Radial Prediction Domain Adaption Classifier for the MIDOG 2022 challenge

Jonas Annuscheit[1,2]

[1]Center for Bio-Medical image and Information processing (CBMI)
[2]University of Applied Science HTW, Berlin 12459

In this paper, we describe our contribution to the MIDOG 2022 challenge without using additional data. A challenge to handle the distribution shift between different tissues for detection of mitosis cells. The main characteristics parts can be distinguished into three parts:

- **We modify the Radial Prediction Layer (RPL) to integrate the layer in a domain adaption classifier, the Prediction Domain Adaption Classifier (RP-DAC). This developed variant learns prototypes for each class and brings more related classes closer. We used this to learn the scanner, the tissue, and the case id.**
- **We used multiple trained YOLO models with different modified input variants of the image. We combine the outputs of the model with an ensembling strategy.**
- **We use the HED color space for data augmentation by calculating different magnitudes for each scanner/tissue type to create more variance in the training set.**

Domain Adaption Classifier | Radial Prediction Layer | Data Augmentation | Ensemble Learning | Uncertainty

Correspondence: ***Jonas.Annuscheit@HTW-Berlin.de***

Introduction

Digital pathology allows it to scan the histology slides and save them in high resolution so that the images can be seen with virtual microscopy. However, analyzing such histology slides is very time-consuming and requires much expertise. There are two important differences between virtual histology slides and natural images: First, we know the resolution of a pixel and can match the resolution to know precisely the size of the cell. Second, we have tiny color space variants inside one tissue type and one scanning process. Deep Learning can help to reduce the time-consuming parts like counting mitoses and decrease the variability of the predictions. However, the colorspace from different laboratories can look vastly different. This was tackled in the MIDOG 2021 challenge(1) by using different scanners. In the new MIDOG 2022 challenge(2), unseen tissue types are available on the test dataset. This increases the domain shift enormously.

To handle the domain shift in the training and the tests set, there exist three possible solutions and was analyzed already in some works (3):

- Using different strategies to augment the training dataset, the domain space from the source gets enlarged.
- Normalization techniques decrease the diversity and overlap the source and target domains.
- Training the neural network so the domain-specific features are not used in the dataset.

In this work, we build our work on the scheme developed for the Radial Prediction Layer (4). That training prototypes instead of fix classes is possible could be shown in the paper of the Radial Predicton Layer(4). That allow us to learn a network that not only removes the information of which scanner or which tissue type an input comes from, but also removes the information to which case it belongs.

Material and Methods

A. Dataset. We used only the dataset that was provided by the MIDOG 2022 challenge. The trainset consists of 9501 mitotic figures from four scanners and six different tissue types, for one of the tissue types where not provide any labeled information. The dataset was split into 80% for the training set, 10% for the validation set, and 10% for an intern validation test set. The unlabeled data was used in the training process to train the RP-DAC and remove the domain information from the network.

B. YOLOv5. Our base model was the YOLOv5s (5) model that was trained on the COCO dataset. We made minor changes by adding learnable parameters to the residual connection layer to allow the network to remove the domain-specific information. This was done for the layers from 6 to 12, 14 to 19, and 10 to 22. The model was trained with AdamW (6) for 800 epochs with small learning rates between 0.002 to 0.0005.

C. Data Augmentation. To enlarge the source domain, we used the technique introduced by Tellez et al. (7) that manipulates the image's hematoxylin, eosin, and dab channel by multiplication it with a factor. This factor is a hyperparameter. We use deconvolution (8) to convert an image from RGB to HED and, after the transformation, back from HED to RGB. To find fair values for this hyperparameter for each scanner/tissue type, we sampled 100 images and calculated the mean of each HED channel. We use the mean of the lowest and the highest value to sample possible factors for each scanner/tissue type separately. This, in combination with a beta distribution to sample possible factors, we get realistic color transformation for each scanner/tissue type.

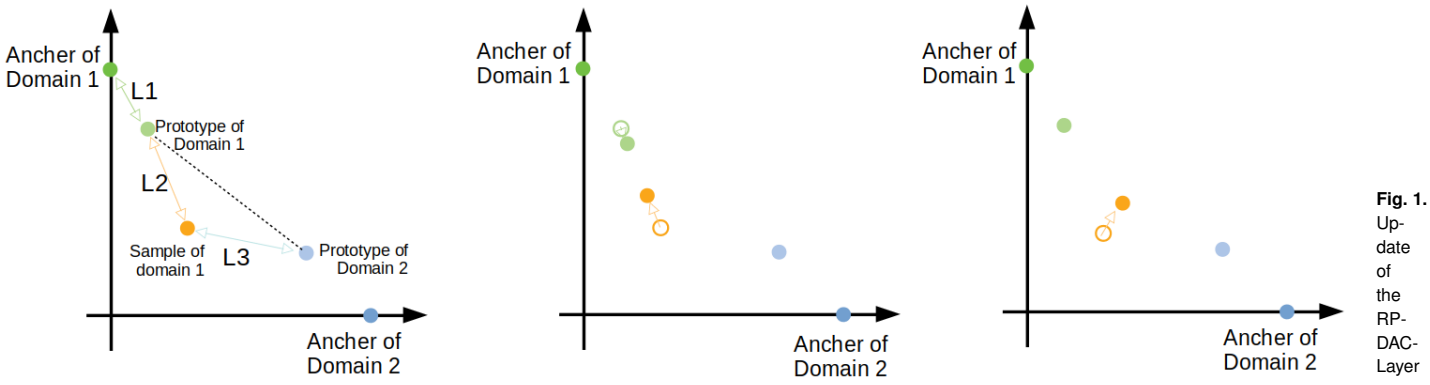

Fig. 1. Update of the RP-DAC-Layer

D. RP-DAC. We took the idea of the Radial Prediction Layer (4) and modified it such that it can be used as a domain adaption classifier with moving prototypes. For each n domain class, we create an n dimensional space with n prototypes, initialized with a constant to one ax. The starting point of the prototypes is hence an proportional to the identity matrix. The training phase can be divided into two alternating steps. 1. The training of the RP-DAC by using not augmented datasets as input and predicting the domain as output. The loss is calculated by the distance between the prediction and the belonging prototype and the distance from the used prototype to the starting point of the prototype by using the mean squared error. Only the RP-DAC weights, including the prototypes' location, are trained in this steps. The two losses can be weighted to allow more freedom for moving the prototypes in the space. 2. Training of the Detection Network includes augmented examples of the image. The RP-DAC loss is the distance from each prediction to each prototype so that the detection network tries to set all predictions of the RP-DAC to one single point by only updating its own weights and removing the domain information as much as possible. The training procedure allows us to train for the scanner's prediction, tissue type, and case id as a domain. It also can handle different data augmentation like described above, which would lead to different domains. For visualization of the losses of the RP-DAC, see figure 1. Left shows an example with two domains. In the phase one, the update of the RP-DAC weights are calculated by the loss L1 and L2, the middle graph shows the result after the update. In steps two, the detection network is updated using the loss L2 and L3; the right graph shows the result after the update. The dashed lines show the space where the cost of the training sample is minimized; If a dataset is far away from this line, there is a way that the network is uncertain about this sample. The not normed uncertainly can be calculated with the Manhatten distance to each prototype divided by the Manhatten distance from the center of all prototypes to all prototypes.

E. Ensembling of the models. In the test phase, we wanted to use an ensembling of different trained models by using different variants of input colorspaces (HE, HED, RGB, GRAY) and test time augmentation like mirroring. However, the run on the test set failed, so we needed to remove this ensembling, to decrease the execution time.

Results

The results of this technique can be found under the leaderboard of the MIDOG 2022 challenge and will be updated as soon as possible in this preprint. Each trained model without ensembling has an F1 score of around 0.76 for our intern validation.

Discussion

In this work, we showed our contribution to the MIDOG challenge 2022. Our solution shows that it can train on prototypes and not on fixed classes. The learning with the prototypes gives much potential for future work, to use smarter strategies in the learning process, to sample or weight trainings data so that the domain shift can be reduced even more. The residual connections of the Yolo network could be using the strategies from (9), so that the domain features do not get transferred. We see create potential in the usage of prototypes for domain adaption classification.

ACKNOWLEDGEMENTS
The authors acknowledge the financial support by the Federal Ministry of Education and Research of Germany (BMBF) in the project deep.Health (project number 13FH770IX6). We also thank Dr. Christian Krumnow for his helpful feedback.

Bibliography

1. Marc Aubreville, Nikolas Stathonikos, Christof A Bertram, Robert Klopleisch, Natalie ter Hoeve, Francesco Ciompi, Frauke Wilm, Christian Marzahl, Taryn A Donovan, Andreas Maier, et al. Mitosis domain generalization in histopathology images–the midog challenge. *arXiv preprint arXiv:2204.03742*, 2022.
2. Marc Aubreville, Christof Bertram, Katharina Breininger, Samir Jabari, Nikolas Stathonikos, and Mitko Veta. Mitosis domain generalization challenge 2022. In *25th International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI 2022)*, 2022. doi: 10.5281/zenodo.6362337.
3. Karin Stacke, Gabriel Eilertsen, Jonas Unger, and Claes Lundström. Measuring domain shift for deep learning in histopathology. *IEEE Journal of Biomedical and Health Informatics*, 25 (2):325–336, 2021. doi: 10.1109/JBHI.2020.3032060.
4. Christian Herta and Benjamin Voigt. Radial prediction layer, 2019.
5. Glenn Jocher. ultralytics/yolov5: v3.1 - Bug Fixes and Performance Improvements. https://github.com/ultralytics/yolov5, October 2020.
6. Ilya Loshchilov and Frank Hutter. Decoupled weight decay regularization, 2017.
7. David Tellez, Maschenka Balkenhol, Irene Otte-Höller, Rob van de Loo, Rob Vogels, Peter Bult, Carla Wauters, Willem Vreuls, Suzanne Mol, Nico Karssemeijer, et al. Whole-slide mitosis detection in h&e breast histology using phh3 as a reference to train distilled stain-invariant convolutional networks. *IEEE transactions on medical imaging*, 37(9):2126–2136, 2018.
8. Arnout C Ruifrok, Dennis A Johnston, et al. Quantification of histochemical staining by color deconvolution. *Analytical and quantitative cytology and histology*, 23(4):291–299, 2001.
9. Juepeng Zheng, Wenzhao Wu, Yi Zhao, and Haohuan Fu. Transresnet: Transferable resnet for domain adaptation. In *2021 IEEE International Conference on Image Processing (ICIP)*, pages 764–768, 2021. doi: 10.1109/ICIP42928.2021.9506562.