Optimized Color Decomposition of Localized Whole Slide Images and Convolutional Neural Network for Intermediate Prostate Cancer Classification

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INTRODUCTION

Prostate cancer shows a favorable long-term prognosis with more than five years of survivor after diagnosis [1]. The 10-year prostate cancer specific survival rate for 3+4 (92.1%) was significantly higher than that for 4+3 (76.5%) [2]. Gleason score is the grading system for prostate cancer. It is based on analyzing patterns of glandular and nuclear morphology [3]. We intend to delineate irrelevant image information such as benign glands and stroma, so that the training data sets consist only malignant glands. We propose optimized hematoxylin decomposition on localized images, followed by convolutional neural network to classify Gleason patterns 3+4 and 4+3 without handcrafted features or gland segmentation.

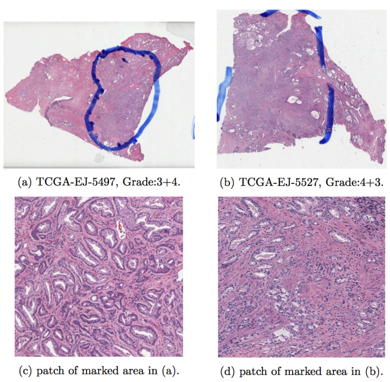
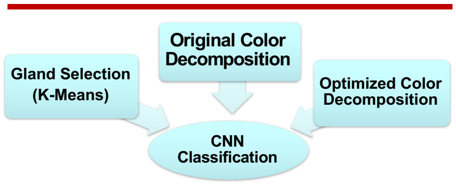


Figure 1. The intermediate prostate cancer image examples.

DATA

The original whole slide images are downloaded from The Cancer Genome Atlas (TCGA). We use 31 Grade 3+3 WSIs and 34 Grade 4+4 WSIs as our training set. For validation, 3 Grade 3+3 WSIs and 3 Grade 4+4 WSIs are used. In the testing stage, 99 Grade 3+4 WSIs and 70 Grade 4+3 WSIs are utilized.

METHODS



Gland Selection:

The localized areas (glands) of WSI for further analysis are segmented by K-Means algorithm in L*a*b* color space. The final binary patch masks are generated to localize gland areas for further color decomposition and classification.

$$\underset{s}{\operatorname{argmin}} \sum_{i=1}^{k} \sum_{x \in S_i} \|x - \mu_i\|^2$$

x: a pixel value in L*a*b* color space;
k: the number of clusters;
S_i: pixels in the i^{th} cluster;
μ_i: the mean value in the i^{th} cluster.

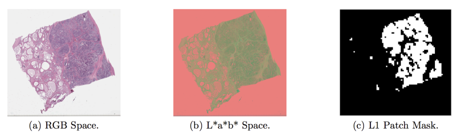


Figure 2. K-Means clustering algorithm on WSI.

Original Color Decomposition:

In Dr. Ruifrok's paper [4], each pure stain (hematoxylin, eosin and diaminobenzidine (DAB)) is characterized by a specific optical density (OD) for the light through each of the three RGB channels. Given an 8-bit RGB image I(x,y,c), its OD is computed as:

$$O(x,y,c) = -\log\left(\frac{I(x,y,c)+1}{256}\right)$$

Three stain absorption vectors:

$$M = [u, v, w] \in \mathbb{R}^{3\times3}$$

Decomposition vectors:

$$S = M^{-1} \cdot R$$

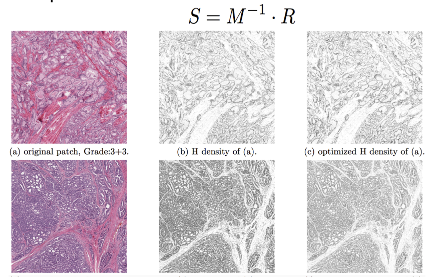


Figure 3. The original and optimized color decomposition results.

Optimized Color Decomposition:

We propose regularized minimization of sum of DAB stain decomposition and the change in matrix $M^{-1}(D)$.

$$\begin{aligned} E(D) &:= \int\int \|S(3)\|^2 dxdy + \lambda\|D - \bar{D}\|^2 \\ &= \int\int \|DO(x,y,c)\|^2 dxdy + \lambda\|D - \bar{D}\|^2 \\ &= \int\int (\boldsymbol{d} \cdot O(x,y,c))^2 dxdy + \lambda\|D - \bar{D}\|^2 \end{aligned}$$

We use quasi-newton algorithm to minimize E(D).

Convolutional Neural Network :

We adopted the CNN architecture from [5], with appropriate modifications for our application. We use caffe [6], an implementation of CNN, which was mainly developed by the Berkeley Vision and Learning Center.

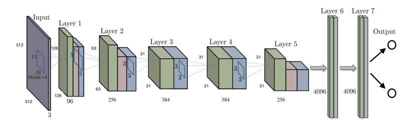


Figure 4. The convolutional neural network architecture.

RESULTS

The results of our prostate cancer classification experiments are shown in Table 1. We can tell that the optimized color decomposition (OOD) has positive effect on prediction performance. The area under ROC curve of OOD method is 0.7247, which can be considered as accurate compared to other methods.

Experiments	Accuracy
Baseline (Originally Informative Patches)	46.15%
Color Decomposition	53.25%
Optimized Color Decomposition	49.70%
Baseline + K-Means	46.75%
Color Decomposition + K-Means	**67.46%**
Optimized Color Decomposition + K-Means	**70.41%**

Table 1. The prediction results of 6 experiments.

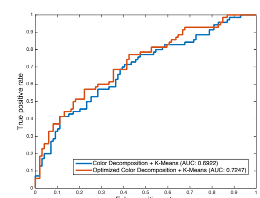


Figure 5. The ROC Curves for the results of proposed methods.

CONCLUSIONS

1. **Experimentations have demonstrated that the optimized color decomposition of localized WSIs can achieve feasible classification accuracy.**
2. **We provides a new approach for intermediate prostate cancer grading without handcrafted ground truth.**
3. **The fully automation framework makes large-scale processing possible.**

REFERENCES

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6. Y. Jia, T. Darrell, "Caffe: Convolutional architecture for fast feature embedding."

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