Rotation Invariance and Extensive Data Augmentation: a strategy for the Mitosis Domain Generalization (MIDOG) Challenge

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Abstract

Automated detection of mitotic figures in histopathology images is a challenging task: here, we present the different steps that describe the strategy we applied to participate in the MIDOG 2021 competition. The purpose of the competition was to evaluate the generalization of solutions to images acquired with unseen target scanners (hidden for the participants) under the constraint of using training data from a limited set of four independent source scanners. Given this goal and constraints, we joined the challenge by proposing a straightforward solution based on a combination of state-of-the-art deep learning methods with the aim of yielding robustness to possible scanner-related distributional shifts at inference time. Our solution combines methods that were previously shown to be efficient for mitosis detection: hard negative mining, extensive data augmentation, rotation-invariant convolutional networks.

We trained five models with different splits of the provided dataset. The subsequent classifiers produced \(F_1\)-score with a mean and standard deviation of 0.747±0.032 on the test splits. The resulting ensemble constitutes our candidate algorithm: its automated evaluation on the preliminary test set of the challenge returned a \(F_1\)-score of 0.6828.

Dataset Preparation

The organizers of MIDOG 2021 [1] provided annotated images from 150 cases (50 cases each from 3 different source scanners). 50 images from a fourth scanner were provided but we chose not to use them in order to present a solution based solely on a supervised learning framework, thus leaving room for improvements for future work.

We created five folds of three splits such that we were able to train and validate multiple models with varying data distributions. For each fold, we partitioned cases in splits with the following distribution: training(80%), validation(10%) and test(10%), such that the distribution of scanners was identical within each split. With this partition we intended to use as much available source data as possible for training while keeping a small proportion for internal validation and model selection.

Model Architecture

We modeled the conditional likelihood of the mitosis class given an input image patch of size 77×77 at magnification 40× using convolutional neural networks (CNNs). Motivated by the benefits of rotation invariance properties of deep learning models for computational pathology tasks [2–5], we used roto-translation equivariant convolutional layers with a 8-fold discretization of the orientation axis [4]. As this structure guarantees the roto-translation equivariance of the internal activations and invariance of the output of the models with respect to the orientation of the input, rotation augmentation at training and inference time becomes an unnecessary step. Furthermore, this gained invariance property prevents learning possible biases related to the orientation of the images.

Figure 1: Precision-Recall analysis of five models trained and evaluated on the different test sets for each fold of the dataset. Dark blue circles show the performances achieved by the models using the operating points that maximized the \(F_1\)-score on the validation sets.
Table 1: Architecture of the CNN used in this work. Shape of output tensors are written with the following format: \((\text{Orientations} \times \text{Channels} \times \text{Height} \times \text{Width})\).

Shape of operator tensors are written with the following format: \((\text{Orientations} \times \text{In.Ch.} \times \text{Out.Ch.} \times \text{Height} \times \text{Width})\).

* indicates that the operation is followed by a Batch Normalization layer and a leaky ReLU non-linearity (coefficient 0.01).

| Layer Type | Operator Shape | Output Shape |
|------------|----------------|--------------|
| Input      | \(3 \times 77 \times 77\) | \(3 \times 77 \times 77\) |
| Lifting Convolution * | \(16 \times 3 \times 4 \times 4\) | \(8 \times 16 \times 4 \times 4\) |
| Max Pooling | \(2 \times 2\) | \(8 \times 16 \times 33 \times 37\) |
| SE(2,8)-Convolution * | \(8 \times 16 \times 16 \times 4 \times 4\) | \(8 \times 16 \times 34 \times 34\) |
| Max Pooling | \(2 \times 2\) | \(8 \times 16 \times 17 \times 17\) |
| SE(2,8)-Convolution * | \(8 \times 16 \times 16 \times 4 \times 4\) | \(8 \times 16 \times 14 \times 14\) |
| Max Pooling | \(2 \times 2\) | \(8 \times 16 \times 7 \times 7\) |
| SE(2,8)-Convolution * | \(8 \times 16 \times 16 \times 4 \times 4\) | \(8 \times 16 \times 4 \times 4\) |
| SE(2,8)-Convolution * | \(8 \times 32 \times 16 \times 4 \times 4\) | \(8 \times 32 \times 11 \times 11\) |
| Maximum Projection | | 32 |
| Fully Connected * | \(64 \times 32\) | 64 |
| Fully Connected + Sigmoid | \(1 \times 64\) | 1 |

The detailed architecture we used is described in Table 1.

Training Procedure and Data Augmentation

We trained our models with batches of size 64 balanced between mitotic figures and non-mitotic objects, and optimized the weights of the models via minimization of the cross-entropy loss. We used the Adam optimizer (learning rate \(3 \times 10^{-4}\)), with a step-wise decay by a factor 0.8 every 5000 iterations, and stopped training after convergence of the training loss. We used weight decay with coefficient \(2 \times 10^{-4}\). For inference time, we kept the weights of the model that achieved the minimum validation loss.

In order to ensure the generalization of our model to variations of appearance related to unseen scanners, we opted for an extensive and aggressive data augmentation strategy. For this purpose, we applied a series of random transformations according to the protocol described in Table 2. Examples of transformed image patches are shown in Figure 2. This approach is motivated by related works showing the effectiveness of data augmentation for mitosis detection [3, 7].

Table 2: Data augmentation protocol: for each input image patch, we scanned the following list of transformations and applied it with a given probability, after random sampling of a set of coefficients.

| Transformation | Coefficients | Probability |
|---------------|--------------|------------|
| Transposition |              | 50%        |
| Color Shift   | \(c_{r,g,b} \sim U[-13,13]\) | 50%        |
| Gamma Correction | \(\gamma_{r,g,b} \sim U[0.9,1.5]\) | 50%        |
| Hue Rotation  | \(h \sim U[0,1]\) | 50%        |
| Spatial Shift | \(\Delta x,y \sim U[-12px,12px]\) | 100%       |
| Spatial Scale | \(s \sim U[-13%,13%]\) | 50%        |
| Additive Gaussian Noise | \(c_{r,g,b} \sim N(0,9)\) | 50%        |
| Cutout [8] (random color/size) | \(s \sim U[8px,16px]\) | 50%        |

Generating training batches via random sampling of non-mitotic image patches is known to be a suboptimal approach for mitosis detection as models are less exposed to challenging non-mitotic objects during training [9]. Therefore, to encourage the model to discriminate challenging non-mitotic objects, for each fold, we sequentially resampled the dataset by removing easy classified patches using a protocol derived from Cireșan et al. [9] using first versions of the models trained via random sampling of the training sets.

Inference Time

At inference time, the fully convolutional structure of our models enables their dense application on large test images which produces probability maps. Candidate mitotic figures are identified as local maxima after applying non-maxima suppression within a radius of 30px. Our models are then turned into binary classifiers by setting a cutoff threshold (operating point) that is selected such that the F1-scores on the validation sets were maximized. We applied this procedure to generate a classifier for each fold, and then gathered the 5 models to form an ensemble. The performance of these classifiers on the source test sets are reported in Figure 1. For new test images the detections of each classifier are considered as votes for candidate mitoses and we filter out detections that get less than 2 votes.

Conclusions and Discussion

We proposed a straightforward approach combining multiple state-of-the-art solutions to tackle the generalization problem for scanner-related distributional shifts in the context of the MIDOG2021 competition. We report a lower performance of our solution on the preliminary test set provided by the organizers compared to the performances we obtained on the source test sets, suggesting that the generalization of our model is limited to some extent. We hope that our methodology can be considered as a baseline, that could potentially be improved using additional training components for domain generalization. In future work, we will aim at investigating the reasons of the generalization limitations of the presented method.

Figure 2: Example of mitosis-centered image patches transformed according to our random data augmentation protocol.
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