Regression based Deep Neural Networks for Epithelium Segmentation in Histopathology Images

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Introduction: Automated Pathology for Early Detection of Cervical Cancer

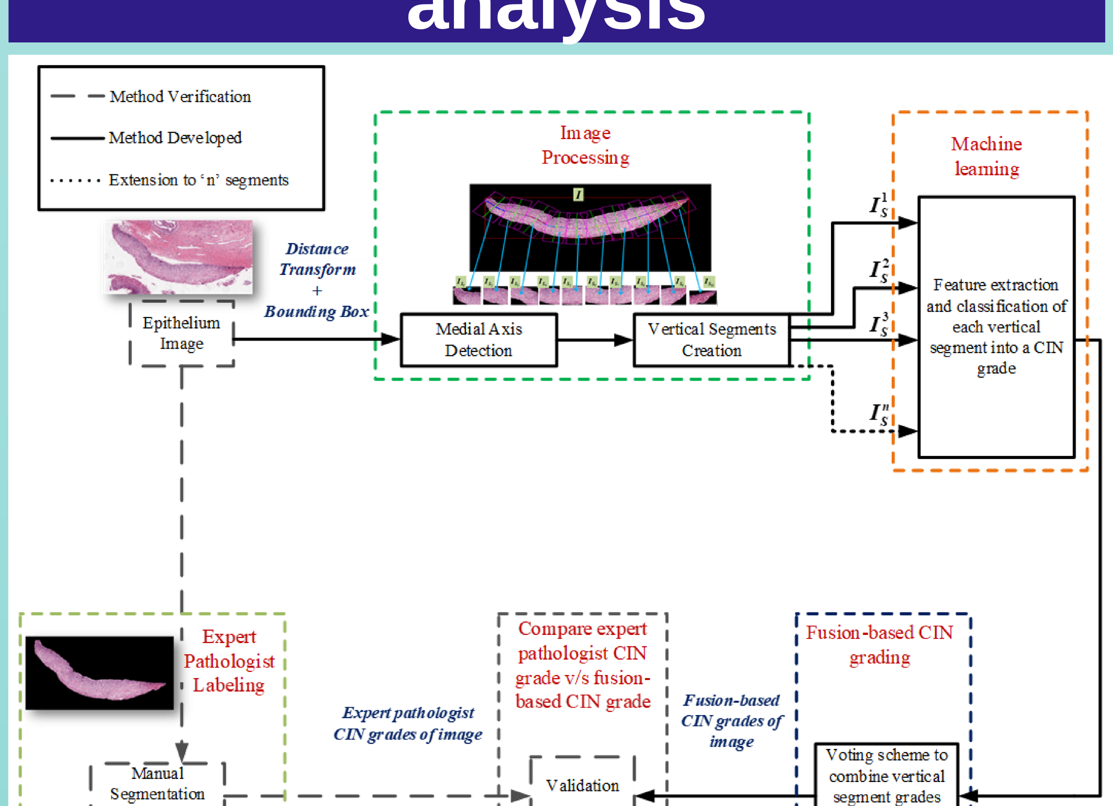
- Cervical cancer, 4th most common cancer affecting women world wide.
- 2018 Statistics:
  - Estimated new cases: 570,000.
  - Low and middle income countries account for 90% of deaths.
- Prevention of cervical cancer mortality is possible with diagnosis at the pre-cancer stage.
- Segmentation of epithelium in cervical histology images is crucial for analysis of nuclei and other image features needed to classify the squamous epithelium into cervical intraepithelial neoplasia (CIN) grades.
- This study presents EpithNet, a deep regression approach for automated epithelium segmentation in digitized cervical histology images.

Manually generated mask

The Challenge: Automatic Detection of Epithelium in Histology Images

- The task is challenging due to:
  - Varying levels of Hematoxylin and Eosin (H&E) staining.
  - Varying shapes of epithelial regions.
  - Varying density and shape of cells.
  - Presence of blood in the tissue sample.
  - Presence of columnar cellular regions.
- We explore the possibility of constructing small-scale but efficient convolutional neural networks (CNNs) to solve the difficult automated segmentation task.

Previous usage of Epithelium analysis

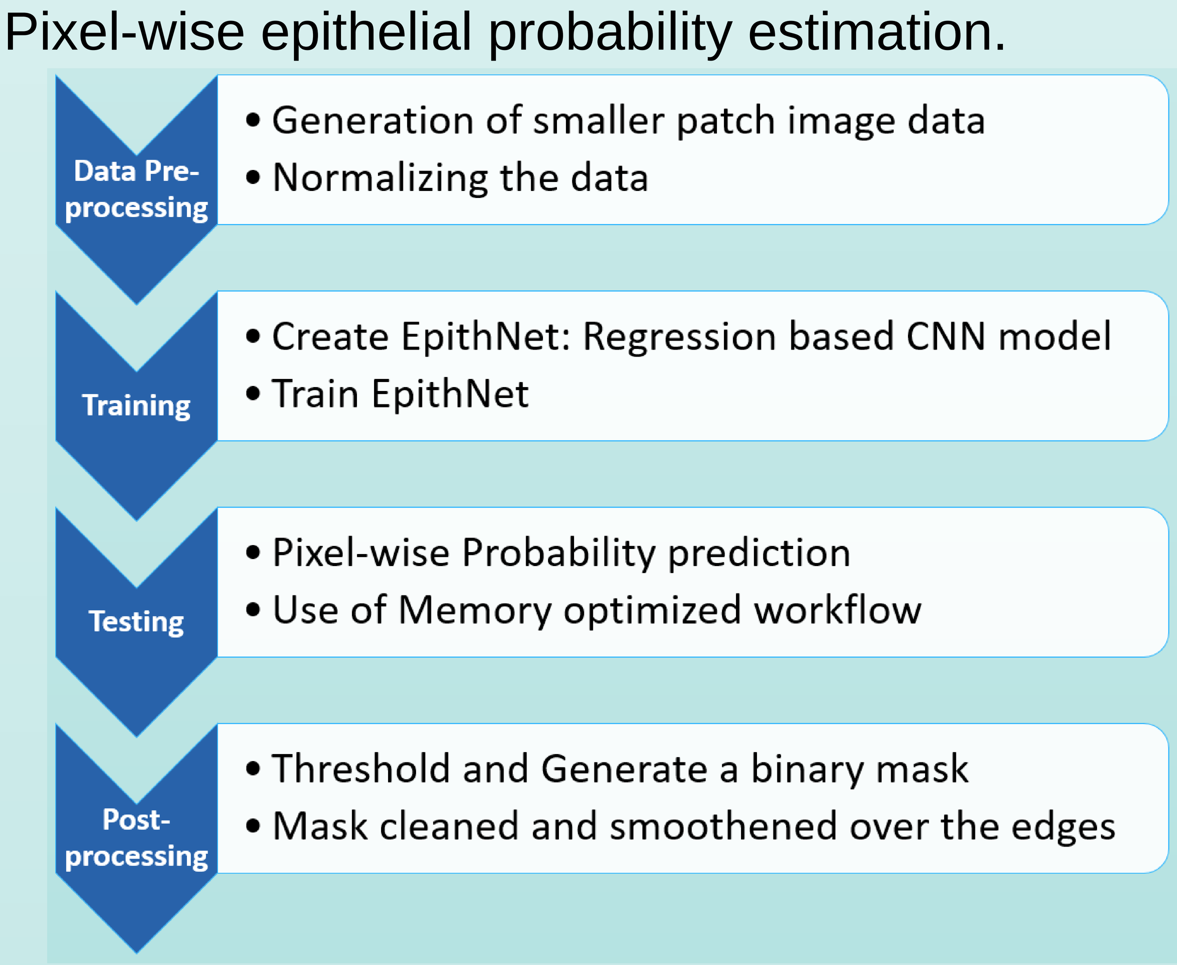


Epithelium Analysis

- Epithelium analysis process used in previous research based on a manually segmented epithelium.

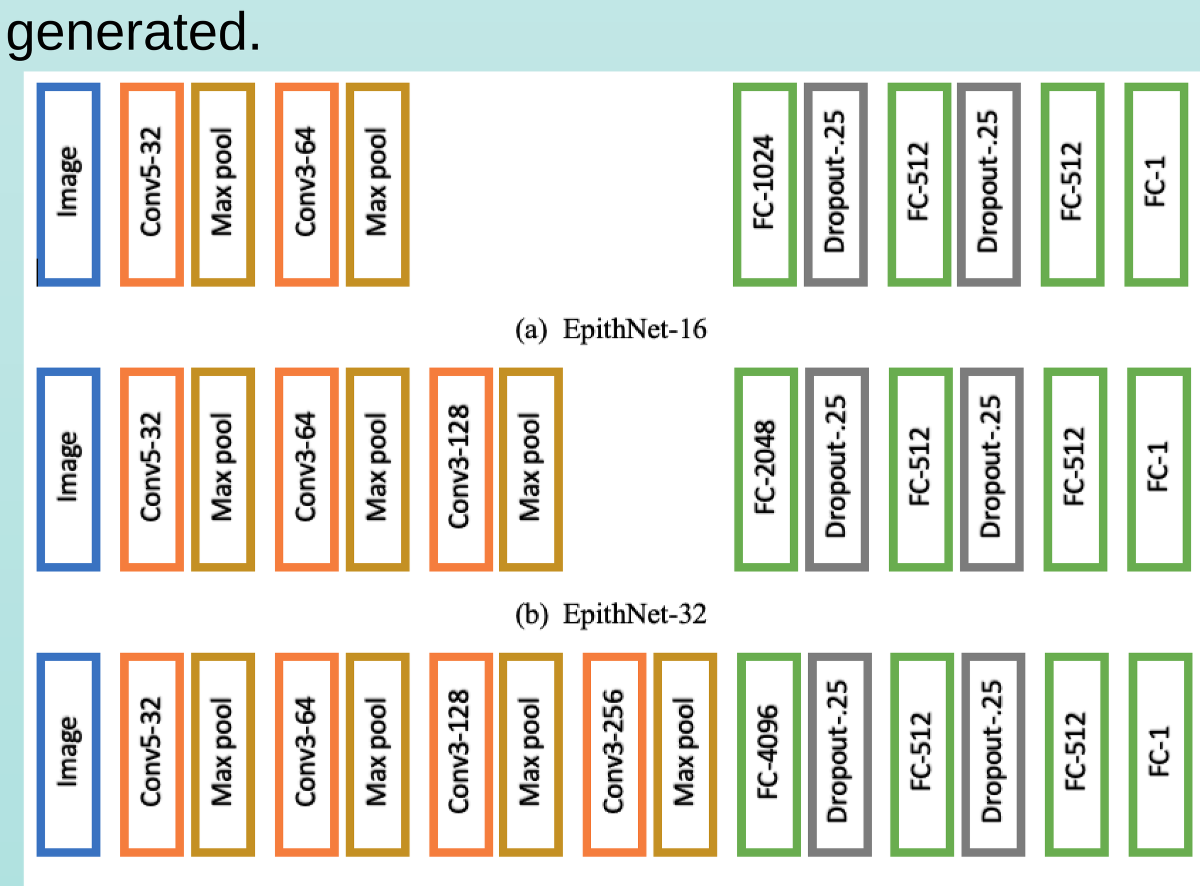
Proposed Model

- Based on the idea:
  - Information provided by a pixel depends on the surrounding spatial proximity in the image plane.
- Pixel-wise epithelial probability estimation.



EpithNet

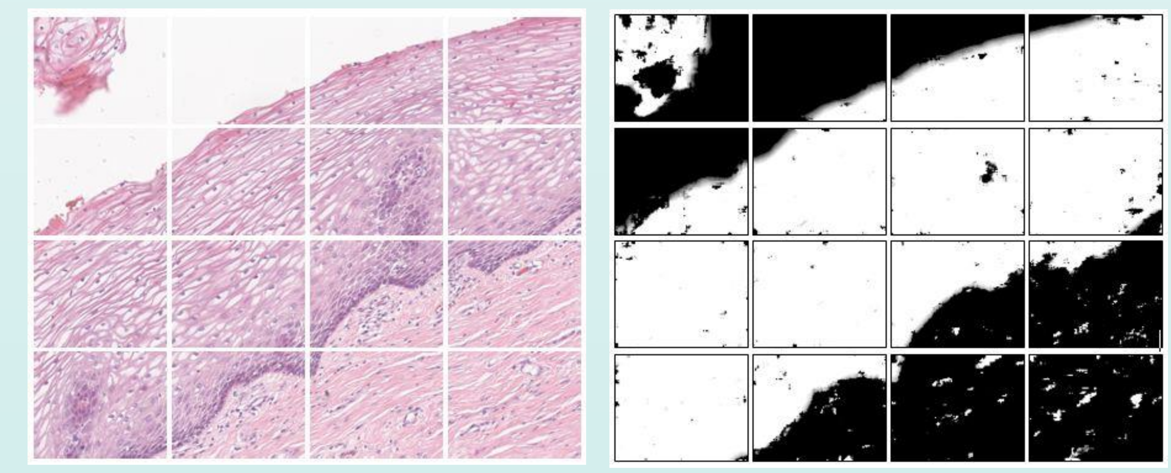
- Models are named after input image sizes: EpithNet-16, EpithNet-32 and EpithNet-64.
- Considered 40 histology images
- 254,514 image patches of size $n \times m \times 3$ were generated.



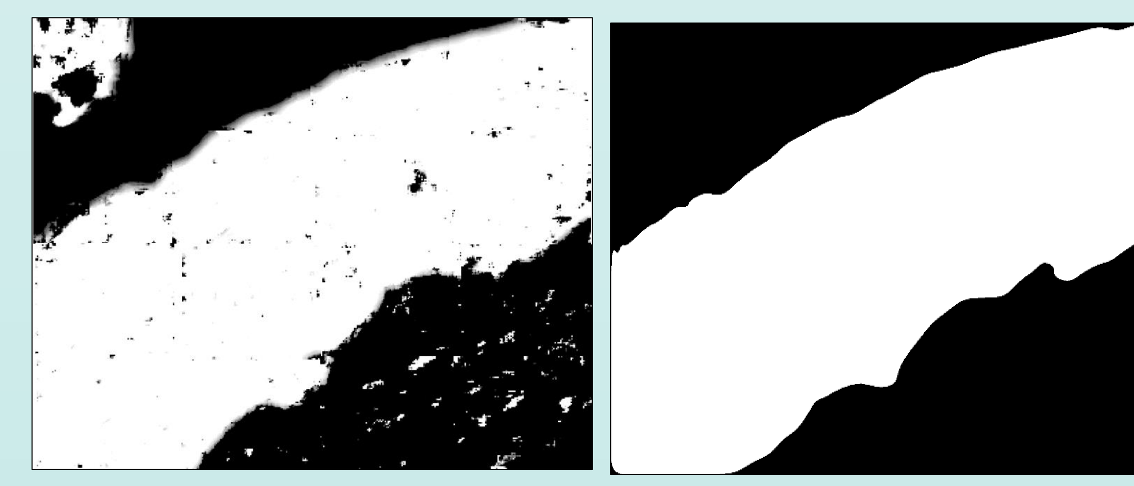
Algorithm

% Preprocess
Generate (n, m) patches with stride s
Calculate the respective ground-truth probabilities,
$y_{gt}^{k} = \frac{1}{mn}\sum_{x=0}^{m-1}\sum_{y=0}^{n-1} p_{mask}^{k}(x, y)$
% Train
Initialize weights and bias
For i=1: N_epochs, do
Forward Pass, predict $\hat{y}^k$
L1 Loss: $L = \sum_{k=1}^{n} |y_{gt}^{k} - \hat{y}^{k}|$
Backpropagate,
Update weights with Adadelta optimizer: $\theta_{i+1} = \theta_i + \Delta\theta_i$
End For
Save model and weights
% Test
Load model and weights
Pad image: $pad_r = n_r s - rem(M, n_r s)$, $pad_c = n_c s - rem(N, n_c s)$
Slice image to (p, q) sub-images,
$n_t = \left\lceil \frac{MN}{pq} \right\rceil$, $n_r = \left\lceil \sqrt{n_t} \right\rceil$, $n_c = \left\lceil \frac{n_t}{\sqrt{n_t}} \right\rceil$
Generate (n, m) patches with stride 4
Predict the probability of each pixel
Combine the predictions to form a gradient mask
Upscale the mask by factor of 4
% Post-process
Threshold the mask
Smooth the mask edges with quadratic Bezier curve,
$B(t) = P_{i+1} + (1-t)^2(P_i - P_{i+1}) + t^2 P_{i+2}$

Automatic Epithelium Segmentation



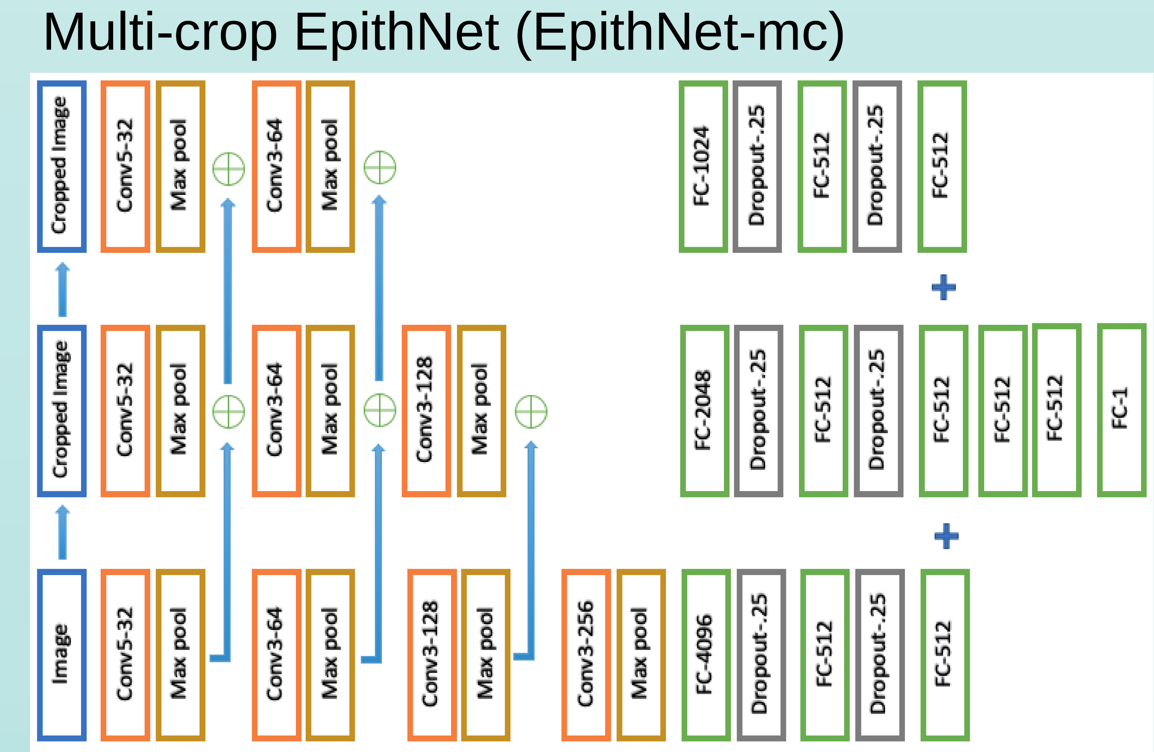
Slice and Predict



Post-processing

Experimental Models

- Unet-64
- Multi-crop EpithNet (EpithNet-mc)



- Designed to read 64×64 image.
- Combined proposed models with center-crop and concatenation of features.

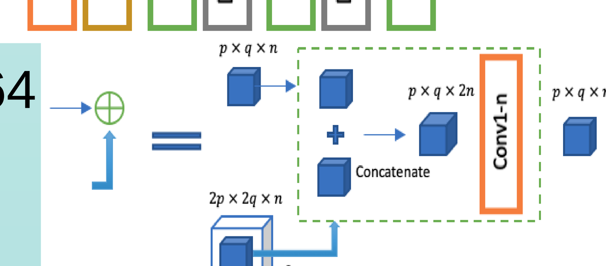


Table I. Model Complexity

Model	UNet-64	EpithNet-16	EpithNet-32	EpithNet-64	EpithNet-mc
Parameters ($\times 10^6$)	31.032	1.071	1.669	3.013	6.856

Results

Table II. Results on 311 cervical histology test data.

Model		J	DSC	PA	MI	FWI
UNet-64	median	0.738	0.849	0.845	0.709	0.740
	mean	0.676	0.789	0.822	0.692	0.712
	std	0.190	0.160	0.116	0.153	0.154
EpithNet-16	median	0.939	0.969	0.965	0.959	0.921
	mean	0.915	0.954	0.951	0.943	0.897
	std	0.070	0.043	0.045	0.049	0.081
EpithNet-32	median	0.947	0.973	0.970	0.966	0.933
	mean	0.931	0.964	0.961	0.954	0.916
	std	0.049	0.028	0.029	0.037	0.059
EpithNet-64	median	0.950	0.974	0.972	0.939	0.945
	mean	0.935	0.966	0.963	0.920	0.930
	std	0.049	0.028	0.032	0.062	0.054
EpithNet-mc	median	0.952	0.976	0.974	0.942	0.949
	mean	0.940	0.969	0.966	0.926	0.936
	std	0.041	0.023	0.026	0.052	0.046

Conclusions

- This new deep learning technique is more accurate for this architectural segmentation than a state-of-the-art technique (UNet-64).
- EpithNet-mc could serve as a useful tool for pathologists.