

Computer-Aided Diagnosis Systems in the Classification of Neuroblastoma Histological Images

A Thesis Submitted for the Degree of
Doctor of Philosophy

By

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Dated: December 2019

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CERTIFICATE OF ORIGINAL AUTHORSHIP

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Table of Contents

Table of Contents	vii
List of Tables	viii
List of Figures	xii
Abstract	1
Table of Symbols	5
1 Introduction	8
1.1 Computer-Aided Diagnosis Systems in Pathology	9
1.2 Research Significance	10
1.3 Research Challenges	11
1.4 Research Hypotheses	14
1.5 Research Objectives and Contributions	15
1.6 Research Structure	19
2 Literature Review	21
2.1 Biological Domain	21
2.1.1 World Health Organisation Peripheral Neuroblastic Tumour Classification	24
2.2 Computer-based Approaches	29
2.2.1 Segmentation Based Methods for Classification of Malignant Tumours	32
2.2.2 Low-level Feature Extraction	35
2.2.3 High-level Feature Extraction Methods	42
2.3 Classification of Neuroblastoma Histological Images	54
2.4 Classifiers Used in This Thesis	55

2.4.1	Support Vector Machine	56
2.4.2	k-Nearest Neighbour	57
2.4.3	Bag of words model in computer vision	57
2.5	Clustering Approaches Used in This Thesis	60
2.5.1	k-means clustering	60
2.6	Metrics Used in This Thesis	61
2.7	Cross-Validation	63
2.8	Parameter Tuning Methods Used in This Thesis	63
2.8.1	Greedy Method	63
2.8.2	Wrapper Approach	64
2.9	Research Gaps	65
3	Models of Computer-Aided Diagnosis Systems Based on Low-level Features	67
3.1	Data Collection and Cropping	68
3.2	Patched Completed Local Binary Pattern	72
3.2.1	Methodology	73
3.2.2	Experiment Results	81
3.3	Scale Invariant Feature Transform	86
3.3.1	Methodology	87
3.3.2	Experiment Results	91
3.3.3	Sensitivity to Dataset	97
3.4	Discussion, Contribution and Conclusion	103
4	Models of Computer-Aided Diagnosis Systems Based on High-level Features	107
4.1	High-level Feature Extraction	108
4.1.1	Convolutional Deep Belief Networks	110
4.1.2	Convolutional Neural Network	123
4.1.3	Sensitivity of Test Samples	129
4.1.4	Discussion, Contribution and Conclusion	132
5	Conclusion	134
5.1	Discussion	139
5.2	Future Research Directions	141

List of Tables

2.1	Histopathological definitions in neuroblastic tumours	27
2.2	Different subtypes of neuroblastic tumours (Shimada et al. 1999) . . .	28
2.3	Specification of favourable and unfavourable histology groups (Robson 2001) based on the Shimada classification (Shimada et al. 1999) . . .	30
2.4	Popular kernel functions	56
2.5	Confusion Matrix. Abbreviation N (Negative) and P (positive)	61
3.1	Number of different categories of neuroblastic tumour cropped images and number of patients	73
3.2	Average classification accuracy of SVM over neuroblastic tumour dataset using different C values	84
3.3	Average classification accuracy of SVM over neuroblastic tumour dataset using different kernel functions	85
3.4	Weighted average precision, recall, and F-measure obtained by the pro- posed method (PCLBP) and Spanhol’s method (CLBP).	87
3.5	Average classification accuracy of the SIFT over ten experiments on the neuroblastic tumour dataset using different values for σ , $C_c = 0.03$, $C_E = 10$	92

3.6	Average classification accuracy of SIFT over the neuroblastic tumour dataset using different values for the contrast threshold (C_C), $\sigma = 1.7$, $C_E = 10$	92
3.7	Average classification accuracy of SIFT over the neuroblastic tumour dataset using different values for the edge threshold (C_E), $\sigma = 1.7$, $C_c = 0.04$	93
3.8	Average classification accuracy of the SIFT over the neuroblastic tumour dataset using bag of features with different values of the codebook size.	93
3.9	Weighted average precision, recall and F-measure of the SIFT method and other benchmarks. The bold value indicates the best F-measure achieved by combination of SIFT with bag of features and SVM (histogram intersection)	95
3.10	A representative confusion matrix of applying SIFT over the neuroblastoma images. Abbreviations: UD (undifferentiated neuroblastoma), PD (poorly-differentiated neuroblastoma), D (differentiating neuroblastoma), GNB (ganglioneuroblastoma) and GN (ganglioneuroma) . .	97
3.11	The actual and predicted classification for dataset from University of Bristol. Abbreviations: UD (undifferentiated neuroblastoma), PD (poorly-differentiated neuroblastoma), D (differentiating neuroblastoma), GNB (ganglioneuroblastoma) and GN (ganglioneuroma)	98
3.12	Image distribution of BreakHis dataset by magnification factor and type	102
3.13	Best average recognition rates (%) of the classifiers trained with different descriptors reported in Spanhol et al. (2016)	103

3.14	Average recognition rate (%) of SIFT + bag of features and PFTAS over the BreakHis breast cancer dataset in different magnifications	104
4.1	Average classification accuracy of the CDBN over the constructed dataset using a different number of hidden layers. Number of groups in the first, second, third layers and number of mini batches are 24, 20, 40 and 4, respectively.	115
4.2	Average classification accuracy of the CDBN over neuroblastic tumour dataset using a different number of groups in the hidden layers. Number of hidden layers and number of mini batches are 3 and 4, respectively.	116
4.3	Average classification accuracy of the CDBN over the constructed dataset for a different number of mini-batches. The number of hidden layers and number of hidden groups in the first, second and third layer are 3, 24, 20 and 40, respectively.	117
4.4	Average classification accuracy of the CDBN over the neuroblastic tumour dataset with different values of the codebook size.	118
4.5	Information of different layers of CDBN	118
4.6	Weighted average precision, recall, and F-measure of the CDBN and the benchmarks over the constructed dataset consisting of 1043 neuroblastoma images. Bold values mean the best precision, recall and F-measure.	120
4.7	T-test for a comparison of CLBP and PCLBP with the combination of CDBN with the bag of features and the histogram intersection kernel SVM, with a significance level $\alpha = 0.05$	122

4.8	A representative confusion matrix. Abbreviations: UD (undifferentiated neuroblastoma), PD (poorly-differentiated neuroblastoma), D (differentiating neuroblastoma), GNB (ganglioneuroblastoma) and GN (ganglioneuroma)	123
4.9	Average weighted average precision, recall, and F-measure obtained by convolutional neural network and the benchmarks. Bold values mean the best precision, recall and F-measure.	128
4.10	T-test for the comparison of the combination of CDBN with the bag of features and SVM histogram intersection kernel with VGG-16, VGG-19, and AlexNet, significance level $\alpha = 0.05$	129
4.11	Weighted average precision, recall, and F-measure of the convolutional deep belief network over randomly selected subimages in 138 TMA cores	132

List of Figures

1.1	An example of high intra-class variation in the shape and intensity of differentiating neuroblast cells, H&E images with scale $80 \times 80\mu\text{m}$. . .	12
1.2	High intra-class variation in the size of the neuroblast cell, H&E images with scale $80 \times 80\mu\text{m}$	13
1.3	Thesis RQs and contribution structure	16
2.1	Sympathetic nervous system shown in yellow (Children’s-Oncology-Group 2016)	22
2.2	Differentiation of neural tumour. Differentiation increases from Neuroblastoma (least differentiated) to ganglioneuroma (most differentiated).	23
2.3	Classification tree diagram of NT based on the Shimada classification (Shimada et al. 1999), where UH indicates unfavourable histology and FH indicates for favourable histology. Histopathologists place the patient’s tumour into the favourable and unfavourable groups.	25
2.4	Blue regions are cellular regions and pink regions are neuropil regions in a H&E stained histological image	31

2.5	The scheme of keypoint detecting. Each point is compared to its eight neighbours in the current image (middle image) and nine neighbours in the scale above (top image) and below (down image).	39
2.6	Orientation calculation: (a) orientations for 64 neighbour pixels around the keypoint (b) orientation histogram	42
2.7	Keypoint descriptor: a) gradient magnitude and orientation in local neighbourhood of keypoint. b) orientation corrections and spatial coordinate transformations. c) SIFT descriptor establishment	43
2.8	Overall framework of the Convolutional Neural Network (Lecun et al. 1998). It consists of a convolutional layer, subsampling layer and fully-connected layer.	45
2.9	An example RBM with three visible units and two hidden units . . .	51
2.10	Construction of a Convolutional Restricted Boltzmann Machine (CRBM) with probabilistic max-pooling, based on Lee et al. (2011)	53
2.11	Pyramid bag of features. At level 0, decomposition consists of just a single cell and the representation is equivalent to a standard bag of features. The image is subdivided into four and 16 quadrants, extracting four and 16 feature histograms in level 1 and 2, respectively (Lazebnik et al. 2006)	58
3.1	A sample of tissue microarray (TMA) slide	69
3.2	A sample of core from a single tumour	70

3.3	Representative images in neuroblastic tumour categories: (a) undifferentiated neuroblastoma, (b) poorly-differentiated neuroblastoma, (c) differentiating neuroblastoma, (d) ganglioneuroblastoma, and (e) ganglioneuroma.	71
3.4	Quantitative relative and actual size of tissue cores and cropped images	72
3.5	The scheme of the proposed method which consists of four stages: 1) patched images, 2) sign and magnitude binary patterns, 3) histogram of sign and magnitude binary patterns and 4) classification.	75
3.6	Coordinates in the patched image. Here, this research assumes $W = N/2$ for better visualisation.	77
3.7	An 8-neighbourhood around (X_0^{pq}, Y_0^{pq})	78
3.8	An example of the computed Magnitude Binary Pattern (MBP) and Sign Binary Pattern (SBP): (a) original image, (b) MBP, and (c) SBP. We assume $W = 150$ pixels in this image for better visualization. However, the real W is 60 pixels.	79
3.9	Concatenation of patches' histograms: (a) patched image, (b) histogram of patches, and (c) concatenation of patches' histograms. . . .	81
3.10	Division of dataset with 1043 neuroblastoma images	82
3.11	Accuracy of k -NN classifier versus patch width (W) and k in parameter tuning of k -NN classifier	83
3.12	Comparison between the proposed method (PCLBP) and Spanhol's method (CLBP)	86
3.13	The scheme of the combination of SIFT with feature encoding	88

3.14	Scheme of the feature encoding block: a) selected keypoints by SIFT b) 128-D extracted features from keypoints c) clustering the 128-D extracted features d) construction of the codebook using clustering e) histogram of codewords in codebook	90
3.15	Comparison between SIFT + the bag of feature approach with CLBP and PCLBP	96
3.16	a) Whole tissue section 4906 with actual classification PD b) Pre- dicted classes for ten randomly cropped images from the whole tis- sue section. Abbreviations: D = differentiating neuroblastoma, PD = poorly-differentiated neuroblastoma	100
3.17	a) Whole tissue section 4909 with actual classification GNB b) Pre- dicted classes for ten randomly cropped images from the whole tissue section. Abbreviations: D = differentiating neuroblastoma, GNB = ganglioneuroblastoma	101
4.1	a) Schematic of deep learning network b) High-level feature extrac- tion by deep learning networks. A deep learning network deconstructs the input image into pixels and combine them to reproduce high-level features (Djuric et al. 2017)	109
4.2	The overall framework based on the CDBN which consists of whitening, partitioning, CDBN, feature encoding, and classification. The yellow squares show the mini-batches.	111

4.3	The scheme of the feature encoding block: (1) extracted high-level features by the CDBN algorithm from the test images, where each feature belongs to one test image, (2) clustering the extracted features using the k-means cluster, (3) finding the centroid of each cluster to construct a codebook consisting of codewords (4) visualisation of the constructed codebook consisting of codewords (5) Histogram of codewords which shows the number of each codeword in the codebook	113
4.4	The visualization of the weights of CDBN (a) weights between the input layer and first hidden layer (b) weights between the first and second hidden layer (c) weights between the second and third hidden layer	119
4.5	Comparison between the proposed algorithm (CDBN + feature encoding) and the benchmarks (CLBP, PCLBP)	121
4.6	Examples of actual and predicted images: a) examples of the differentiating type which are identified by the computer as the poorly-differentiated type b) actual poorly-differentiated type	124
4.7	Overall framework of the Convolutional Neural Network (CNN). It consists of the convolutional layer, subsampling layer, fully-connected layer and SVM classifier	125
4.8	Comparison between CDBN + feature encoding and CLBP, PCLBP, CNN (VGG-16), CNN (VGG-19), and CNN (AlexNet)	130
4.9	A sample of a TMA core with randomly selected sub-images. They are likely to include the common artefacts seen in TMA cores.	131

Abstract

Neuroblastoma is the most common extracranial solid malignancy in early childhood. Optimal management of neuroblastoma depends on many factors, including histopathological classification. Although histopathological classification by a human histopathologist is considered the gold standard, computers can help to extract many more features, some of which may not be recognisable by the human eye. Neuroblastoma histological images have a complex texture with complicated features which are different from appearance-based features. Computer-aided diagnosis (CAD) systems facilitate the analysis and classification of neuroblastoma histological images which are non-trivial tasks due to the differences in staining, intensity, and instrumentation. This motivates the thesis to work on the classification of neuroblastoma histological images.

In the past, a small number of methods were proposed by previous studies for the classification of neuroblastoma histological images. These methods are based on the geometry and appearance of the different cells. However, there is a high intra-class variation of intensity and size of the neuroblast cells within the same classification group. Therefore, these methods are not applicable to neuroblastoma histological images. This research proposes a solution based on traditional machine learning approaches and deep learning approaches to extract non-appearance-based

features in small regions. This thesis will investigate two research areas of feature extraction: low-level feature extraction and high-level feature extraction. Low-level features are minor details of the image such as lines, curves and edges. However, high-level features are on top of the low-level features to detect object and larger shape in the image. Feature extraction is aggregated with the classifier in this research to classify neuroblastoma histological images into five categories.

This thesis makes four contributions. Contribution 1 is the construction of a dataset comprising neuroblastoma histological images which are labeled by an expert histopathologist. Contribution 2 is the proposal of a local feature extraction method which can extract local features which are robust to high intra-class variations of intensity. Contribution 3 is the extraction of discriminative features which are robust to high intra-class variation of scale of the neuroblast cells within the same class. Contribution 4 is the proposal of deep networks to extract high-level features which are difficult for the human eye to recognise. The performance of all the proposed methods in this research is evaluated on a dataset collected from The Children's Hospital at Westmead, Sydney, Australia. As there was no publicly available dataset in this field, the proposed algorithms were evaluated on the second dataset of neuroblastoma provided by the University of Bristol and the public breast cancer dataset. All the results are compared with state-of-the-art methods. The results indicate the effectiveness of the proposed algorithms.

This is the first time that neuroblastoma histological images have been classified into five subtypes using low-level and high-level features. However, there are limitations in this research. The specificity is not 100% compared with the gold standard.

Moreover, the proposed algorithms are confused in the distinction between poorly-differentiated and differentiating neuroblastoma, a distinction that human pathologists also find difficult in limited fields of view.

Publications

Following is the list of publications resulting from the work in this thesis:

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Table of Symbols

Symbol	Description
CAD	Computer aided diagnosis
PCLBP	Patched completed local binary pattern
SIFT	Scale-invariant feature transform
CDBN	Convolutional deep belief network
CNN	Convolutional neural network
CT	Computed tomography
CLBP	Completed local binary pattern
SBP	Sign binary pattern
MBP	Magnitude binary pattern
DSBP	Decimal sign binary pattern
DMBP	Decimal magnitude binary pattern
HSBP	Histogram of sign binary patterns in image
HMBP	Histogram of magnitude binary patterns in image
LH	Local histogram
k-NN	k nearest neighbour
SVM	Support vector machine
RBF	Radial basis function

C_C	Contrast threshold
C_E	Edge threshold
UD	Undifferentiated neuroblastoma
PD	Poorly-differentiated neuroblastoma
D	Differentiating neuroblastoma
GN	Ganglioneuroma
GNB	Ganglioneuroblastoma
QDA	Quadratic Discriminant analysis
GLCM	Gray level co-occurrence matrices
LPQ	Local phase quantization
ORB	Oriented fast rotated brief
PFTAS	Parameter-free threshold adjacency statistics
CDBN	Convolutional deep belief network
CRBM	Convolutional restricted botzmann machine
H	Hidden layer
V	Visible layer
TMA	Tissue microarray
MKI	Mitosis karyorrhexis Index
H & E	Hematoxylin and eosin
$G(x, y)$	Gaussian function
$L(x, y, \sigma)$	Scale space of an image
x and y	Image coordinates
σ	Width of Gaussian function
DoG	Difference of gaussian

F_l	Feature maps of convolutional layer l
$y_{i,j}^{\phi,l}$	Output of neuron (i, j, ϕ, l) at position i, j
$w_{\Delta i, \Delta j}^{\phi, \phi', l}$	Weight of each connection between the neurons in convolutional layer (i, j, ϕ, l) and all the neurons in the previous subsampling layer ϕ'
b_j	Hidden unit biases for neuron j
c_i	Visible unit biases for neuron i