A regularization term for slide correlation reduction in whole slide image analysis with deep learning

Hongrun Zhang[1], Yanda Meng[1], Xuesheng Qian[4], Xiaoyun Yang[5], Sarah E. Coupland[2,3], Yalin Zheng[1]

1. Department of Eye and Vision Science, University of Liverpool, Liverpool, UK
2. Liverpool Ocular Oncology Research Group, University of Liverpool, Liverpool, UK
3. Liverpool Clinical Laboratories, Liverpool University Hospitals NHS Foundation Trust, Liverpool, UK
4. Chinese Academy of Sciences (CAS) IntelliCloud Technology Co., Ltd., Shanghai, China
5. Remark Holdings, London, UK

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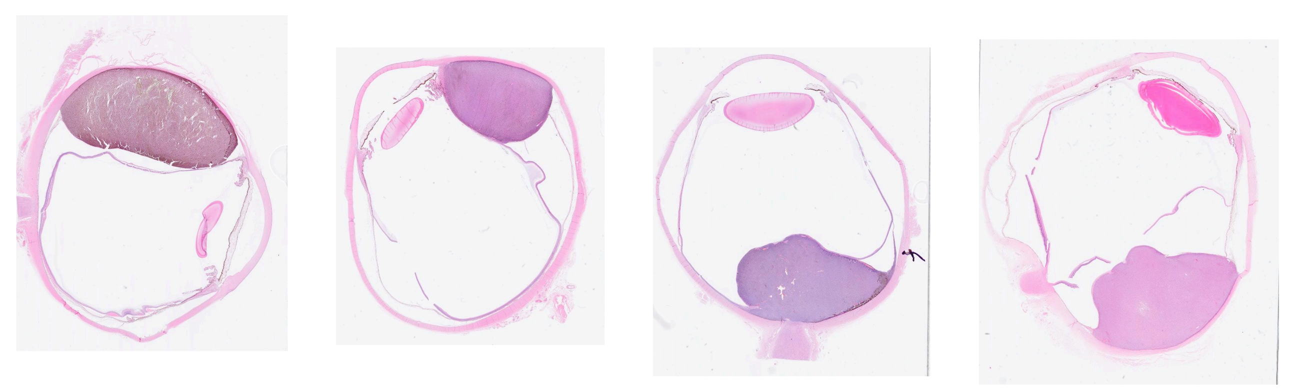
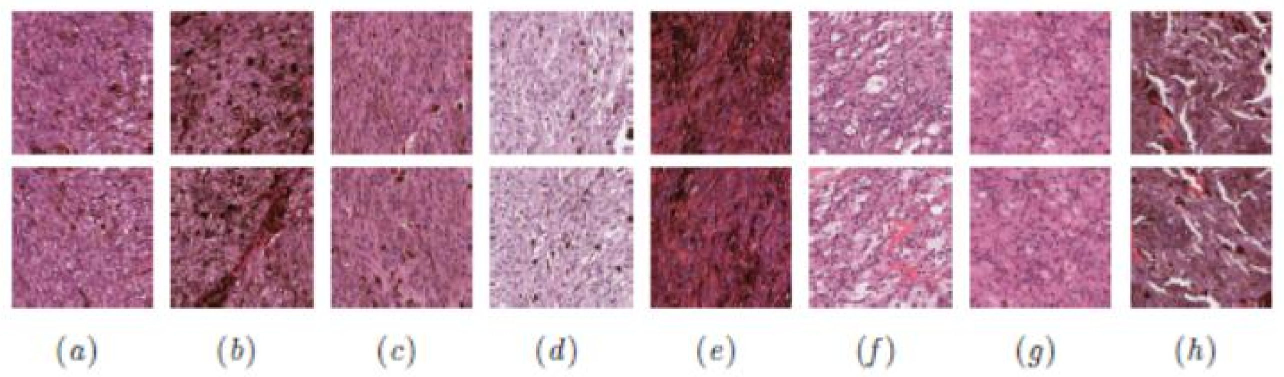
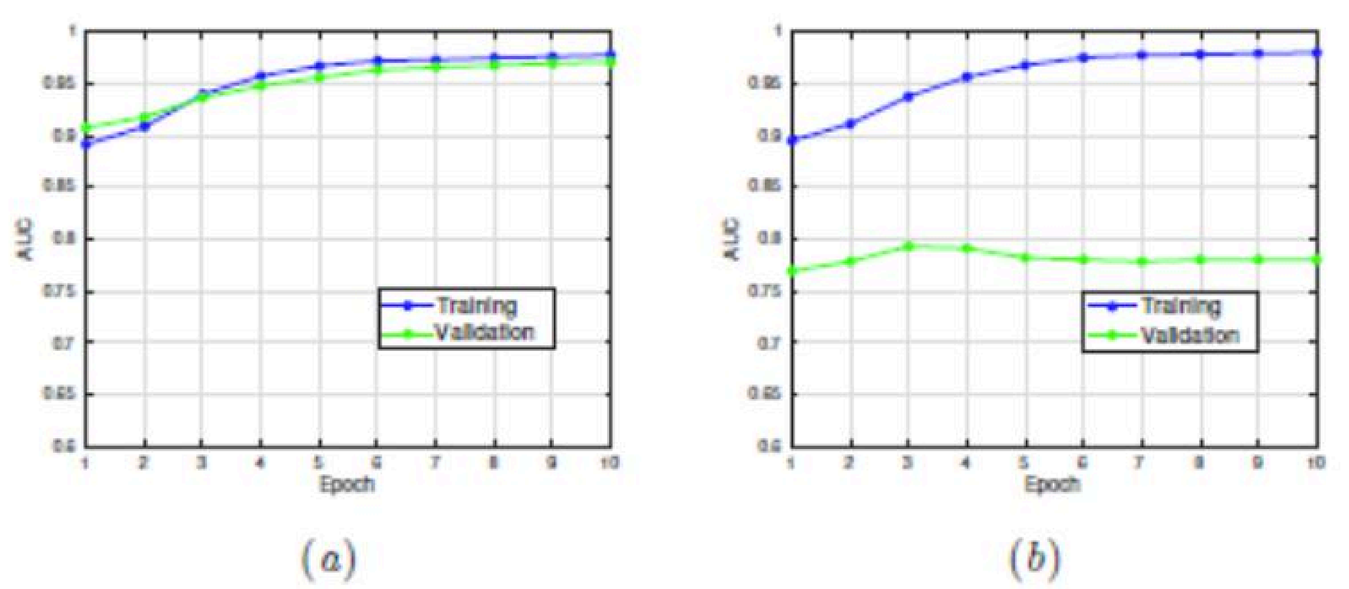
Motivation





Patches from the same slide of this tumour type are very similar, and the shared features may not be relevant for diagnosis, and thus could deteriorate the generalization capability of a trained model.



The experimental results from the two figures above demonstrate further the highly correlation of patches from the same slide, where: (a) Patches from the same slide are mixed into training set and validation set, while (b) Patches from the same slide all exist only in the training set or validation set.

Method

We propose to directly reduce the correlations among the learnt features of patches from the same slide, in order to improve the generalization capability of a trained model. It is implemented by the following regularization term added to regular loss functions.

$$\mathcal{L}_{\mathrm{cr}}(\hat{F}, s) = \frac{1}{D}\mathcal{S}(\hat{F}^T\hat{F} \odot M), \quad M_{i,j} = \begin{cases} 1, & \text{if } s_i = s_j \\ 0, & \text{otherwise} \end{cases}$$

(a) Without SCR. ResNet-18 (b) Without SCR. ResNet-50

(c) With SCR. ResNet-18 (d) With SCR. Resnet-50

When trained with the proposed regularization term, the learnt features of the patches contain less slide information.

Conclusions

- The proposed regularization term is able to increase the generalization capability of trained models
- The regularization term is intuitive and easy to implement
- It is expected to be feasible in wider applications.

Results

Network	Method	Accuracy	Recall	Specificity	F1	AUC
Resnet18	Baseline	$0.649_{0.011}$	$0.875_{0.001}$	$0.521_{0.017}$	$0.645_{0.007}$	$0.776_{0.015}$
	SDA	$0.600_{0.027}$	$0.812_{0.001}$	$0.478_{0.042}$	$0.596_{0.016}$	$0.772_{0.015}$
	SCR	$0.622_{0.031}$	$0.887_{0.024}$	$0.471_{0.057}$	$0.631_{0.017}$	$\mathbf{0.834}_{0.002}$
Resnet50	Baseline	$0.519_{0.007}$	$0.955_{0.028}$	$0.270_{0.026}$	$0.591_{0.005}$	$0.801_{0.021}$
	SDA	$0.545_{0.038}$	$0.574_{0.025}$	$0.528_{0.052}$	$0.479_{0.028}$	$0.650_{0.018}$
	SCR	$0.584_{0.031}$	$0.937_{0.001}$	$0.382_{0.049}$	$0.621_{0.018}$	$\mathbf{0.889}_{0.003}$
AlexNet	Baseline	$0.813_{0.029}$	$0.887_{0.053}$	$0.771_{0.069}$	$0.776_{0.021}$	$0.889_{0.004}$
	SDA	$0.895_{0.018}$	$0.899_{0.030}$	$0.892_{0.039}$	$0.862_{0.018}$	$0.916_{0.001}$
	SCR	$0.795_{0.062}$	$0.912_{0.050}$	$0.728_{0.120}$	$0.769_{0.049}$	$\mathbf{0.920}_{0.006}$
DenseNet121	Baseline	$0.836_{0.009}$	$0.737_{0.025}$	$0.892_{0.001}$	$0.766_{0.016}$	$0.880_{0.005}$
	SDA	$0.859_{0.026}$	$0.812_{0.068}$	$0.885_{0.014}$	$0.806_{0.043}$	$0.881_{0.003}$
	SCR	$0.822_{0.017}$	$0.887_{0.025}$	$0.785_{0.039}$	$0.784_{0.012}$	$\mathbf{0.918}_{0.005}$
VGG16	Baseline	$0.695_{0.027}$	$0.875_{0.001}$	$0.592_{0.042}$	$0.676_{0.019}$	$0.891_{0.007}$
	SDA	$0.672_{0.030}$	$0.75_{0.001}$	$0.628_{0.048}$	$0.625_{0.021}$	$0.809_{0.002}$
	SCR	$0.695_{0.018}$	$0.937_{0.001}$	$0.557_{0.028}$	$0.691_{0.012}$	$\mathbf{0.893}_{0.010}$

Table 1: Performance of the baseline method, slide domain adversarial (SDA) and the proposed regularization term of slide correlation reduction (SCR). The subscripts are the standard deviation values. The best AUC values are in bold.

Network	Method	Accuracy	Recall	Specificity	F1	AUC
Resnet18	Baseline+SN	$0.850_{0.011}$	$0.774_{0.030}$	$0.892_{0.001}$	$0.789_{0.018}$	$0.890_{0.002}$
	Baseline+CJ	$0.873_{0.016}$	$0.892_{0.028}$	$0.862_{0.012}$	$0.8367_{0.021}$	$0.927_{0.002}$
	SDA+CJ	$0.899_{0.011}$	$0.937_{0.001}$	$0.878_{0.017}$	$0.872_{0.012}$	$0.9334_{0.002}$
	SCR+CJ	$0.889_{0.022}$	$0.928_{0.021}$	$0.867_{0.031}$	$0.859_{0.026}$	$\mathbf{0.951}_{0.005}$
Resnet50	Baseline+SN	$0.854_{0.023}$	$0.800_{0.025}$	$0.885_{0.026}$	$0.800_{0.029}$	$0.899_{0.006}$
	Baseline+CJ	$0.777_{0.009}$	$0.937_{0.002}$	$0.685_{0.014}$	$0.753_{0.007}$	$0.936_{0.005}$
	SDA+CJ	$0.809_{0.018}$	$0.862_{0.025}$	$0.778_{0.034}$	$0.766_{0.016}$	$0.919_{0.008}$
	SCR+CJ	$0.845_{0.017}$	$0.937_{0.001}$	$0.792_{0.026}$	$0.815_{0.016}$	$\mathbf{0.953}_{0.002}$
AlexNet	Baseline+SN	$0.831_{0.023}$	$0.800_{0.072}$	$0.850_{0.014}$	$0.774_{0.040}$	$0.887_{0.004}$
	Baseline+CJ	$0.850_{0.011}$	$0.812_{0.001}$	$0.871_{0.017}$	$0.797_{0.012}$	$0.911_{0.003}$
	SDA+CJ	$0.799_{0.030}$	$0.875_{0.001}$	$0.757_{0.047}$	$0.761_{0.027}$	$0.915_{0.003}$
	SCR+CJ	$0.859_{0.022}$	$0.875_{0.039}$	$0.850_{0.052}$	$0.819_{0.019}$	$\mathbf{0.932}_{0.002}$
DenseNet121	Baseline+SN	$0.768_{0.009}$	$0.600_{0.030}$	$0.864_{0.014}$	$0.652_{0.018}$	$0.877_{0.002}$
	Baseline+CJ	$0.836_{0.009}$	$0.862_{0.025}$	$0.821_{0.001}$	$0.792_{0.014}$	$\mathbf{0.955}_{0.003}$
	SDA+CJ	$0.836_{0.009}$	$0.875_{0.001}$	$0.814_{0.014}$	$0.795_{0.008}$	$0.929_{0.002}$
	SCR+CJ	$0.863_{0.014}$	$0.850_{0.030}$	$0.871_{0.017}$	$0.819_{0.019}$	$0.947_{0.004}$
VGG16	Baseline+SN	$0.795_{0.020}$	$0.612_{0.061}$	$0.899_{0.014}$	$0.683_{0.041}$	$0.870_{0.007}$
	Baseline+CJ	$0.745_{0.037}$	$0.762_{0.027}$	$0.735_{0.059}$	$0.685_{0.031}$	$0.863_{0.010}$
	SDA+CJ	$0.777_{0.033}$	$0.8125_{0.055}$	$0.757_{0.057}$	$0.726_{0.034}$	$0.874_{0.017}$
	SCR+CJ	$0.872_{0.011}$	$0.837_{0.030}$	$0.892_{0.001}$	$0.826_{0.017}$	$\mathbf{0.968}_{0.003}$

Table 2: Performance of the baseline method, slide domain adversarial (SDA) and the proposed slide correlation reduction (SCR), with stain normalization (SN) and color jitter (CJ) serving as the extra pre-precossing methods. The subscripts are the standard deviation values. The best AUC values are in bold.

The proposed regularization indeed improve the performances of models of different backbone architectures.

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中科智云 IntelliCloud

Liverpool Ocular Oncology Research Group

LOORG Liverpool Ocular Oncology Research Group

Remark AI UK

UNIVERSITY OF LIVERPOOL

Contact details: Hongrun.Zhang@liverpool.ac.uk, S.E.Coupland@liverpool.ac.uk, Yalin.Zheng@liverpool.ac.uk