trial containing 2770 scans where a high sensitivity of 91% with an average false positive count of 0.5 is achieved. Incorporation of contextual information at different scales is also explored. Finally, superior performance is shown upon comparing with Support Vector Machine (SVM), Random Forest and variant of an MRF.

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## 1. Introduction

The task of pathology segmentation in medical imaging is a challenging problem due, in part, to the shortage of robust shape, size and location priors, and to the difficulty in modeling intensities and texture patterns given their large variability over a population. There exists a wide and diverse set of contexts, where it would be important to first detect and then to segment (possibly very small) pathologies among other candidates, which can be quite similar in appearance (Baek et al., 2012; Johnson et al., 2013; Karimaghaloo et al., 2012b). In many cases, early detection of these pathologies can be crucial in disease staging and in assessing treatment outcome. This includes the domain where contrast-enhancing agents, such as Gadolinium, are injected into patients, resulting in images where new pathological activity, such as within cancer cells or lesions, becomes enhanced in some imaging modalities and thereby easier to see (Fig. 1(a)–(c)). In these contexts, the problem is more difficult than in a typical pathology segmentation context because, for one thing, other healthy structures are often enhanced as well, rendering the primary task the detection of all the pathologies of interest. These structures can vary substantially in size, location and texture and can be as small as 3 or 4 voxels, leaving little margin for error. In fact, failing to detect an existing pathology (i.e. False Negative – FN) or incorrectly labeling a healthy structure as pathology (i.e. False Positive – FP) have huge ramifications in both the diagnosis and the assessment of treatment effect. The problem is further complicated because the contrast between the target and background can be very low. Some non-probabilistic approaches such as those defined in Datta et al. (2007); He and Narayana (2002) have been proposed to

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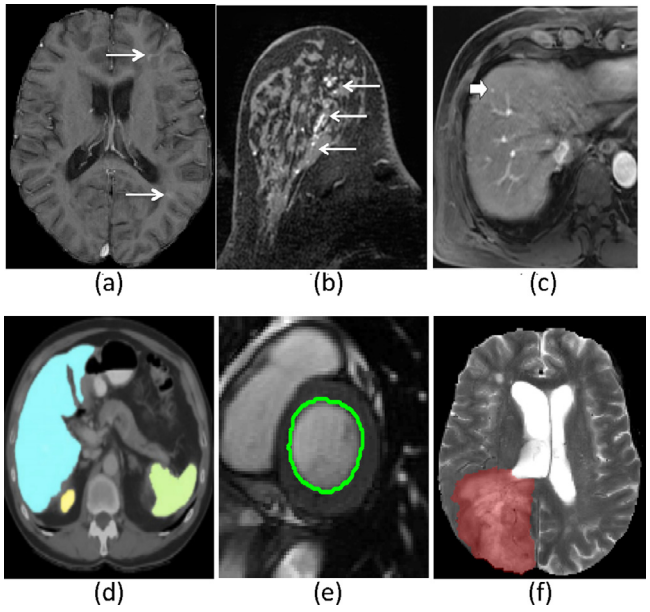


**Fig. 1.** First row shows examples of small pathologies that required detection. Arrows point to: (a) enhanced MS lesions in brain MRI (Karimaghaloo et al., 2012b), (b) ductal carcinoma in breast cancer (Johnson et al., 2013) and (c) hepatocellular carcinoma in liver cancer (Baek et al., 2012). Second row shows examples of large structure segmentations in medical imaging: (d) shows different abdominal organs to be segmented from CT (liver in cyan, spleen in green, right kidney in yellow) (Linguraru et al., 2010), (e) shows segmentation of left ventricle (Ayed et al., 2009) and (f) shows segmentation of a brain tumor (in red) (Subbanna et al., 2013). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).

address this issue. However, they depend on prior segmentation of other structures in order to remove the FPs.

In the field of computer vision, probabilistic graphical models in the form of random fields have provided a principled way for capturing neighboring data dependencies. As a result, methods such as Markov Random Fields have been extensively used to model many segmentation problems (Blake et al., 2011; Li and Singh, 2009). However, computation of the joint distribution becomes intractable in the generative MRF resulting in simplifying assumptions (such as observations independencies). Furthermore, incorporation of data dependent interactions is not straight forward in a traditional MRF. Hence, discriminant variants of MRF i.e. Conditional Random Fields (CRF) (Lafferty and et. al., 2001) have been proposed and are widely used both in computer vision and medical imaging (Ayed et al., 2009; Bhole et al., 2014; Boix et al., 2012; He et al., 2004; Hu et al., 2008; Kohli et al., 2009; Kumar and Hebert, 2006; Ladicky et al., 2009; L'ubor Ladickỳ et al., 2010; Shotton et al., 2006). However, most of these methods are focused on the context of segmenting a central object or a healthy structure from the surrounding tissue in a known general region of interest (Fig. 1(d) and (e)). In these contexts, often rich features can be extracted based on intensity or texture patterns, that render the object distinctive from the surrounding background. Moreover, location, size and shape models can be learned and exploited in order to further improve the segmentation results. In the context of pathology segmentation, where the pathology of interest is large, and there is only one in the image (e.g. brain tumors – Fig. 1(f)), techniques have managed to exploit some prior knowledge and texture information to delineate the pathology, particularly if one can leverage texture homogeneity within sub-regions (Bauer et al., 2011; Hao et al., 2012; Lee et al., 2008; Subbanna et al., 2013).

There has been some work (Karimaghaloo et al., 2012a, 2010, 2012b) where adaptations of CRFs were proposed for the context of small enhanced pathology segmentation and were shown to outperform standard MRF, SVM and linear regression models. While Karimaghaloo et al. (2010, 2012b) incorporates mainly local, voxel-level features, Karimaghaloo et al. (2012a) includes some higher order terms but the features used are not expressive enough to characterize the context and hence FPs still remain. Intensities at each pixel might be distorted due to the presence of noise or other artifacts. Hence, higher order textural patterns that are robust to local intensity distortions should be incorporated into the model to remove the FPs.

In this work, we propose an Adaptive Multi-level Conditional Random Field (AMCRF) classifier for the task of small enhanced pathology (commonly known as enhancing *lesion*) segmentation. The proposed model (Fig. 2) works at two different levels of graphical modeling: in the first stage, we introduce a voxel-level CRF model, with cliques of up to size 3, to generate candidate lesions. At this level, the classifier is tuned to be highly sensitive at the expense of additional FP detections. Voxel-level labels are used to group together and identify candidate lesions. In the second stage, as we are left with only a relative few candidates, the model can now efficiently incorporate more computationally expensive higher order features. As opposed to traditional hierarchical graphical models, a novel *adaptive* CRF is developed to both remove FP lesion candidates and refine the boundaries of the detected lesions. To this end, both voxel-wise interactions *AND* additional higher order features are optimized together at the second stage of inference. The method extends preliminary work (Karimaghaloo et al., 2013) in several ways including exploring the effect of different texture models (independently and combined) such as: local intensity histogram descriptors (spin image) (Lazebnik et al., 2005), Rotationally Invariant Feature Transform (RIFT) (Lazebnik et al., 2005), and Local Binary Pattern (LBP) (Ojala et al., 2002). These textural descriptors encode intensity patterns and gradient orientations around a reference point and are invariant to rotation and local intensity distortions. Moreover, the relatively simple graphical structure used in Karimaghaloo et al. (2013) is replaced with a more complete model where higher order nodes and their corresponding pairwise edges are included to better capture variables interactions.

A CRF-based segmentation approach is proposed in Hao et al. (2012) for the context of breast lesion segmentation where different hypothesis based on all image cues are included to train a single CRF framework. However, their framework highly relies on texture homogeneity within sub-regions and the performance is only shown on relatively large breast lesions. Hence, the efficacy of their approach

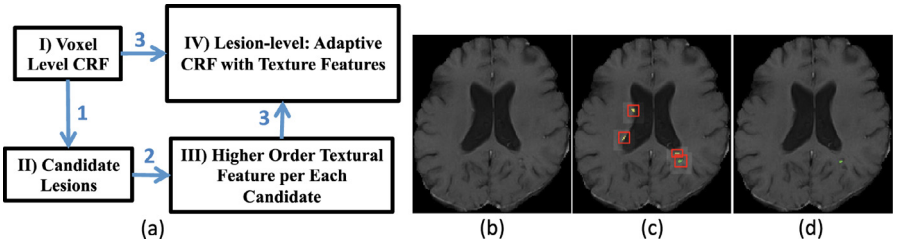


**Fig. 2.** Adaptive multi-level CRF framework. (a) Shows different stages of the algorithm. Numbers on the arrows indicate the order of the process. (b) Shows a test image. (c) Shows the result of the voxel-level CRF together with the bounding box surrounding each candidate (stage II). (d) Shows the final results of the AMCRF model (stage IV) with the incorporation of higher order features along with the voxel-wise interactions.

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