Spatial Attention-based Deep Learning System for Breast Cancer Pathological Complete Response Prediction with Serial Histopathology Images in Multiple Stains

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Motivations & Challenges

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- In early prediction of PCR to Neoadjuvant chemotherapy, except for H&E images explored before, IHC images stained with KI-67 and PHH3 biomarkers can provide decisive information as well.
- Among the whole slide images, only little part of the images are crucial to the final decision. This is what pathologists will do but CNNs cannot.

- Main problem we attempt to solve is:
  - A CNN system which can process H&E and IHC images simultaneously for a comprehensive analysis.
  - Rather than ask CNN to implicitly learn the patters, more special attention need to be paid to areas where usually are important (tumor cells and TILs)

Methods – Cell Detection Module

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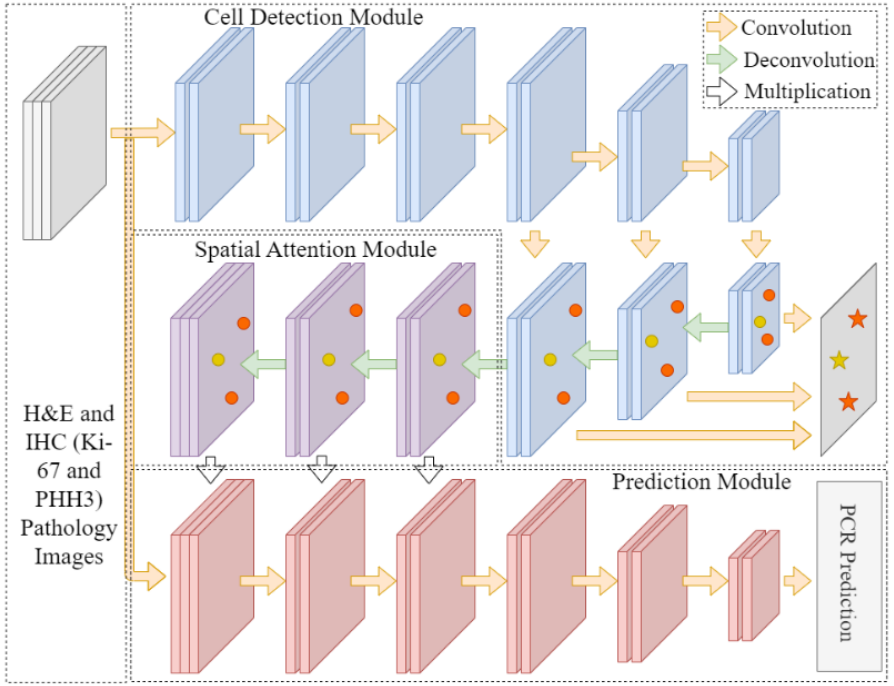
Cell Detection Module (CDM), the first module in the system, is designed to detect all tumor cells and TILs in the pathology images.

The feature maps from the last several convolutional layers in CDM are believed to contain spatial information on the locations of tumor cells and TILs, areas which are important for the final prediction.



Methods – Spatial Attention Module

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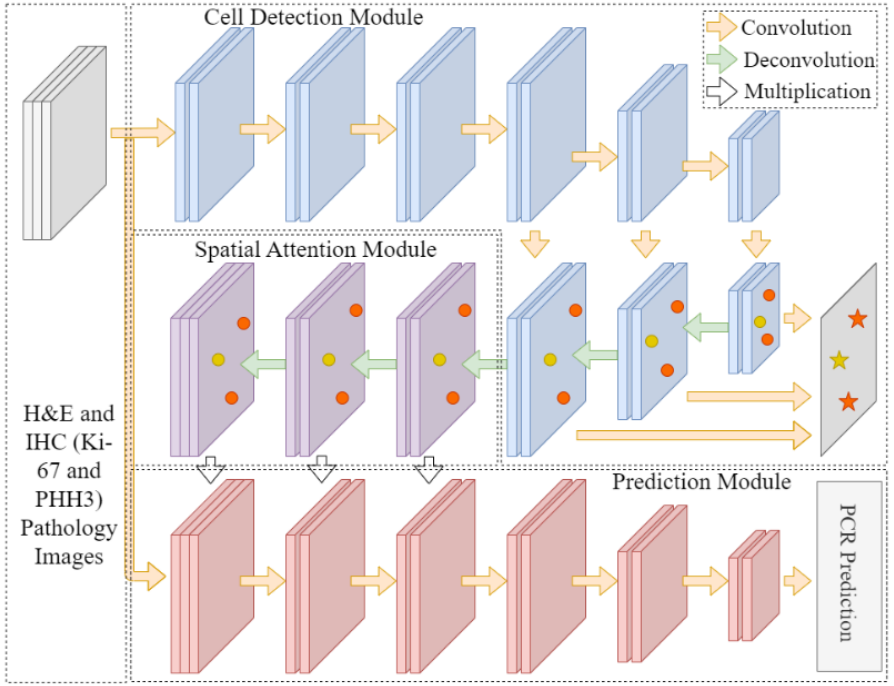
Spatial Attention Module (SPM) is designed to, by several convolutional and deconvolutional layers, resize the features maps to the same size with the original pathology images.

These importance distribution map will be directly applied to the original images (by overlapping/masking), to emphasis the area where has more tumor cells and TILs.



Methods – Prediction Module

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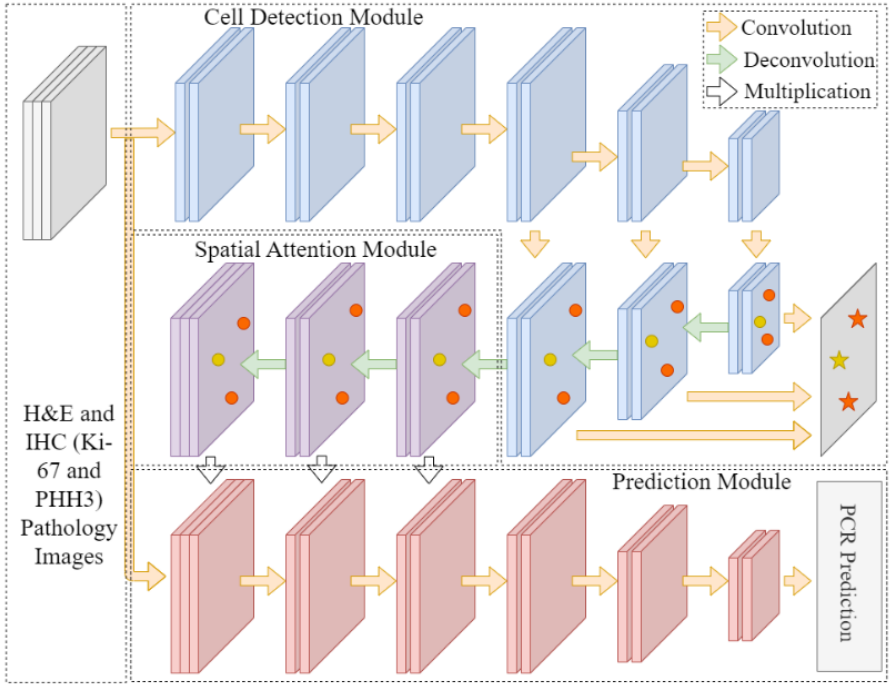
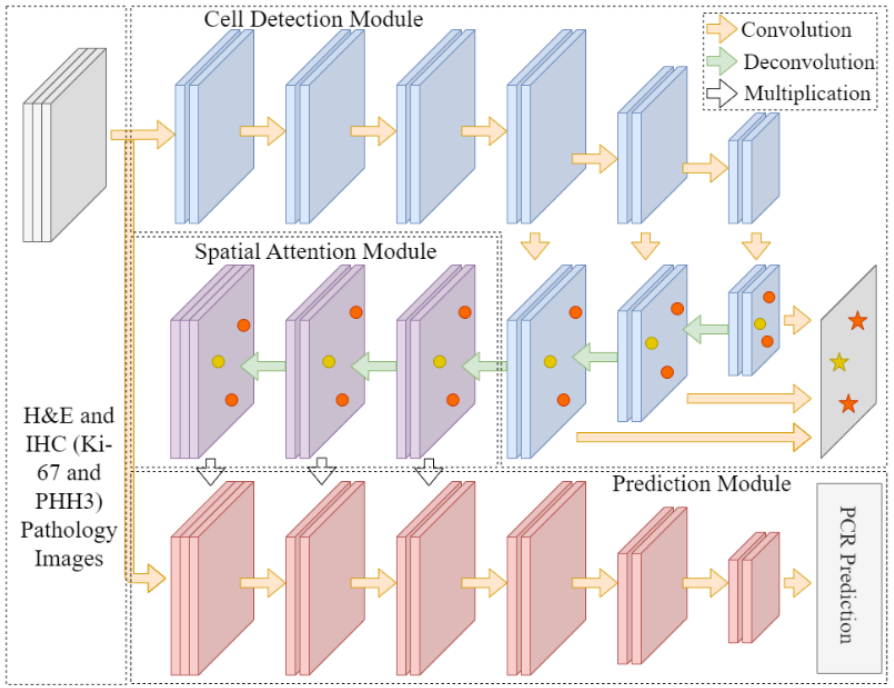
The original H&E and IHC images overlapped with importance distribution maps will be fed into Prediction Module for the final PCR prediction.

The Prediction Module we used here is VGG-19 model considering the performance and computing burden and it can be replaced with other CNN models.



Dataset

- First, the Cell Detection module will be trained on a dataset consisting of 868 H&E images for tumor cell and TILs detection (53,314 tumor cells and 20,966 TILs).
- Second, freezing the trained CDM, all three modules together will be trained on another dataset consisting of 75 patients, 1038 H&E images for PCR prediction.



Results

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Table 1. Comparison of PCR prediction performance of progressively improved deep learning models at the image patch level by metrics of accuracy, AUC, sensitivity, specificity, and balanced accuracy (BA).

	Single Stain + Prediction Only	Multi-stain + Prediction Only	Single Stain + SAM Prediction	Multi-stain + SAM Prediction
Accuracy	0.507	0.635	0.709	0.783
AUC	0.622	0.644	0.762	0.803
Sensitivity	0.726	0.625	0.765	0.701
Specificity	0.467	0.612	0.664	0.829
BA	0.596	0.619	0.715	0.765

Table 2. Prediction performance comparison at patch, region, and patient-level with the number of corrected predictions, total cases, and accuracy.

	Single Stain + Prediction Only	Multi-stain + Prediction Only	Single Stain + SAM Prediction	Multi-stain + SAM Prediction
Patient Level	18/40 (45.0%)	27/40 (67.5%)	32/40 (80.0%)	35/40 (87.5%)
Region Level	289/583 (49.6%)	387/583 (66.4%)	446/583 (76.5%)	488/583 (83.7%)
Patch Level	23325/46029 (50.7%)	29248/46029 (63.5%)	32674/46029 (70.9%)	36059/46029 (78.3%)

Results

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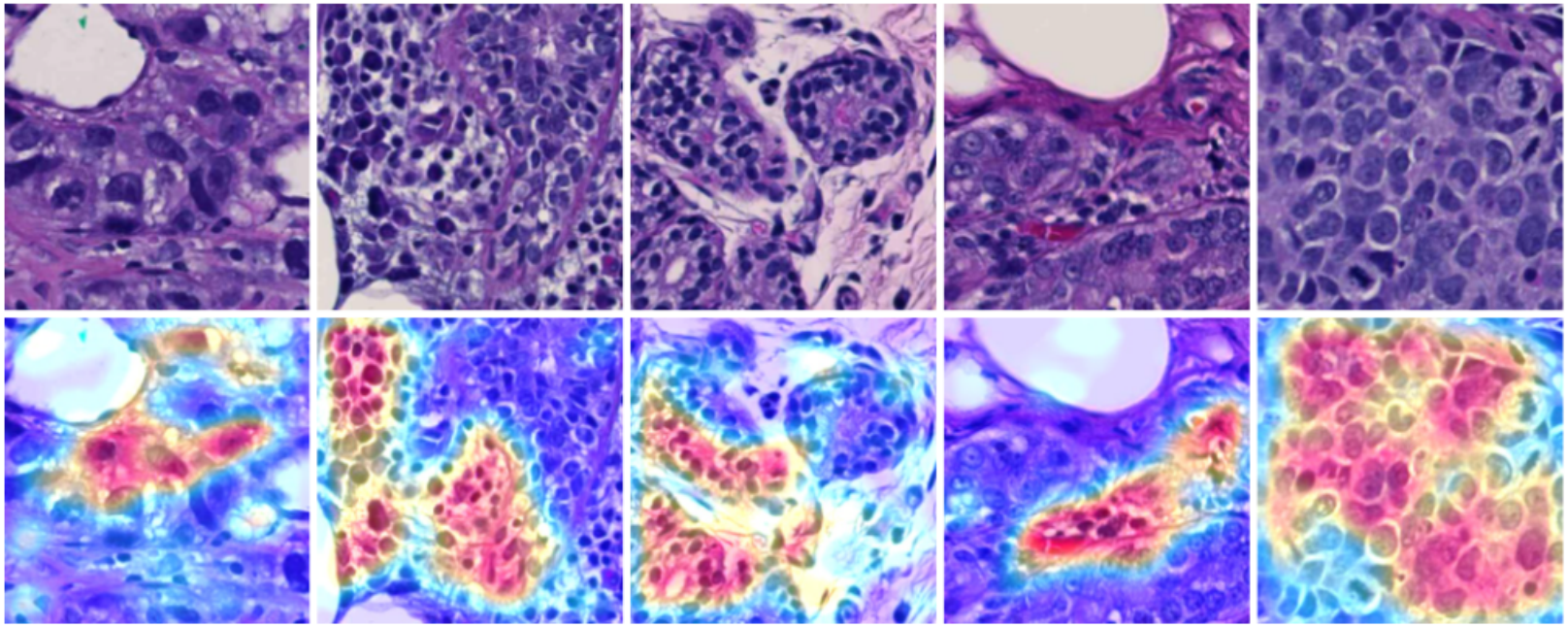

Limits &Future Work

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- The system needs to be tested in other dataset with more clinical cases.
- we will explore incorporating non-imaging features tothe PCR prediction system, as several non-imaging clinical variables are provento be correlated with the PCR.
- since our current system requires imagesin three stains to be well registered, we will study improving the reliability ofthe system for unregistered multi-stained images.
- besides PCR, we willexpand the prediction to additional clinical outcomes such as recurrence andoverall survival.