Assessing Uncertainty in Neural Network Models for Predicting Gene Mutation Status in Brain Tumor Patients

Dingkun Guo
Instructor: Xun Huan

INTRODUCTION

Background

- Deep learning has been widely used for building data-driven models in medical diagnosis
- Most models only report single-value predictions but cannot provide prediction uncertainty resulting from noisy and limited training data

Objective

- To develop computational capability for quantifying uncertainty in neural network (NN) models in a systematic manner
- To determine most sensitive factors; to decide whether a model is trained with adequate data

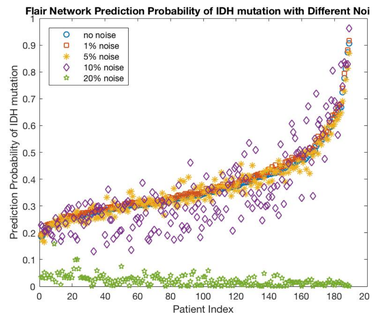
Model

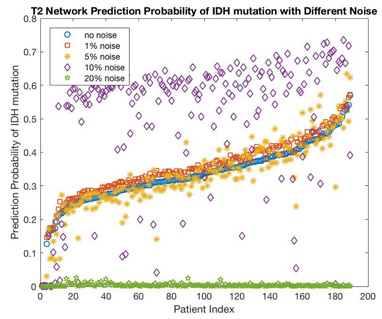
- A residual convolutional NN model developed to predict isocitrate dehydrogenase (IDH) mutation status in gliomas from preoperative brain magnetic resonance imaging (MRI)
- 44,898 NN model weights trained using only 496 data points: uncertainty quantification is crucial

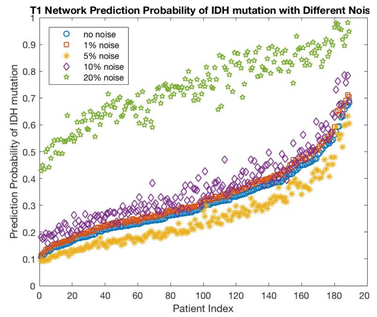
METHODS

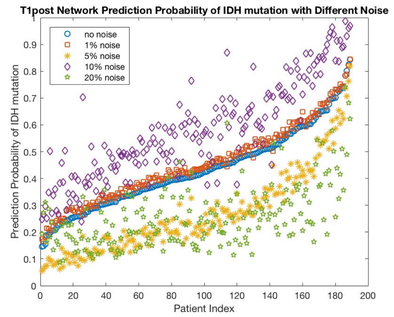
- Use the model to make predictions for 63 patients from The Cancer Genome Atlas (TCGA) database
- Analyze the sensitivity of model predictions with respect to the trained model weights
- Use a Monte Carlo sampling approach, where random noise (1%, 5%, 10%, 20%) is added to the trained NN model weights

RESULTS









- A 5% perturbation to the weights can alter the prediction probability of IDH mutation up to 10%
- FLAIR and T2 Networks failed when 20% random noise is added to model weights
- FLAIR Network is the least sensitive when noise is small (1% and 5%)
- T1 Network is less sensitive to relatively large noise

Root Mean Square Error After Adding Random Noise

	FLAIR	T2	T1	T1 Post
1%	**0.0103**	0.0218	0.0219	0.0245
5%	**0.0254**	0.0438	0.0604	0.1685
10%	0.0799	0.2437	**0.0641**	0.1670
20%	0.3755	0.3417	0.4309	**0.2109**

CONCLUSION

Predictions from neural network models studied here can be quite sensitive to noise in model weights, which are affected by the quality of training data. Uncertainty qualification in these models is thus important for decision making for patient treatments.

WHAT'S NEXT

- Analyze the four networks as a combined model
- Incorporate other variables such as age in analysis
- Compare with other competing models
- Conduct formal global sensitivity analysis where uncertainty contributions can be identified
- Compute the actual uncertainty on NN weights from original model training procedure
- Develop Bayesian inference methods for NN models to assess uncertainty from noisy and limited data

REFERENCE

- Chang *et al.* (2018) Residual Convolutional Neural Network for the Determination of IDH Status in Low- and High- Grade Gliomas from MR Imaging, Clin Cancer Res, 24(5).
- Pedano *et al.* (2016) Radiology Data from The Cancer Genome Atlas Low Grade Glioma [TCGA-LGG] collection. The Cancer Imaging Archive.

ACKNOWLEDGMENT

Srikanth Kuthuru, Nicholas Wang, and Prof. Arvind Rao (University of Michigan Department of Computational Medicine & Bioinformatics, Department of Radiation Oncology)