



**Midterm Report** (Undergraduate Creative Independent Study in Electrical & Electronic Engineering)

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**Classification of the Undergraduate Creative Independent Study**

- H/W Implementation ☐
- S/W Implementation ☒
- Theory and Survey ☐

# Fmri noise reduction via deep learning trained by synthetic data

## Current Progress

The definition of MRI is ‘magnetic resonance image’ It is a non-invasive way and non-radioactive way to obtain images of the objects with magnetic dipole moments. There are three magnetic fields produced by an MRI machine. First, the main field  $B_0$  is a static field in the direction of  $z$ . (If a human lie down on the machine,  $z$  can be a human head direction) This field polarizes the magnetic moment vectors. Since atoms with the odd number of protons have magnetic dipole moment, hydrogen is the dominant atom affecting MRI images. Also, this field creates the nuclear spins where the frequency is proportional to a magnetic field. (called Larmor frequency). This is shown on Fig. 1,2.

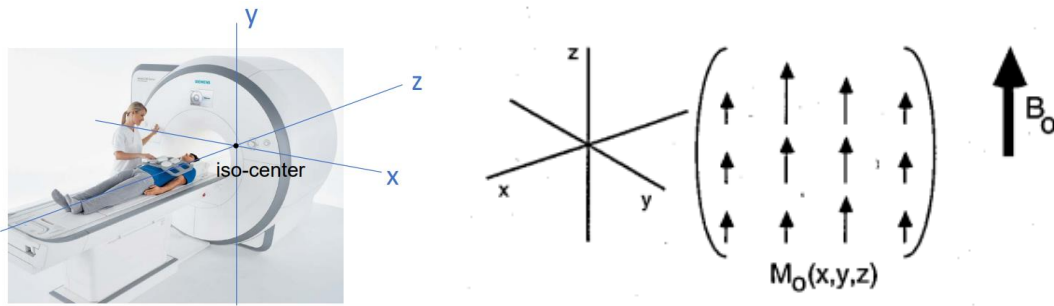


Fig. 1.(left) The coordinates of x-y-z, Fig .2. (Right) The  $B_0$  magnetic field

Second magnetic field is  $B_1$  or radiofrequency field (Fig. 3.). This magnetic field is tuned to Larmor frequency circulating on the x-y plane. The result of this field is traversing the magnetic dipole to x-y plane. This is called excitation. Last magnetic field a linear gradient field  $G$ . This field is applied linearly proportional to x-y coordinates heading to z-direction. The equation is  $G_x X$  or  $G_y Y$ .  $G_x$  and  $G_y$  are constants and  $X$  and  $Y$  are coordinates. (Fig. 4.) Since these two directions are toward z-direction, they also added to Larmor frequency with  $B_0$ . From these three magnetic fields can make the k-space of the MRI images. (or Fourier space) Considering only  $G_x$ , the example of received signal can be presented as Fig. 5, where  $m(x, y)$  is magnetic dipole, and  $w_0$  is Larmor frequency of  $B_0$ . By inverse Fourier transforming this equation we can figure out the intensity of  $m(x, y)$  on the excited field. Strictly speaking, we are going to compare the relaxation time (the time to relax toward z-direction from traversed direction) of  $m(x, y)$ .

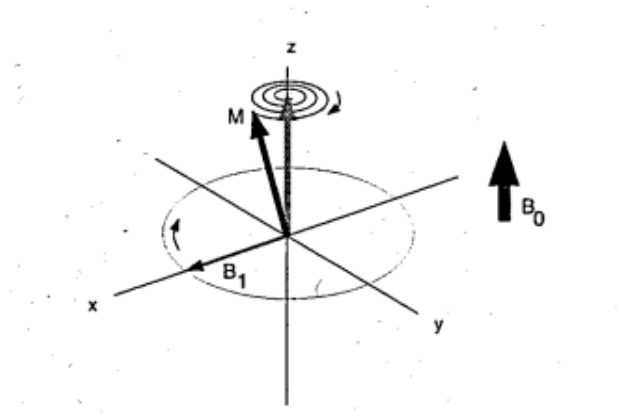


Fig. 3. The B1 magnetic field evoking the excitation to M.

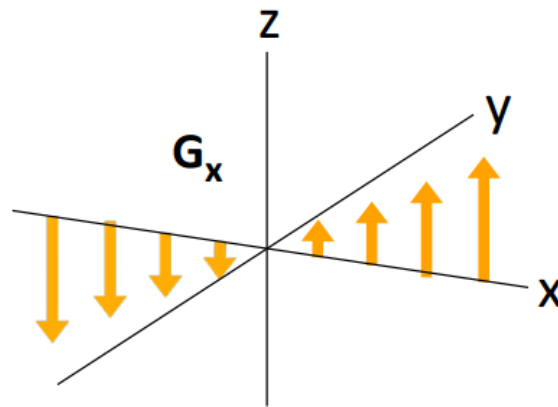


Fig. 4. The linear gradient field example ( $G_x$ )

$$s_r(t) = \int_x \int_y m(x, y) e^{-i\omega_0 t} e^{-iyG_x t} dx dy$$

Fig. 5. The received signal representation from MRI.

Fmri means functional MRI. This is a 4D data that consists of 3-dimensional image with time sequence. This is focused on the activities of a static object often used to check brain function. In my experiment, I used the brain data with two stimuluses during taking images of MRI. Also, I assumed that there would be some spots showing blood-oxygen-level-dependent (BOLD) signal corresponding to the stimuluses. The Bold signal is normally characterized by canonical hemodynamic function which can be referred as a

gamma distribution. The example of a real BOLD signal is below Fig.6. This will be additionally explained later.

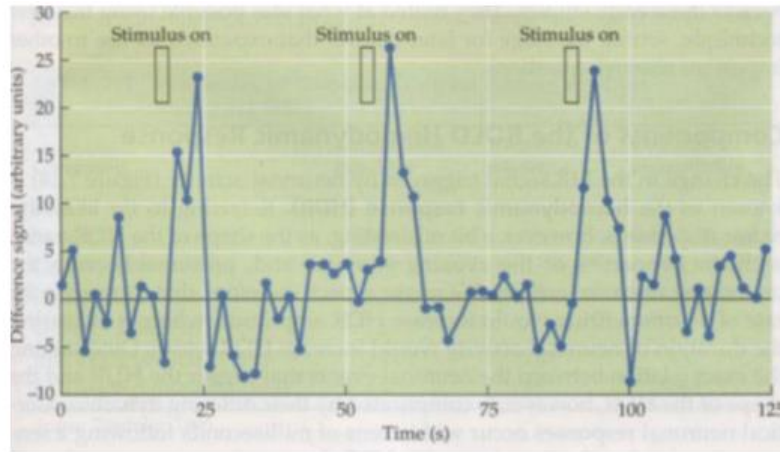


Fig. 6. The BOLD signals example.( data from Blamire et al., 1992.)

Remember that fmri is a time sequence of 3D MRI images, it consists of 4 dimensions. Therefore fmri needs to be taken 3D images repetitively. This leads to the number of insufficient voxels in limited TR (repetition time) and causes low resolution. Fig. 7. is a sample of fmri image. and Fig .8. a sample of fmri in time sequence. There are previous researches to solve this problem[8] such as a motion-related noise reduction, data-driven methods(PCA, ICA) and external recording methods. PCA means principal component analysis and ICA means independent component analysis. Both are famous methods for statistical analysis. In my experiment, a motion-related noise reduction is performed on the pre-processing stage and external recording methods will be excluded since it needs extra cost for recordings. Data-driven methods are comparison group to my experiment. (This comparison group results will be included in the final report) Instead of using PCA, ICA method, I implemented to denoise fmri temporal sequence data with supervised deep learning in this paper. One more point is that I used the synthetic training data because there is no label (not noisy, clean data) for fmri data.

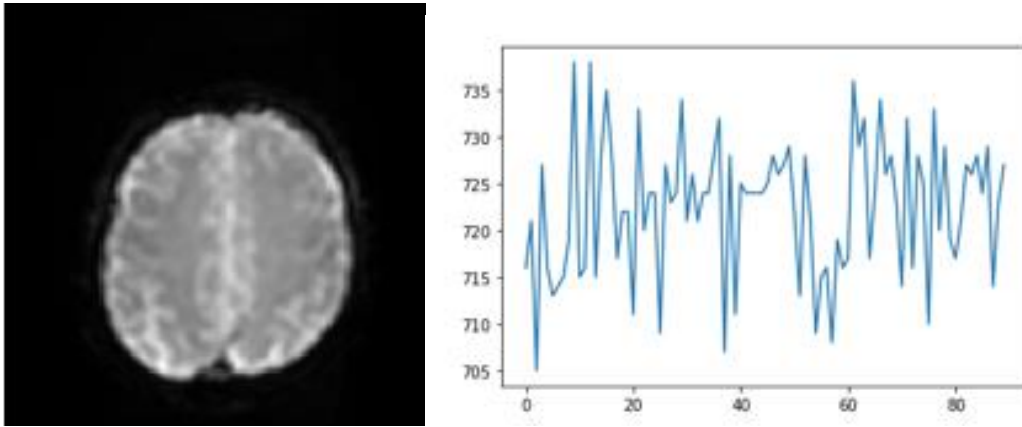


Fig. 7.(Left). Low resolution of a fmri image, Fig. 8.(Right). The time sequence of fmri data of one voxel.

First, before we dive into training the deep learning model, I preprocessed the fmri images with SPM. SPM is a Matlab program that is dominantly used for preprocessing MRI data. I implemented just two preprocessing steps to avoid the result of denoising caused by SPM preprocessing such as segmentation, smoothing. First one is realignment of the functional images. Remind that fmri is functional mri which is a time sequence of 3D mri. The objects could move during taking the MRI images temporally. This step is to warp each image sequences to same places. Second preprocessing step is slice-timing correction. Consider a human head is taking a MRI images. One 3D MRI image isn't made simultaneously. It is made from the bottom slice of head to top slice of head. Therefore, there are time differences between each slice. Slice-timing correction is correcting the MRI images as if it is acquired simultaneously. The reason why I preprocessed these two steps is that these two steps are motion-related noise. Motion-related denoising step needs to be preprocessed regardless of subsequent data-driven denoising.

Second, I made synthetic label data and synthetic training data for training supervised deep learning model. Label data means the clean, not noisy data. The training data means noisy data. (Let  $s(t)$  be the label data, then training data is  $s(t)+n(t)$ .  $n(t)$  is noise.) It would be better to use real world data to train the model, but unfortunately there are no label data for fmri image due to limited time of 1TR data acquisition. The BOLD signal can be modeled with a Gamma distribution as a basis function. This is called canonical hemodynamic response function, HRF. The gamma distribution is shown on Fig. 9 and defined HRF in experiment is shown on Fig. 10. Actually, it can be defined various ways, but I choose the popular one.

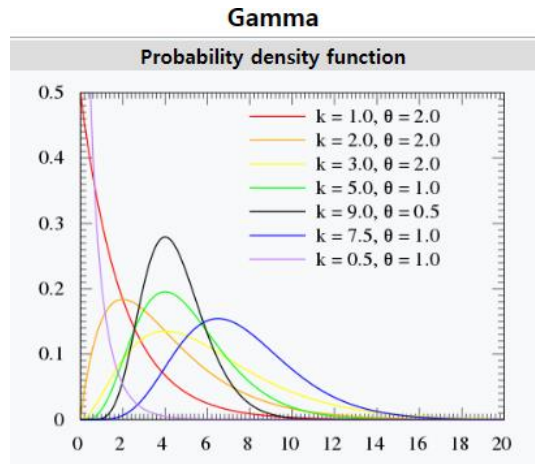


Fig. 9 . Gamma distribution

$$f(x; \alpha, \beta) = \frac{x^{\alpha-1} e^{-\beta x} \beta^{\alpha}}{\Gamma(\alpha)} \quad \text{for } x > 0 \quad \alpha, \beta > 0,$$

Fig. 10. The equation of probability density function of Gamma distribution

```
def hrf(t):
    # Gamma pdf for the peak
    peak_values = gamma.pdf(t, 6)
    # Gamma pdf for the undershoot
    undershoot_values = gamma.pdf(t, 12)
    # Combine them
    values = peak_values - 0.35 * undershoot_values
    # Scale max to random value between 0.01 and 0.1
    random_value = np.random.uniform(0.2, 0.6)
    return values / np.max(values) * random_value
```

Fig. 11. The hemodynamic response function defined in the experiment.

Also, the stimulus to object can be modeled with block functions which start with onsets and have duration of stimulus. (Onset means the start time of a stimulus) The defined HRF and the block functions is on Fig. 12. Synthetic label data are the result of convolution between HRF and the block functions. These are shown on Fig. 13. The training data are made by adding Gaussian noise, respiratory noise and heartbeat noise to label data. This is shown on Figure 14. To avoid overfitting, the two onset times of training data are randomly chosen, where test data have constant onsets. The time stamps of synthetic label and synthetic training data are equally distributed as test data.

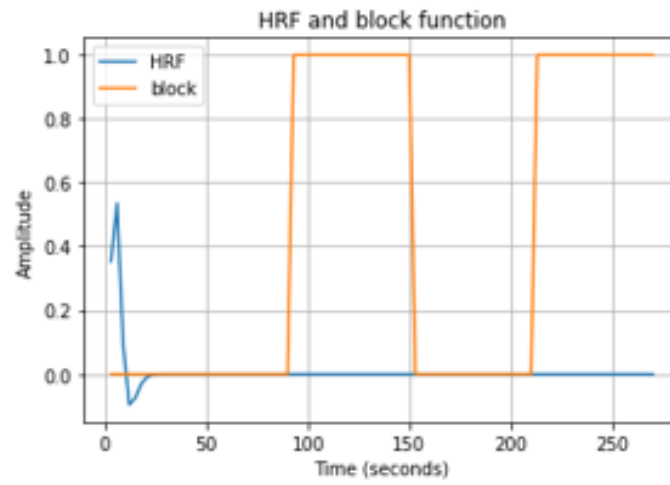


Fig. 12. The defined HRF and block functions.

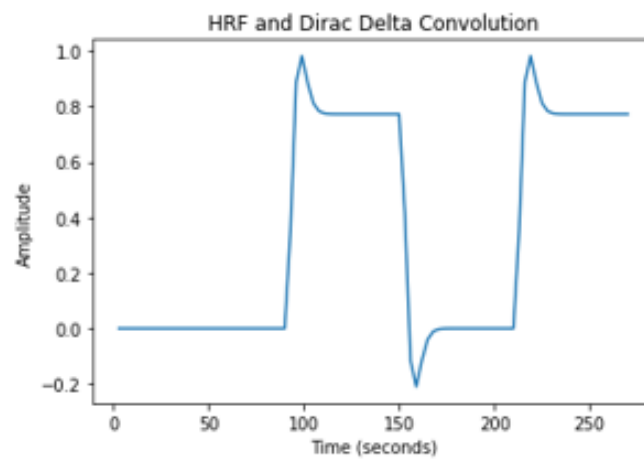


Fig. 13. The label data convolutionized with HRF and block functions.

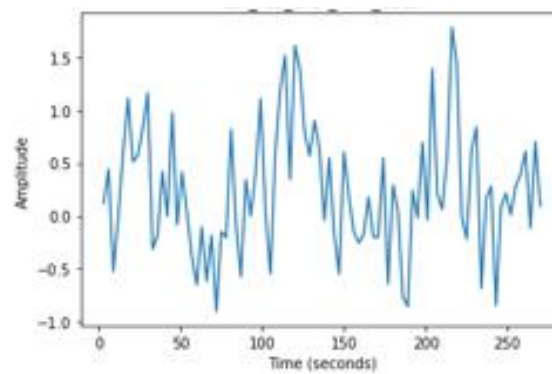


Fig. 14. The training data which is defined by adding noise to the label data.

After that, I normalized all the data including test and training data. Also, I tried to match the histogram of normalized synthetic training data with the histogram of normalized test data. This is because the histogram distribution of normalized data are mainly composed of noise. If the histogram of those training and test data are different, the noisy distribution of both training and test data could be identified different. As a result, the final result would be unreliable considering that the deep learning is the sequence of multiplying the matrixes and we cannot expect the correct denoised results. These histograms are shown on Fig. 15 and Fig. 16.

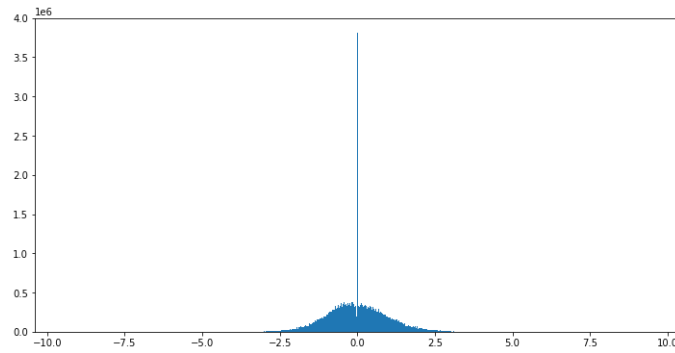


Fig. 15. The histogram of test data. (real data)

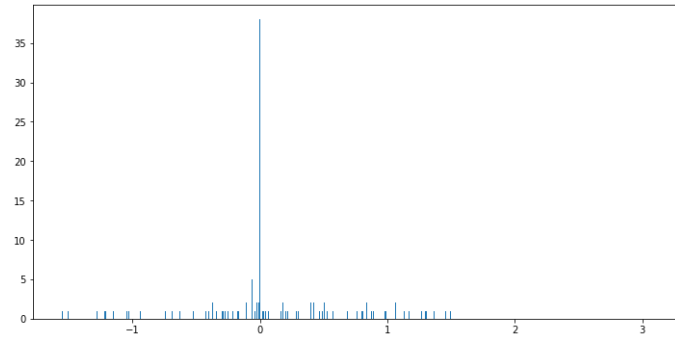


Fig. 16. The histogram of training data. (synthetic data)

Thirdly, I chose the U-net[6] for a deep learning model. U-net is an U shaped model which has several advantages. U-net is a fully convolutional network which means it is not dependent on the size of images. (In my case, it is not dependent on the number of time sequence.) Since medical image could have lots of different size or different time stamps this advantage is adequate for medical data. Another pro of fully convolutional network is spatial invariance. Spatial invariance, which is time invariant in my case, means that the object can be detected spatial invariantly. This can be adopted to my case to find out the HRF independent to its temporal position. U-net consists of four down-samplings and four up-sampling with



two 3X3 convolutional filters before each sampling. (Because my data is temporal, I changed all the 3X3 filters to 1X3 filters.) This leads to 20 receptive fields at the last down-sampling. U-net have skip connections by concatenating previous size which is advantageous for preventing gradient vanishing. The U-net is described on Fig. 17 including how it is skip connected.

In fact, U-net could not be the best choice of deep learning model. However, we will focus on if the synthetic data work for training. I would try other models to train on subsequent experiments.

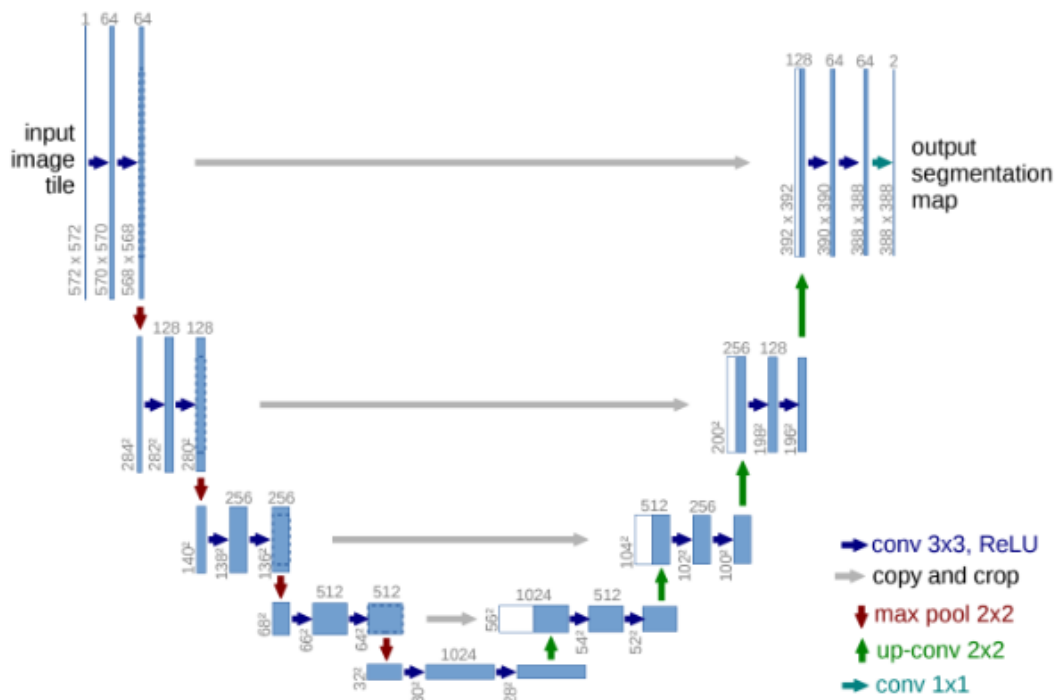


Fig 17. The description of U-net.[6]

Finally, it is time to train the model and show the result. The test data onset time are [90, 210] and their duration are [60, 60] seconds. I followed the number of onsets and duration time. But I choose the onset time randomly as I said above. The learning rate is  $1e-7$ , optimizer is Adam. Epoch is 20, where one epoch has 8000 synthetic training data. Loss function is MSE. After training, I firstly tested the model with synthetic test data which are unseen during training. Figure 18, 19, 20 are samples of the results tested data and labels.

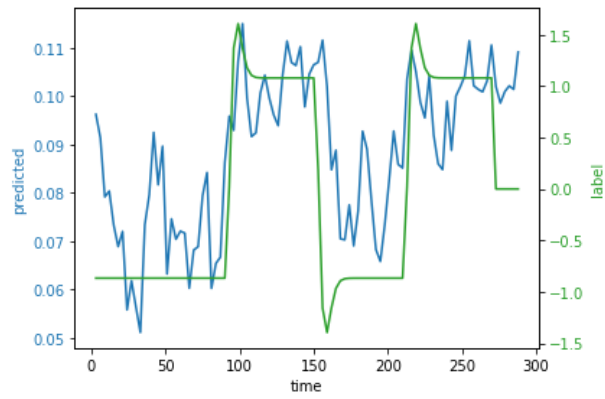


Fig 18. The first example of testing data(Blue) and the label(Green)

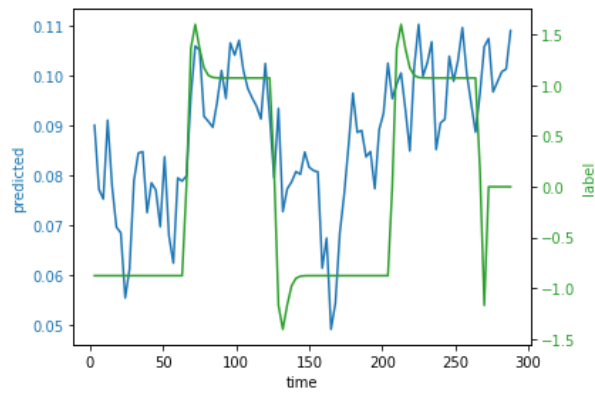


Fig 19. The second example of testing data(Blue) and the label(Green)

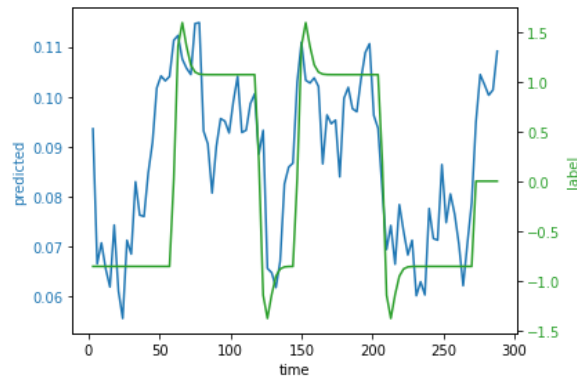


Fig 18. The third example of testing data(Blue) and the label(Green)

We can see the trained model looks pretty work well on synthetic test data. Next, I tested on the real data. Fig. 19. is the raw data which is not trained on deep learning model and Fig 20. is the test data after passing through the model. The red dots are the hrf spots based on the generalized linear model (GLM), which is often used to evaluate the BOLD signal in fmri. We can see the relevant differences of red spots

on the second and the last pictures.

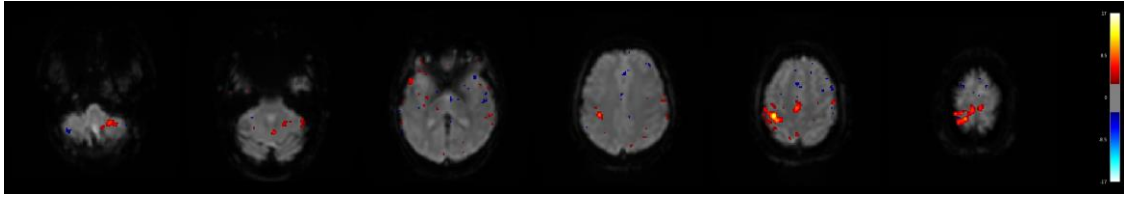


Fig. 19. The raw data and the HRF signal (red dots) found by GLM

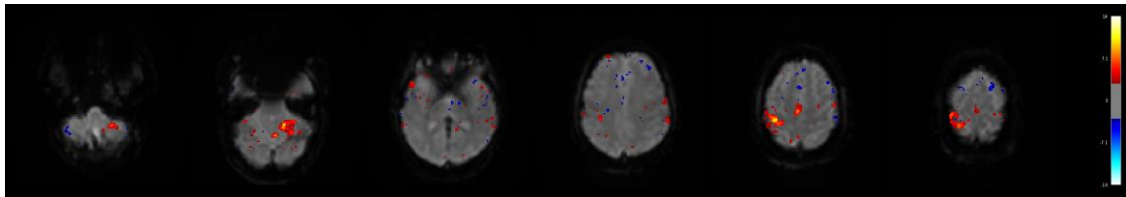


Fig. 20. The tested data and the HRF signal (red dots) found by GLM

Therefore, I brought the comparison of original spots data and changed spots on Fig. 21 to Fig 24. Fig. 21 and Fig.22 are original data that are not passed on the model and Fig. 23, Fig. 24 are changed spots due to the model. Remember that both of them are temporal data. We can check out that the model figured out the bold signal from strongly noised data.

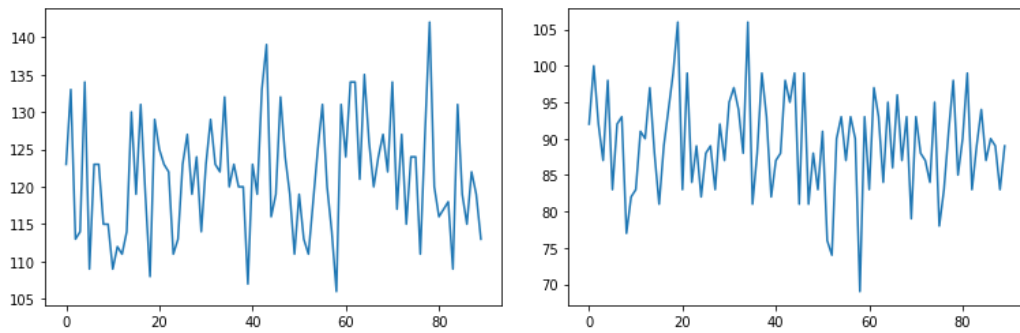


Fig. 21(Left), Fig. 22(Right). The original spots data before tested on the model

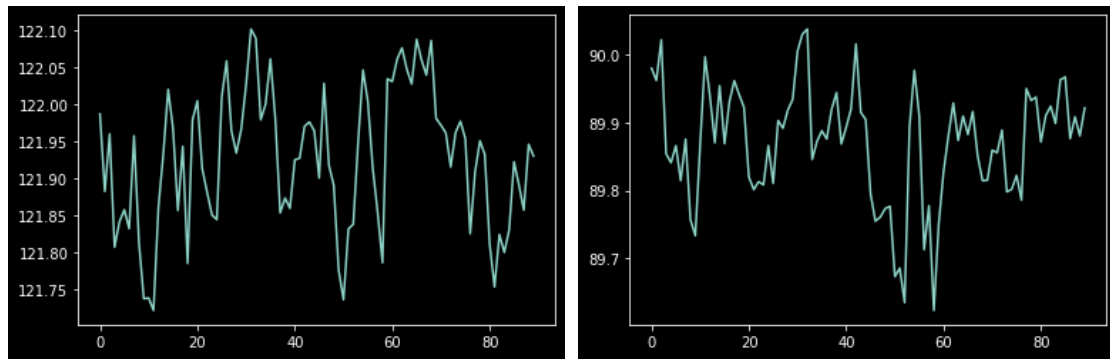


Fig. 23(Left), Fig. 24(Right). The tested spots data after the model

In conclusion, we found out that we are possible to make the meaningful denoising temporal fmri data. However, one major problem is that ‘Is the result data trustable for clinical purpose?’ Let’s go back to the red spots of Fig. 20. second pictures. There are new red spots which is not supposed to appear original data. One hypothesis is that it is less likely to have lots of new red spots on certain space by accident. Therefore, the new red spot is quite reliable. And the next problem is that what if the model ruins the original data? This problem can be dealt with two ways. First one is just using original data as background and use GLM score as red spots. Second one is scale down the normalized data. The test data will be denormalized by the mean and variance, where the mean values have an mainly effect on the intensity of data. To make the model less likely to ruin the original data, we can scale down the normalized data to lei ss ruin the mean.

In addition to try the things above, there are several other things I could do. I should try other synthetic hrf, other models of deep learning, and matching the histogram more precisely. Or I could try to apply domain adaptation research to improve my result. Domain adaptation is the case that the trained domain and test domain are different. In my case, the synthetic data are from source domain, and the real data are from target domain. For example, there was an attempt of segmentation on the real world by training data of computer graphics. This is shown on Fig. 25. Since this is similar to my experiment, I could find another room for development.

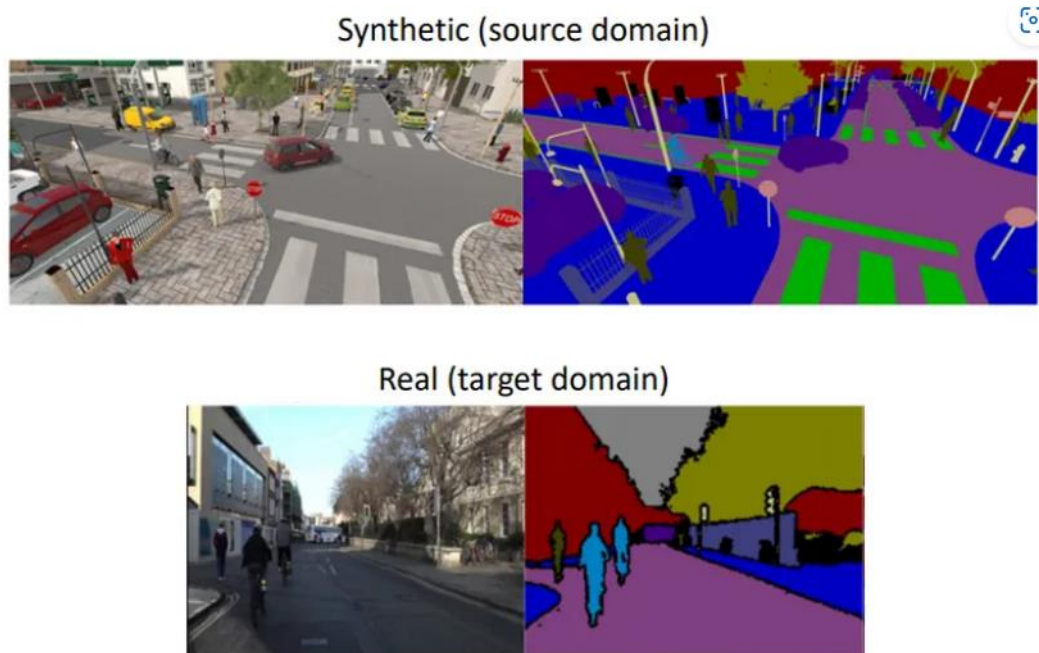


Fig. 25. Image segmentation via training synthetic computer graphics. (ECCV 2020 Domain Adaptation for visual application tutorial part 1, 9 page) [5].

## Schedules

The first week after submitting the midterm reports, I will try other synthetic hrf. function and different noise. Because there are more characterized BOLD signals such as glover and I need to match the histogram more precisely. And also I will try to scale down the synthetic and test data to less likely to ruin the mean of original data.

From second week to fourth week, I will research the possibility to apply domain adaptation (DA) method to my experiment. I only have labeled synthetic data which can be identified as a source domain and unlabeled real word data which can be identified as a target domain. For example, transductive domain adaptation is a method to take a domain shift from labeled source domain to target domain. This could be proper approach to my research.

From fifth week to sixth week, I am going to try other deep learning models that would be better than U-net. U-net may not be the best model for denoising.

From seventh to last week, I discuss about how I could improve reliability of my model. After that I have to write down the final report.

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