Detecting Invasive Ductal Carcinoma with Semi–Supervised Conditional GANs

Editors: Under Review for MIDL 2020

Abstract
Invasive ductal carcinoma (IDC) comprises nearly 80% of all breast cancers. The detection of IDC is a necessary preprocessing step in determining the aggressiveness of the cancer, determining treatment protocols, and predicting patient outcomes, and is usually performed manually by an expert pathologist. Here, we describe initial experiments with a novel algorithm for automatically detecting IDC using semisupervised conditional generative adversarial networks (cGANs). The framework is simple and effective at improving scores on a range of metrics over a baseline CNN.

Keywords: GAN, cGAN, histopathology, breast cancer

1. Introduction
Invasive ductal carcinoma (IDC) comprises nearly 80% of all breast cancers (DeSantis et al., 2011). The detection of IDC is a necessary preprocessing step for determining aggressiveness, treatment protocols, and predicting patient outcomes. This is usually done by performing a visual analysis of tissues slides from regions where IDC has been detected, a costly, time-consuming, and challenging process that involves the pathologist scanning large regions of mostly healthy tissue to identify the relatively smaller regions of IDC. Because precise delineation of the IDC is critical to assessing of the aggressiveness of the malignancy, there is a significant need for highly accurate automatic methods for detecting IDCs.

Many algorithms have been somewhat successful at automatic detection of IDCs (Cruz-Roa et al., 2014; Araújo et al., 2017; Cruz-Roa et al., 2014; Janowczyk and Madabhushi, 2016). Here, we propose a novel approach via conditional generative adversarial networks (cGANs). The proposed framework is simple and effective at improving scores on a range of metrics over a baseline CNN.

2. Conditional Generative Adversarial Networks
A generative adversarial network, or GAN, consists of two neural network models, a generator $G$ and a discriminator $D$, that compete in an adversarial game: the task of the generator is, given some random input $z$, to produce an output $G(z)$ such that the discriminator $D$ cannot distinguish $G(z)$ from a sample taken from the source domain. As $D$ and $G$ are trained in turn, $G$ learns to model the true distribution $p$ of the source domain and $D$ learns to evaluate the divergence between $p$ and the generative distribution $q$, resulting in a competition to reach a Nash equilibrium that can be expressed by the training procedure. The generator and the discriminator can be augmented with conditional data $y$ to produce a conditional GAN, or cGAN. Although often unstable and prone to issues such
as mode collapse, recent developments such as spectral normalization and gradient penalty have significantly improved the stability of GAN training (Miyato et al., 2018; Gulrajani et al., 2017).

By augmenting the discriminator with a network head that performs classification (c.f. Figure 1), the discriminator can be trained to classify samples from the source data. Such a semi–supervised training regime has been shown to be particularly effective when limited training data is available (Salimans et al., 2016).

3. Methodology and Results

The data used for the experiments described here are publicly available\(^1\) data first introduced in (Cruz-Roa et al., 2014). In total, the dataset contains 277,524 50 \times 50 RGB patches, 78,786, or 28\% where IDC is present, and 198,738 patches, or 72\%, without IDC. Detailed background on the dataset is provided in Appendix A. 20\% of the data were held out for testing, and the model was trained on the remaining 80\% of the dataset.

The model proposed here is a cGAN loosely based on the DCGAN architecture (Radford et al., 2015), where the generator is conditioned on the class of the input data, and the discriminator receives no conditioning, giving the value function

\[
\min_D \max_G V(G, D) := \mathbb{E}_{x \sim p}[\log(D(x))] + \mathbb{E}_{z \sim p_z}[\log(1 - D(G(z|y)))],
\]

where \(z \sim p_z\) is white noise.

The generator is a fully convolutional neural network (Long et al., 2015). The discriminator is a CNN with two network heads, one that predicts the presence of IDC, and the other that predicts whether the observed data is real or synthetic. Both the generator and the discriminator use five transposed convolutional (resp. convolutional) layers with 3 \times 3 kernels. The number of filters in each convolutional layer of the discriminator is 64 \times layer \times \omega, where \(\omega\) is a width multiplier used to increase the capacity of the network; the number of filters in each transposed convolutional layer in the generator is calculated

\(^1\) https://andrewjanowczyk.com/wp-static/idc_regular_ps50_idx5.zip
Table 1: Results from semi–supervised experiments. In expressions of the form cGAN$_\omega$, the value $\omega$ is the width multiplier described in Section 3.

| Model   | Accuracy | BAC   | Precision | Recall/Sensitivity | Specificity | F1–score |
|---------|----------|-------|-----------|--------------------|-------------|----------|
| CNN$^2$ | NA       | 84.23%| 65.40%    | 79.60%             | NA          | 71.80%   |
| cGAN$_1$| 86.68%   | 81.15%| 81.94%    | 68.29%             | 94.00%      | 74.50%   |
| cGAN$_2$| 87.45%   | 83.19%| 80.85%    | 73.29%             | 93.09%      | 76.88%   |
| cGAN$_4$| 88.33%   | 83.54%| 84.39%    | 72.41%             | 94.66%      | 77.94%   |

analogously. The generator uses ReLU activations, the discriminator uses leaky ReLU activations with $\epsilon = 0.2$. Downsampling in the discriminator was accomplished by adjusting the stride of the convolutional layers as needed. The discriminator network heads each consist of a single fully connected layer. Spectral normalization was applied to all convolutional and transposed convolutional layers except the first and the last layers in the discriminator and gradient penalty was used (Miyato et al., 2018; Gulrajani et al., 2017). The network was trained for 200 epochs with minibatch size of 128 using the Adam optimization algorithm ($\beta_1 = 0.5, \beta_2 = 0.999$) (Kingma and Ba, 2014) with the learning rate fixed at 0.0002 for the first 100 epochs, then reduced linearly to 0 for the remaining 100 epochs. The model was implemented using PyTorch (Paszke et al., 2017) and trained on a workstation running Ubuntu 18.04 using two Titan Xp GPUs. Results are presented in Table 1.

4. Conclusions and Future Work

In this paper we present the results of a preliminary investigation into the use of cGANs for automatic detection of IDC in breast histopathology images. The advantages of the cGAN framework is that the generator learns during the training process to generate data that follows the distribution of the training data, thus supplementing the training dataset with additional high–quality synthetic training data. These models achieve high accuracy, precision, specificity, and F1–scores, and competitive balanced accuracy scores, while being less sensitive than a conventional CNN model.

There are several avenues for future work in this vein. One of the advantages of semi–supervised GAN training is that in situations with limited data, it is often possible to achieve superior performance over other methods on similarly sized data. Most GAN discriminators are rather shallow in comparison to modern classifier architectures (Mahmood et al., 2019). Semi–supervised training may allow one to increase the capacity of the discriminator over a base classifier CNN and thereby improve performance beyond the results described here, where despite increasing the network width by a factor of four, no signs of overfitting were observed. In addition, other conditioning approaches are possible and may be effective, such as conditioning on the location of the image patch in the whole slide image. Future work will investigate these possibilities.
Acknowledgments

Acknowledgments withheld.

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Appendix A. The Data

As noted above, the data used for the experiments described here are the publicly available data first introduced in (Cruz-Roa et al., 2014). These data consist of digitized histopathology slides from 162 women diagnosed with IDC at the Hospital of the University of Pennsylvania and The Cancer Institute of New Jersey. The slides were digitized via a whole–slide scanner at 40x magnification (0.25μm/pixel resolution), and each whole–slide image was downsampled by a factor of 16:1 to a resolution of 4μm/pixel. The ground truth annotations were obtained manually by an expert pathologist. The data were publicly released as RGB patches of 50 × 50 pixels. In total, the dataset contains 277,524 patches, of which 78,786, or 28% are IDC, while the remaining 198,738 patches, or 72% are healthy tissue. The annotations were performed at 2x magnification or less, and are thus relatively coarse, occasionally admitting some stromal or non–invasive tissue.