M-Protain Diagnostics Using Generative Active Learning

Abstract

With comparatively less labeled data and high labeling cost, most of the medical involved tasks can not be directly tackled by state of art machine learning approaches for their lack of large carefully labeled datasets. Our paper is based on the a dataset of immunofixation electrophoresis(IFE) images used in the M-protain diagnostics that has no annotation. In order to make the diagnostics process more efficient, our paper try to train a binary classifier(normal or not) with only few data instance labeled by human experts and all other unlabeled data. We do the semi-supervised training by combining active learning with generative models. In our proposed method, we do these things iteratively: first we find the most uncertain data instances in the latent space of the generative model using the classifier; then we generate synthetic IFE images for human oracle to annotate; afterwards we add these labeled data back in the training set of the classifier. In addition, according to prior knowledge of the IFE images, we propose a specific explainable generative model based on Gaussian mixture model(GMM) that is only effective in this dataset, and compare the result of it with universal effective generative model like GAN and VAE. In order to figure out the best representation of this dataset, we conduct extensive experiments to demonstrate the difference between applied generative models, evaluate the effect they make on active learning quantitatively, and explore the reason behind the results.

Introduction

As deep models achieve astonishing results in almost every machine learning tasks, some unavoidable problems such as the need for large carefully labeled dataset has troubled researchers from the start. Part of the reason behind the tremendous success in deep learning is the availability of large-scale labeled data(Sun et al. 2017). Although data labeling companies and platforms claim that they can provide inexpensive yet high quality data(Buhrmester, Kwang, and Gosling 2011), achieving such datasets can be extremely costly or even unrealistic in the scenarios where labeling requires high professionality. For instance, some medical image tasks can not be labeled by people without systematic training. However, the small number of these experts has determined that large-scale dataset is difficult to biuld. Plus, they are probably already preoccupied. With the desire to fill this gap, our paper combines active learning and generative model to achieve relatively good results on small datasets.

For instance, a large dataset of medical images regarding M-protain diagnostics is accessible. Nonetheless, each image comes with a diagnostics report without the trainable label that we desire. M-protain stands for Myeloma protein, which can be identified by applying immunofixation electrophoresis(IFE) because its sharp monoclonal band in the image. Different categories of results may indicate MGUS, smouldering myeloma(sMM), or multiple myeloma(MM). It usually takes three doctors to examine the IFE image and reach the final conclusion. Therefore the process is highly time consuming. In real world scenarios, more than half of the electrophoresis results are obviously normal which do not need further concern. Although final decision should be made by doctors, if a classifier can provide an indicating result, then time can be significantly saved. Part of the proposed method can be implemented by manually constructed rules, so in the end, machine learning involved section is narrowed down to a binary classification(normal or abnormal) of one dimensional signal.

Due to the lack of explicit label, this is a classic semi-supervised learning task. Our paper tries to utilize the combination of active learning and generative model to tackle with this unlabeled dataset. Active learning is that a machine learning algorithm that can achieve greater accuracy with same amount labeled training instances if it is allowed to choose the data to be labeled from an unlabeled dataset (Settles 2009). Thus, active learning techniques significantly reduce the amount of labor required compared to manually label all existing data. Deep generative models including GAN and VAE are currently purveiling in a variety of applications. Zhu and Bento made the first attempt(Zhu and Bento 2017) to generate data for active learning process. Since then, a number of research have been conducted to find the most effective way to boost the active learning performance using generative models.

Our paper also tries to utilize the combination of active learning and generative models to gain a task learner, but we made specific augmentations specifically for IFE column binary classification. By generating(decoding) synthetic IFE images based on latent space of the generative models, the model can query the least certain generated instances in the latent space, and thus improve the classifier in the latent space iteratively. In addition, according to prior knowledge of the IFE images, we propose a specific explainable generative model based on Gaussian mixture model(GMM) that is only effective in this dataset, and compare the result of it with universal effective generative model like GAN and VAE. We conduct extensive experiments to demonstrate the difference between applied generative models, evaluate the effect they make on active learning quantitavely, and try to find the reason behind it.

Related Work

Several techniques were widely used by researchers to tackle with small datasets and partially labeled datasets. For example, active learning(Settles 2009) tries to pick the most informative data to label so that models can learn better when the total number of labeled data is limited; generative methods(Kingma et al. 2014)(Springenberg 2015) wish to benifit target classifier using knowledge of data distribution learnt by generative models; data augmentation(Tanner and Wong 1987) enriches small dataset by generating new synthetic data; domain transfer(Pan and Yang 2009) utilizes large, easily acquired datasets in different tasks or different settings to help the training of target learner. In this paper we mainly focus on active learning and generative methods.

Active Learning

In general, active learning has three main settings: membership query synthesis, stream-based selective sampling, and pool-based active learning(Pan and Yang 2009). Among them the last one is mostly refered to. Pool-based active learning gather a large pool of unlabeled data and ranks their informativeness according to an acquisition function that may coevolve with the task learner in the training process. Various acquisition functions have been developed by researchers. For example, some acquisition function can be derived by maximising the uncertainty of the current learner(i.e. finding the most uncertain data in the pool). Another acquisition function maximises the Bayesian Active Learning by Disagreement(BALD)(Houlsby et al. 2011). It can choose pool points that are expected to maximise the information gained about the model parameters through maximising the mutual information between predictions and model posterior.

Generative Methods

Firstly proposed by Goodfellow *et al.* in 2014, generative adversarial nets(GANs) (Goodfellow et al. 2014) drawn a lot attention in the field of computer vision, natual language processing, and etc. Previous researchers inspired by its adversarial structure developed a large amount of variations that can be applied to various kinds of tasks. Some of the most well-known variations of GAN includes WGAN(Arjovsky, Chintala, and Bottou 2017) which stablizes training process and provide solution to mode collapse problem, CGAN(Mirza and Osindero 2014) that firstly introduced models that can generate specific classes according to the label fed as part of the input, BiGAN(Donahue, Krhenbhl, and Darrell 2016) that enables bidirectional transformation, VAEGAN(Larsen et al. 2015) that connects GAN and VAE using a conjuncted generator/decoder, and so on. Variation auto encoder(VAE) on the other hand, tries to develop a generative model in a variation inference kind of way(Kingma and Welling 2013).It tries to capture the most important latent variables that determine how real data are formed. Although more robust to small pertubations in latent space, VAE tends to lose more graphic details(more blurry) when reconstructing the input data compared to GAN due to its pixel-wise reconstruction loss.

Generative Active Learning

Preliminaries

The entire defination of the task can be defined as below. Every IFE image consists of five columns of one dimensional signal. According to an IFE image, a 12 dimensional 0/1 vector will be computed as output.

Proposed Method

Our method make use of

Experiments

I did such experiments

Discussion

After I did these experiments

Conclusion

To sum up

References

Arjovsky, M.; Chintala, S.; and Bottou, L. 2017. Wasserstein gan. *arXiv preprint arXiv:1701.07875*.

Buhrmester, M.; Kwang, T.; and Gosling, S. D. 2011. Amazon's mechanical turk: A new source of inexpensive, yet high-quality, data? *Perspectives on psychological science* 6(1):3–5.

Donahue, J.; Krhenbhl, P.; and Darrell, T. 2016. Adversarial feature learning.

Goodfellow, I.; Pouget-Abadie, J.; Mirza, M.; Xu, B.; Warde-Farley, D.; Ozair, S.; Courville, A.; and Bengio, Y. 2014. Generative adversarial nets. In *Advances in neural information processing systems*, 2672–2680.

Houlsby, N.; Huszár, F.; Ghahramani, Z.; and Lengyel, M. 2011. Bayesian active learning for classification and preference learning. *arXiv preprint arXiv:1112.5745*.

Kingma, D. P., and Welling, M. 2013. Auto-encoding variational bayes. *arXiv preprint arXiv:1312.6114*.

Kingma, D. P.; Mohamed, S.; Rezende, D. J.; and Welling, M. 2014. Semi-supervised learning with deep generative models. In *Advances in neural information processing systems*, 3581–3589.

Larsen, A. B. L.; Snderby, S. K.; Larochelle, H.; and Winther, O. 2015. Autoencoding beyond pixels using a learned similarity metric.

Mirza, M., and Osindero, S. 2014. Conditional generative adversarial nets.

Pan, S. J., and Yang, Q. 2009. A survey on transfer learning. *IEEE Transactions on knowledge and data engineering* 22(10):1345–1359.

Settles, B. 2009. Active learning literature survey. Technical report, University of Wisconsin-Madison Department of Computer Sciences.

Springenberg, J. T. 2015. Unsupervised and semi-supervised learning with categorical generative adversarial networks. *arXiv preprint arXiv:1511.06390*.

Sun, C.; Shrivastava, A.; Singh, S.; and Gupta, A. 2017. Revisiting unreasonable effectiveness of data in deep learning era. In *Proceedings of the IEEE international conference on computer vision*, 843–852.

Tanner, M. A., and Wong, W. H. 1987. The calculation of posterior distributions by data augmentation. *Journal of the American statistical Association* 82(398):528–540.

Zhu, J.-J., and Bento, J. 2017. Generative adversarial active learning. *ArXiv* abs/1702.07956.