



ERCIM "ALAIN BENSOUSSAN"
FELLOWSHIP PROGRAMME



Scientific Report

First name / Family name	Meng/Zhao
Nationality	China
Name of the <i>Host Organisation</i>	Norwegian University of Science and Technology (NTNU)
First Name / family name of the <i>Scientific Coordinator</i>	Hao/Wang
Period of the fellowship	01/05/2019 to 30/04/2020

I – SCIENTIFIC ACTIVITY DURING YOUR FELLOWSHIP

During my ERCIM research programme, I have focused on the topic of “Automatic cancer cell detection system based on machine learning and big data analysis”. Considering this topic, firstly I have established two datasets: the first one is “Pleural Effusion Cell Clusters” consisting of 130 whole slide images; the second one is “White Blood Cells” consisting of 300 whole slide images.

For pleural effusion cells, since they usually appear in clusters, we mainly dealt with the segmentation problem during this research year. Until now, we have successfully realized the precise segmentation of cell clusters, and we are focusing on single cell segmentation from cell clusters, and on basis of this, in the future, we will deal with the problem of abnormal cell detection from cell clusters.

For white blood cells, we mainly solved the problem of instance segmentation from whole slide images, which means that, we do segmentation and classification at the same time and designed an end-to-end network to fulfil a simultaneous segmentation-classification task.

The proposed models are all machine-learning-based methods which corresponds with my research topic.

II – PUBLICATION(S) DURING YOUR FELLOWSHIP

During my fellowship, I have finished two conference papers and two journal papers, in which one conference paper was published, and the other three papers are still under review.

Paper 1-Accepted (published):

Title: Cluster analysis of lung adenocarcinoma cells using PCA and confocal Raman spectroscopy.

Authors: Yan, Jing, Meng Zhao, Fan Shi, Zhe Wang, Yu Yang, and Shengyong Chen.

References: In 2019 IEEE 3rd Advanced Information Management, Communicates, Electronic and Automation Control Conference (IMCEC), IEEE, 2019.

Abstract: This work analysis composition and structure of lung adenocarcinoma cells and normal cells based on confocal Raman spectroscopy. Firstly, confocal Raman spectra of 242 lung adenocarcinoma cells and 231 normal cells are obtained. In addition, Raman spectra are denoised and two evaluation criteria are used to evaluate the Raman spectra. Then, PCA is used to make principal component analysis of the spectrum and observe the process of spectral information changing with PCs. The best number of features is selected to prevent cross-sensitivity and obtain a better model. On this basis, a clustering model of PCA is constructed. The results show that accuracy of 84.57%, sensitivity of 88.02%, specificity of 80.95% and marshall correlation coefficient (MCC) of 69.21% are obtained. The results show that this method is effective in diagnosing cancer cells. Therefore, this model proves the potential of nondestructive detection of lung adenocarcinoma, and has a certain guiding role for the next classification and location. In addition, it can be easily applied in other fields in the future.

Paper 2- pending (submitted to ICPR 2020):

Title: Fused 3-Stage Image Segmentation for Pleural Effusion Cell Clusters

Authors: Sike Ma, Meng Zhao, Hao Wang, Fan Shi, Xuguo Sun, Shengyong Chen, Hong-Ning Dai

References: 25th International Conference on Pattern Recognition (ICPR2020)

Abstract: The appearance of tumor cell clusters in pleural effusion is usually a vital sign of cancer metastasis. Segmentation, as an indispensable basis, is of crucial importance for diagnosing, chemical treatment, and prognosis in patients. However, accurate segmentation of unstained cell clusters containing more detailed features than the fluorescent staining images remains to be a challenging problem due to the complex background and the unclear boundary. Therefore, in this paper, we propose a fused 3-stage image segmentation algorithm, namely Coarse Segmentation-Mapping-Fine segmentation (CMF) to achieve unstained cell clusters from whole slide images. Firstly, we establish a tumor cell cluster dataset consisting of 107 sets of images, with each set containing one unstained image, one stained image, and one ground-truth image. Then, according to the features of the unstained and stained cell clusters, we propose a three-stage segmentation method: 1) Coarse segmentation on stained images to extract suspicious cell regions-Region of Interest (ROI); 2) Mapping this ROI to the corresponding unstained image to get the ROI of the unstained image (UI-ROI); 3) Fine Segmentation using improved automatic fuzzy clustering framework (AFCF) on the UI-ROI to get precise cell cluster boundaries. Experimental results on 107 sets of images demonstrate that the proposed algorithm can achieve better performance on unstained cell clusters with an F1 score of 90.40%.

Paper 3-pending (under review, submitted to Future Generation Computer Systems)

Title: SEENS: Nuclei Segmentation in Pap Smear Images with Selective Edge Enhancement

Authors: Meng Zhao, Hao Wang, Ying Han, Xiaokang Wang, Hong-Ning Dai, Xuguo Sun, Marius Pedersen

Reference: submitted to Future Generation Computer Systems

Abstract: Accurate nuclei segmentation, an indispensable basis and core link for multi-cell cervical image analysis, plays an important role in automatic pre-cancer detection. However, the poor image quality due to the uneven staining, complex background and overlapping cell clusters also poses the great challenge in nuclei segmentation. In this paper, we propose a new Selective-Edge-Enhancement-based Nuclei Segmentation method (SEENS). In the proposed method, selective search is integrated with mathematical operators to segment whole slide cervical images into small region of interest (ROI) while automatically avoiding repeated segmentation as well as eliminating non-nuclei regions. In addition, an edge enhancement method based on the canny operator and mathematical morphology is presented to extract edge information as a weight to enhance the nucleus edge selectively. As a result, the enhanced ROI is then segmented by the Chan-Vese model with a higher accuracy. We evaluate our method with 18 whole slide images for a total of 395 cell nuclei. Experimental results demonstrate that SEENS achieves higher accuracy in cervical nuclei segmentation. Notably our method performs particularly better in low-contrast scenarios than baselines.

Paper 4-pending (finished, submitted to IEEE Sensors Journal)

Title: Microfluidic Chip with Image Processing Technique for Analysis CD14+Monocyte Myeloperoxidase Expression in Acute Myelomonocytic Leukemia Patients

Authors: Meng Zhao, Yan Zhao, Sike Ma, Fan Shi, Xuguo Sun and Hao Wang

Reference: submitted to IEEE sensors journal

Abstract: In the absence of effective detection technology and specific biomarkers, distinction of acute myelomonocytic leukemia (AMML/M4) from other acute myeloid leukemia (AML) may be difficult solely on the basis of bone marrow morphological features. In this study, a microfluidic chip analysis system was established to detect specific markers in leukemia cells in M4 patients and an image processing procedure was designed to process cell images collected by the chip system for the purpose of intelligent analysis leukemia individual information. The established system use myeloperoxidase (MPO) and CD14 as detection indexes, which connected the method enzyme cytochemistry with fluorescence immune-labeling assay. After detecting myeloperoxidase (MPO) expression of different kinds of white blood cells in the peripheral blood, compared the chip CD14+ monocyte MPO expression in M4 patients (n=48) with that in the control (n=52). It was found that the positive rate of MPO expression and the activity of CD14+ monocytes in the bone marrow of M4 patients were significantly higher than those in the bone marrow of the control group ($P < 0.05$). Then, we designed an image processing procedure which was based on different color processing models, to detect cell image signals from microfluidic chip. Subsequent analysis of cell images revealed that the image processing result could show the different cell morphology characteristics and quantified it. Here we reported a method using microfluidic cell chip technology to analyze CD14+ monocyte MPO expression in M4 patients, and a cell image processing model which is expected to become a digital representation for automatic identification of leukocyte image signals in peripheral blood by computer software, for the first time.

III – ATTENDED SEMINARS, WORKHOPS, CONFERENCES

During my research programme, I have attended many seminars and workshops. Every week, there are one or two seminars in NTNU, and I have attended a lot, I will just list several of them.

Seminars:

- (1) Title: Stability of Iris Codes - Why is it important in biometrics?
Date: February 28th, 2020
Place: NTNU Gjøvik
Name: Kiran Raja (associate professor)
- (2) Title: Deep Learning based Malware Detection and Classification
Date: November 29th, 2019
Place: NTNU Gjøvik
Name: Ferhat Ozgur Catak (postdoctoral researcher)
- (3) Title: Using behavioural biometrics beyond gaining access
Date: September 27th, 2019
Place: NTNU Gjøvik
Name: Patrick Bours (professor)

Workshops:

- (1) Title: one-day Workshop on AI and (Medical) Imaging
Date: March 5th, 2020
Place: NTNU Gjøvik
Names: Hao Wang, Marius Pedersen, Tone F. Bathen, Mattijs Elschot, Meng Zhao
- (2) Title: Intra-operative Image Enhancement and Registration for Image Guided Laparoscopic Liver Resection
Date: March 27th, 2020
Place: NTNU Gjøvik
Name: Congcong Wang

IV – RESEARCH EXCHANGE PROGRAMME (REP)

During my research programme, I have finished two REPs.

- (1) Organisation: Inria
Country: France
Department or project: Inria-Rennes - Bretagne Atlantique Research Center
Local scientific coordinator: Shadi.Ibrahim
Dates: 6th April, 2020 to 10th April, 2020
During the REP, we had online discussions about the research work and exchanged ideas for future collaboration.
- (2) Organisation: INSEC-Tec
Country: Portugal
Department or project: Electrical and Computer Engineering, Center for Biomedical Engineering Research
Local scientific coordinator: Aurélio Campilho
Dates: 06th April, 2020 to 17th April, 2020
During the REP, I have presented my research work and we had online discussions about problems within medical image analysis and exchanged ideas for future collaboration.