MITOSIS DETECTION FOR INVASIVE BREAST CANCER GRADING

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Abstract

Mitosis count in histologic slide plays the key role in breast cancer grading. We propose a fast and accurate solution for automatic mitosis detection. Cells are detected in a novel manner using area morphological scale space. The scale space is restricted by maximization of cross-entropy between cells and background for precise cell detection. The Random Forest Classifier classifies the detected cells in mitotic and non-mitotic class. Experiments show promising results on a variety of data.

Introduction

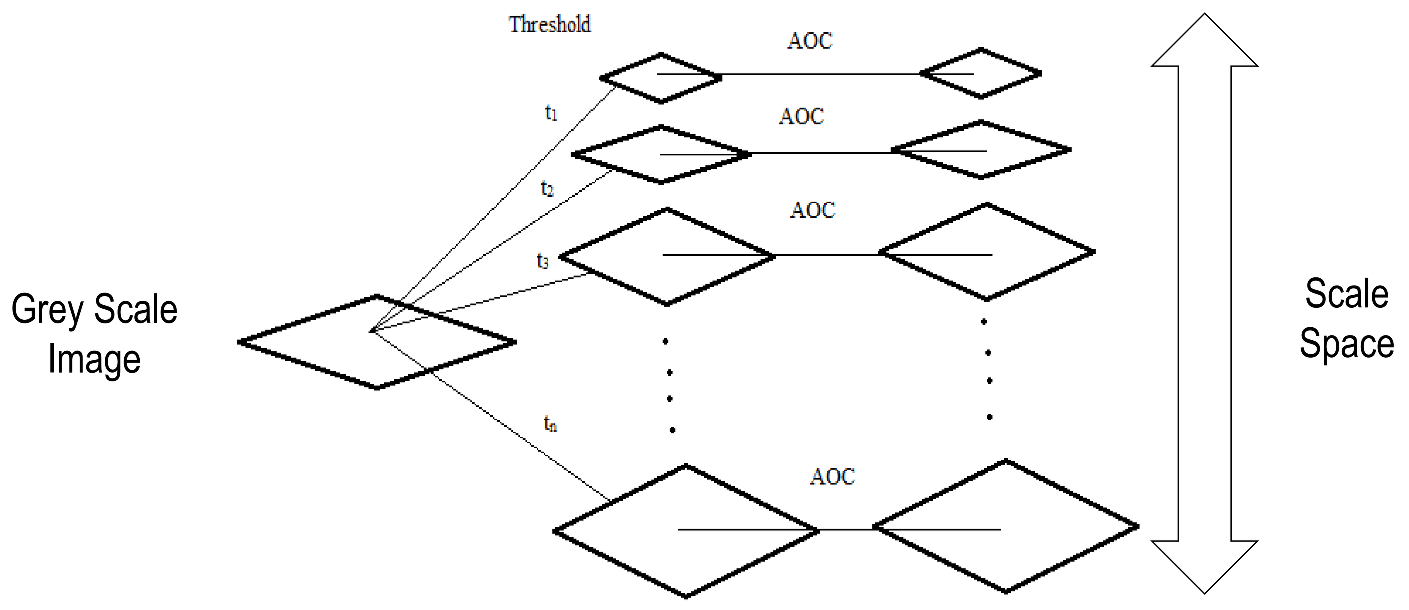
- Mitosis count : A crucial indicator in histologic grading of invasive breast cancer
- Manual Grading: not time efficient and prone to observer variability
- Goal: Automatic cancer grading from histopathological images
- Input: Regions extracted from whole-slide images
- Output: Number of mitotic figures in the region
- Mitotic cells: Various different forms of appearance at different phases
- Non mitotic objects like apoptotic nuclei may look similar to mitotic cells
- So, mitotic cells are difficult to classify precisely

Proposed Methodology

- Detection of the cells from the input image
- No shape or intensity pattern of the cell has been assumed unlike [1]
- No appearance model has been used for cell detection
- Extraction of the cell features from the detected cells
- Classification of the detected cells
- Two class problem: Mitotic and Non mitotic

Cell detection

- Accurate cell detection is very important for proper feature extraction
- This leads to good classification using simple features
- We employ area morphological scale space for cell detection
- Successive application of area morphology operator opening and closing (AOC)
- Scale space: generated by thresholding the grey scale image at different grey levels and applying AOC on them (see figure below)



- Use of the entire range of grey levels for generating the scale space often lead to diffusion of the object boundary [2], and hence inaccurate detection
- So, we propose to use only the grey levels, restricted by maximum cross entropy (between object and background) of the image to generate the scale space
- We define *Inter Class Entropy* between object (ob) and background (bg) as:

$$H_{int} = \sum_g p_g \log \frac{1}{p_g} \; : g = I(x,y) \; \forall \, (x,y) : [(x,y) \in \; ob \; and \; \exists i : \; (x'_i, y'_i) \in bg]$$

(x'_i, y'_i): i^{th} neighbour of (x,y); p_g: Occurrence probability of grey level g

- Clearly, H_{int} is the entropy contributed by the pixels on the edge region
- We define *Within Class Entropy* of object (ob) and background (bg)as:

$$\begin{cases} H_{ob} = \sum_g p_g \log \frac{1}{p_g} \; : g = I(x,y) \; \forall \, (x,y) : \left[(x,y) \in \; ob \; and \; \forall i : \; (x'_i, y'_i) \in ob\right] \\ H_{bg} = \sum_g p_g \log \frac{1}{p_g} \; : g = I(x,y) \; \forall \, (x,y) : \left[(x,y) \in \; bg \; and \; \forall i : \; (x'_i, y'_i) \in bg\right] \end{cases}$$

- H_{ob}, H_{bg} are the entropies, contributed by the pixels of object and background respectively
- For accurate object detection: maximize the separation information between *ob* and *bg*
- So, reduce H_{ob} and H_{bg} (Similarity information): Requires smoothing of *ob* and *bg* region
- Preserve H_{int}(Separation information): Requires preservation of edge region
- *ob*, *bg*: regions of low intensity variance; Edge: regions of high intensity variance
- Image update equation (I^t : image at time *t*):

$$I^{t+1}(x,y) = I^t(x,y) - \lambda \exp\left(-\beta\left\{var\left(L^t(x,y)\right)\right\}t\right)\left(I^t(x,y) - \mu_L^t\right)$$

$$\lambda, \beta : constant; \; L^t(x,y) : \; neighbouring \; region \; of \; (x,y); \; \mu_L^t : mean \; of \, L^t(x,y)$$

- After updating, we find the grey level that maximizes the total *Cross entropy* of the image:

$$i_t = \arg \underbrace{max}_{i} \left\{H_{pq} = \int p(i) \log\left(\frac{1}{q(i)}\right) di\right\}$$

$$p(i) = pdf \; of \; grey \; level \; i : i > i_t$$
$$q(i) = pdf \; of \; grey \; level \; i : i \leq i_t$$

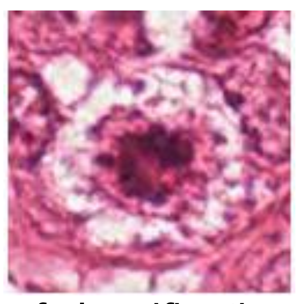
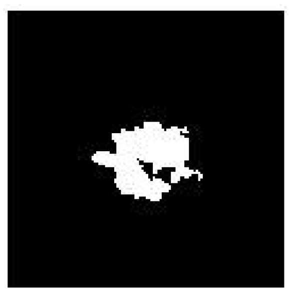
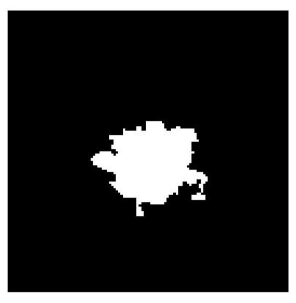
- Scale space is constructed with grey levels $i_t \pm \Delta i$, where Δi is the 3-dB point in entropy-grey level curve
- Objects (cells) are detected based on pixel classification in the scale space images using FCM algorithm

Cell Classification

- Nonlinear classification problem
- Random forest classifier: Nonlinear, less parameters, independent of data size [3]
- Features: colour histogram of the cells (red and blue channel histogram since green channel does not provide distinctive features here)
- Split points at nodes of random tree chosen using maximum information gain
- Features for growing each tree chosen randomly with replacement

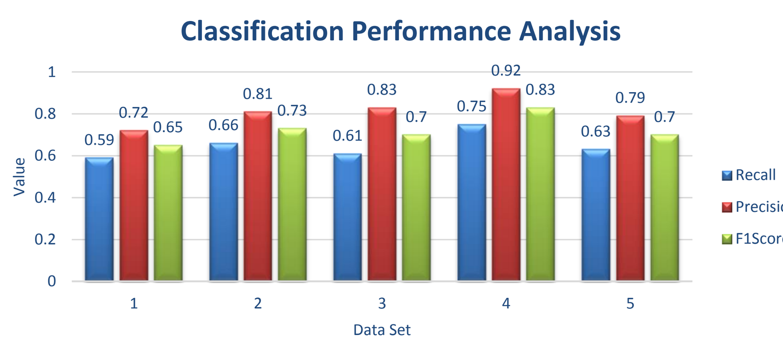
Experiments and Results

- Data : MITOS-ATYPIA 14 [4] data set (Aperio scanner, 40X magnification)
- 5 different data set; Total number of frames:480; Total number of mitosis: 614
- For cell detection, only red channel of the RGB image is used
- Results of cell detection using area morphological scale space with and without entropy restriction: original image (left), with (middle) and without (right) entropy restriction

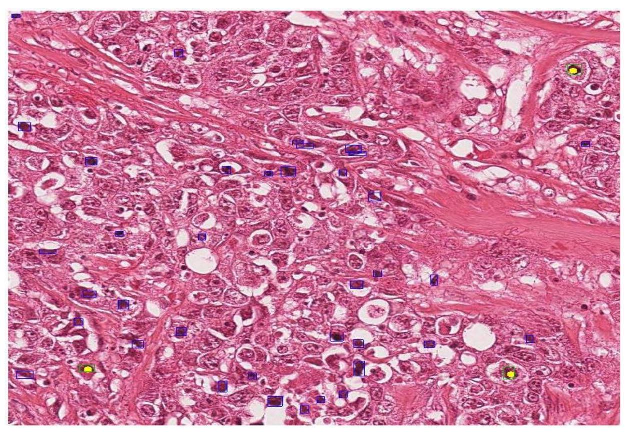
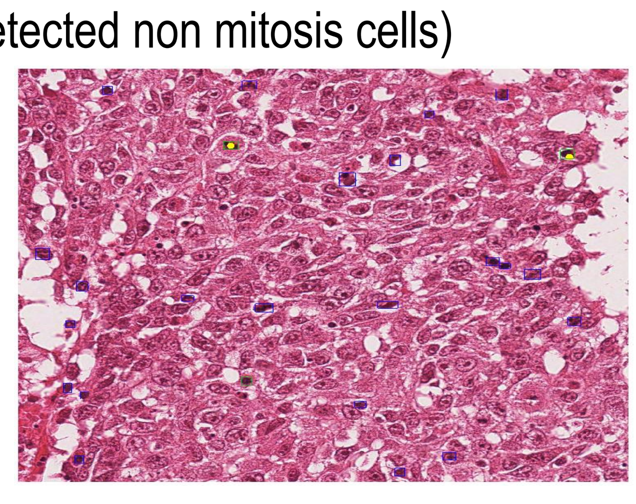
  

- Results of classification:

Data Set	Recall	Precision	F1 score
1	0.59	0.72	0.65
2	0.66	0.81	0.73
3	0.61	0.83	0.7
4	0.75	0.92	0.83
5	0.63	0.79	0.7
Average	0.648	0.814	0.722



- Classification results on the images: Solid yellow region (ground truth), green rectangle (detected mitosis cells), blue rectangle (detected non mitosis cells)

- The average processing time (detection and classification)for each image is 24 sec.

Conclusion

- Mitosis detection algorithm from the images of histopathological slides
- Accurate cell detection: Entropy restricted area morphological scale space
- Cell classification: Random forest classifier with color histogram features
- Fast algorithm and provides better F1 score compared to other existing algorithms

References

1. Pal, N. R. (1996). On minimum cross-entropy thresholding. *Pattern Recognition*, *29*(4), 575-580.
2. Acton, S. T., & Mukherjee, D. P. (2000). Scale space classification using area morphology. *Image Processing, IEEE Transactions on*, *9*(4), 623-635.
3. http://mitos-atypia-14.grand-challenge.org/dataset/
4. Breiman, L. (2001). Random forests. *Machine learning*, *45*(1), 5-32.