PhD Thesis Title: Classification and Denoising of Objects in TEM and CT Images Using Deep Neural Networks

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ABSTRACT:

The digitization of biomedical images has benefited the clinicians in comprehending (or detecting) obscure abnormalities. However, manual analysis is labour-intensive and time-consuming. Since the last few decades, computer-aided detection (CAD) systems employing learning-based methods and conventional image analysis-based methods have successfully paved the landscape for the detection (and/or classification) of deadly abnormalities. Lately, the inception of deep neural networks (DNN) (often synonymized as deep learning) as a powerful recognition module has shifted the research interest from problem-specific solutions to increasingly problem-agnostic methods that rely on learning from data. In particular, convolutional neural networks (CNNs) have rapidly become a primary choice for many CAD systems due to their astonishing results. This impulse has been sparked by increased computational power (graphical processing units) and the evolution of learning-based methods. However, the performance of CAD systems has mostly stagnated in the past decade.

This thesis presents a total of five solutions: four DNN-based solutions for classification of structures in biomedical images, and one solution for denoising of biomedical images to improve the image quality. This thesis is focused on the applications of two variants of DNN: the CNN, and the multi-layer perceptrons (MLP).

From a biomedical image analysis perspective, the first solution is associated with improving the performance of automated workflow for primary ciliary dyskinesia (PCD) analysis. To classify cilia and non-cilia structures in low-magnification (LM) transmission electron microscopy (TEM) images, a CNN-based classifier is developed as a false positives (FP) reduction module. Although computing discriminative features of cilia structures at very low magnification is challenging, the developed CNN classifier substantially improves the F-score from 0.47 to 0.59 [1].

The second solution takes a side step from classification and focuses on denoising. Denoising is often considered as a pre-processing step to improve the image quality for automated analysis. Given this, the second solution is associated with enhancing the structural information in short exposure high-magnification (HM) TEM images. A novel multi-stream CNN-based model is developed to denoise 100 short exposure high-magnification images acquired at the same spatial location in the cell section. Three different strategies for combining denoising and image merging are investigated to determine the optimal structure enhancing strategy. The CNN denoising model is only trained for one strategy and used as it is for other two strategies, thus presenting the transfer learning perspective of DNN as

a potential add-on to automated analysis. The presented model achieves an improved PSNR of 40.84 dB [2].

From a medical image analysis perspective, the third solution is associated with improving the performance of a CAD system for the early detection of multiple sizes of nodules (3-30 mm) in computed tomography (CT) scans. To classify nodules and non-nodules, a MLP-based classifier is developed as a FP reduction module. The CAD is extensively tested on four publicly available CT datasets; this makes it the only system to be successfully validated on such large scale. The developed CAD system achieves a high sensitivity of 85.6 % with only 8 FPs/scan [3].

Until recently, conventional CAD systems employing learning-based methods depended on handcrafted representations (features). Designing features by hand is challenging and often result in limited discriminative power; thus, this is insufficient to classify micronodules ($\leq$ 4 mm) and cross-sectional vessels. The fourth solution is associated with developing a CAD system for the detection of micronodules in CT scans. To classify micronodules and small cross-sectional vessels, a novel 3D CNN classifier is developed as a FP reduction module. Using the largest publicly available CT dataset, the developed CAD system achieves a high sensitivity of 86.7 % with only 8 FPs/scan [4].

The fifth solution is associated with improving the performance and efficiency of automated workflow for detecting multiple sizes of vascular nodes in CT angiography (CTA) scans. To classify cross-sections of different sizes of vessel and non-vessel nodes, a patch-based CNN classifier is developed as a FP reduction module. On the given 25 CTA volumes from the clinical routine, the presented classifier substantially improves the F-score from 0.43 to 0.82 [5].

References to author publications that relate specifically to the dissertation:

1. **Gupta A**, Suveer A, Lindblad J, Dragomir A, Sintorn I-M, and Sladoje N. Convolutional Neural Networks for False Positive Reduction of Automatically Detected Cilia in Low Magnification TEM Images. In *Proceedings of the 20th Scandinavian Conference on Image Analysis* (SCIA), June 2017, LNCS-10269, 407-418. DOI: /10.1007/978-3-319-59126-1_34
2. Bajic B*, Suveer A*, **Gupta A*,** Pepic I, Lindblad J, Sladoje N, and Sintorn I-M. Denoising of Short Exposure Transmission Electron Microscopy Images for Ultrastructural Enhancement. In *Proceedings of the 15th International Symposium on Biomedical Imaging (ISBI)*, Washington D.C., USA, April 2018. DOI: 10.1109/ISBI.2018.8363721
3. **Gupta A**, Saar T, Märtens O, and Moullec YL. Automatic detection of multi–size pulmonary nodules in CT images: Large-scale validation of a multilayer perceptron based false-positive reduction step. *Medical Physics*, 2018;45(3):1135-49. DOI: 10.1002/mp.12746
4. Lidayova K*, **Gupta A*,** Frimmel H, Sintorn I-M, Bengtsson E, Smedby O. Classification of Cross-sections for Vascular Skeleton Extraction Using Convolutional Neural Networks. In Proceedings of the 21th Medical Image Understanding and Analysis (MIUA), Scotland, July 2017.DOI: 10.1007/978-3-319-60964-5_16