

A Novel Information Theoretic and Bayesian Approach for fMRI data Analysis

Chandan Reddy^{*a}, Alejandro Terrazas^{b,c}

^aDepartment of Computer Science and Engineering, ^bDepartment of Telecommunications, Michigan State University, ^cVRSciences, East Lansing, MI.

ABSTRACT

Functional Magnetic Resonance Imaging (fMRI) is a powerful technique for studying the working of the human brain. The overall goal of the project is to develop a novel method for the analysis of fMRI data in order to discover the activation of a network of regions involving most likely the hippocampus, parietal cortex and cerebellum as a person is navigating in a virtual environment. Spatially sensitive voxels are extracted by selecting voxels that have high mutual information. Each of these extracted voxels is then used to create a response curve for the stimulus of interest, in this case spatial location. Following the voxel extraction stage, the set of extracted voxel time series would be treated as a population and used to predict the location of the subject at any randomly selected time in the experiment. The population of voxels essentially “votes” with their current activity. The approach used for prediction is the Bayesian reconstruction method. The ability to predict the location of a subject in the virtual environment based on brain signals will be useful in developing a physiological understanding of spatial cognition in virtual environments.

Keywords: Monte Carlo simulation, Place cells, fMRI, Mutual Information, Bayesian Reconstruction, voxels, time series.

1. INTRODUCTION

Functional Magnetic Resonance imaging (fMRI) is a powerful tool for investigating the brain activity. fMRI is a non-invasive imaging modality with good temporal and spatial resolution. It reflects the brain tissue haemodynamics that are spatially related to the metabolic demands of the brain tissue caused by neuronal activity. Therefore, indirectly, fMRI can capture brain neuronal dynamics at different sites while being activated by sensory input, motor performance or cognitive activity. In our paper, we discuss how the voxels in an fMRI scan that are responsible for spatial position are identified and analyzed. After finding them, we also discuss whether these voxels can be used to find out the position of a person when had such intensity values.

In this paper, we develop a novel information theoretic approach for analyzing the fMRI data. Mutual information is shown to be a better approach because it solves problems even if the waveforms are nonlinear and stochastic. Complex relationships between the voxel time response and the physical positional waveform are easily identified using mutual information maps. Assuming that the physical variables like the location of the body in space are coded as activity level in the population of neurons, we try to discover those groups that have high coincidence with the positional variable. Once we find all the neurons that are responsible for the position, we can use that information to reconstruct the position based on the neuronal activity of that group of voxels. The approach we followed for reconstruction is Bayesian reconstruction which is the most optimal one and it works well in a probabilistic framework.

Section 2 of this paper describes the relevant work done in the past in the field of fMRI analysis. The way in which we acquired the data and registered the images is explained in section 3. Next section clearly

* reddycha@msu.edu; Phone: 1 517 353 5964; Fax: 1 517 355 1292; <http://www.msu.edu/~reddycha>; Media Interface and Network Design Lab, 251 Communication Arts Building, Michigan State University, East Lansing MI 48823

illustrates our methods and simulations of the fMRI data we captured. Section 5 shows some of our results. The last section concludes our approaches and findings giving some ideas to future research in this area.

2. RELEVANT BACKGROUND

There had been tremendous advancement in the area of fMRI acquisition techniques but unfortunately the analysis of these data has been inadequate for many problems. A very simple and naïve approach used was direct subtraction^[7] which calculates the difference between two mean intensities of each voxel where one mean value is the average value of the temporal responses acquired during the task and others are the average of all the temporal responses of other voxels during the non-task control period. This works based on the underlying assumption that the temporal measurements of a given voxel can be partitioned into two data groups. The correlation coefficient^[8, 16] has also been used for fMRI analysis in the case where one make an *a priori* assumption about a reference waveform with which the measurement waveform is cross correlated and normalized. However, the choice of reference waveform is vital and with so many unknown parameters in measuring brain activation, it is difficult to pin point which reference waveform will bring the optimum solution. General Linear Model (GLM) was developed for this type of analysis^[14] and also depends on assumptions about the response waveforms. Tsai *et al.*^[2] has applied mutual information to fMRI analysis and compared the results with other previous analysis methods. This work differs from Tsai *et al.* in its use of continuous variables.

Estimating the physical variables based on the neuronal activity is termed *reconstruction* or *decoding*. This part of the work is based on the method developed for the analysis of populations of simultaneously recording neurons in the hippocampus of the rats. These neurons, called place cells, fire in restricted areas of space as the rat moves around an environment. Modeling the place cells can be done using Template Matching Method^[17] which yields a scalar distribution function at any given time. Until recently, the most popular method for reconstruction was the population vector method developed by Georgopolous^[9]. This method overcomes the drawback of the template matching method in that it yields a single vector which specifies a single point in the space where the reconstruction is to be applied. However, this approach will be more suitable for the estimation of the directional vectors (vectors representing the direction) than that of the positional vectors (vectors representing the position) because scaling a directional vector will yield the same direction where as scaling a positional vector will yield a different position. We apply Bayesian Reconstruction method^[5] that uses a probabilistic framework to overcome many drawback of the previous methods.

3. EXPERIMENTAL SETUP

3.1. Data Acquisition

Existing data was collected at the NIH using 1.5 Tesla GE Signa Magnet and a spiral fMRI pulse sequence. Full brain scans were acquired at the rate of 2 seconds each. Each full brain scan is represented in terms of 38 2-dimensional slices with each slice having 64 * 64 voxels (Fig 1). A total of 612 full brain volumes were acquired while the subject was engaged in a virtual reality spatial task written in Java 3D^[11].

Each subject was instructed to drive around the circular environment and to “discover” to correct goal locations through trial and error. Three goal locations were used. The goal locations were initially set to 20 degrees each. As the subject began to find the goal correctly, the area was systematically reduced in increments of one degree. Missing the goal, relaxed the requirement by one degree. The subject received instructions at the top of the screen indicating the next goal location to find and the results of the previous trajectory. The ratio of correct stops to incorrect stops was also indicated.

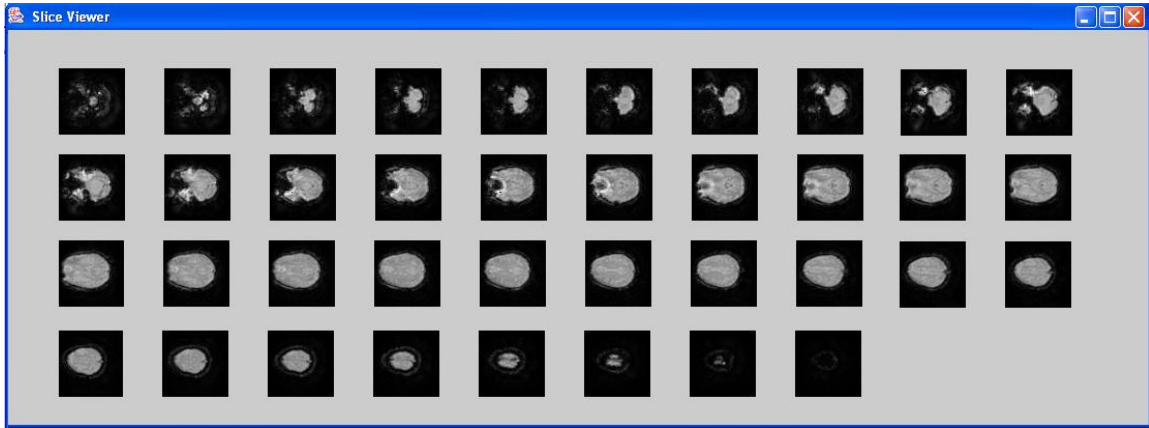


Fig 1. The 3D volumetric brain is represented as 38 slices of 2D images. Each Slice consists of 64 *64 voxels. This is the output of our Slice Viewer module.

3.2. Image Reconstruction and Registration

The data is reconstructed using multi-frequency deblurring technique. The technique corrects the spiral k-space trajectory for field inhomogeneities and susceptibility artifacts based on an acquired field map taken prior to scanning. After reconstruction, all images were registered to the initial time point using cubic spline registration method ^[12].

4. OUR METHODOLOGY

From the data we have acquired, it is possible to make a time series of activity for each voxel that is analyzed with respect to the physiological stimulus. We used a novel approach to the analysis of fMRI data and found the activation of a network of regions involving the hippocampus, parietal cortex and the cerebellum as the subject navigated in the virtual environment. The task related voxels are extracted by selecting voxels with high mutual information. Each of these extracted fMRI time series is then used to create a tuning curve (or response curve) for the stimulus of interest. In the case of spatial navigation, the tuning curve is computed for the location of the subject in space. The stimulus value of peak activity is termed the “preferred stimulus” of the voxel. The set of extracted voxel time series is treated as a population and used to predict the location of the subject at a random time in the experiment by essential “voting” with their current activity. The approach used for prediction is the Bayesian reconstruction method.

4.1. Mutual Information Map

The concept of mutual information ^[1] cannot be adequately described within the scope of this paper. However, we try to simplify the definition of our experiment. Mutual information is a measure of information that one random variable conveys about the other. It is represented in terms of bits of information. Using mutual information for analyzing the fMRI data is a kind of novel approach which promises to deliver better results ^[2] than other methods. In this technique, we calculate the mutual information between the temporal response of the voxel and behavioral response. This value is used to quantify the relationship between the two waveforms. Activation map is produced by computing a statistical test of the data. The mutual information between two random variables X and Y is given by

$$I(X;Y) = H(Y) - H(Y|X) = H(X) - H(X|Y)$$

Where H (Y) is the entropy which gives the randomness of Y and H (Y | X) gives the conditional randomness of Y given the randomness of X. In our case, X will be the time series of the neuron and the

variable Y represents the behavioral activity of the neuron. In order to calculate the mutual information between the two signals.

To calculate the entropy of the signal, we have the formula

$$H(Y) = -\sum_{y \in Y} P(y) \log(P(y))$$

$$H(Y | X) = -\sum_{x \in X} P(x) H(Y | X = x) = -\sum_{x \in X} P(x) \sum_{y \in Y} P(y | x) \log(P(y | x))$$

Since X is a discrete random variable in our case, the condition always reduces uncertainty to ($H(X | Y) \leq H(X)$), Y can convey at most $H(X)$ bits of information about X . Hence the value of the mutual information will be between 0 and $H(X)$. We can see from the above formula that we are not assuming anything about the nature of the waveforms. In other words, we don't have any *a priori* knowledge about the waveforms. The advantage of using the mutual information is that it does not assume anything about the nature of the relationships between the two waveforms. Also, Mutual Information will be helpful for analyzing the continuous variables like what we have.

4.2. Bayesian Reconstruction

The two variables we have here are the positional waveform and the intensity level of the voxel. Let x be the position of the subject at any given time. Correspondingly, let n represent the vector of intensity levels of all the voxels of interest. Now, given the n value at any point, we need to estimate the x value. The reconstruction is based on the formula for the conditional probability.

$$\mathbf{P}(x | n) \mathbf{P}(n) = \mathbf{P}(n | x) \mathbf{P}(x)$$

$P(x | n)$ is the probability of the subject to be at position x given the intensity values to be n .

$P(n | x)$ is the conditional probability that the intensity value is x given that the position of the subject is x

$P(x)$ is the probability of the subject to be at position x

$P(n)$ is the probability of the intensity values to be n

Using this method, the peak position or the most probable position is taken as the reconstructed position of the subject.

4.3. Simulation of the experiment

We simulated the fMRI data based on the experiment we have conducted. The experiment requires subject to navigate on a circular field within the virtual environment. The subject is required to stop in goals. The stop is used to dissociate periodicities in time from spatial location. Thus, the positional waveform is simulated to include random stops twice for every complete 360° . There are some 1000 voxels in the simulation. The voxels were modeled to have high mutual information with the positional waveform.(see figures 2 and 3).

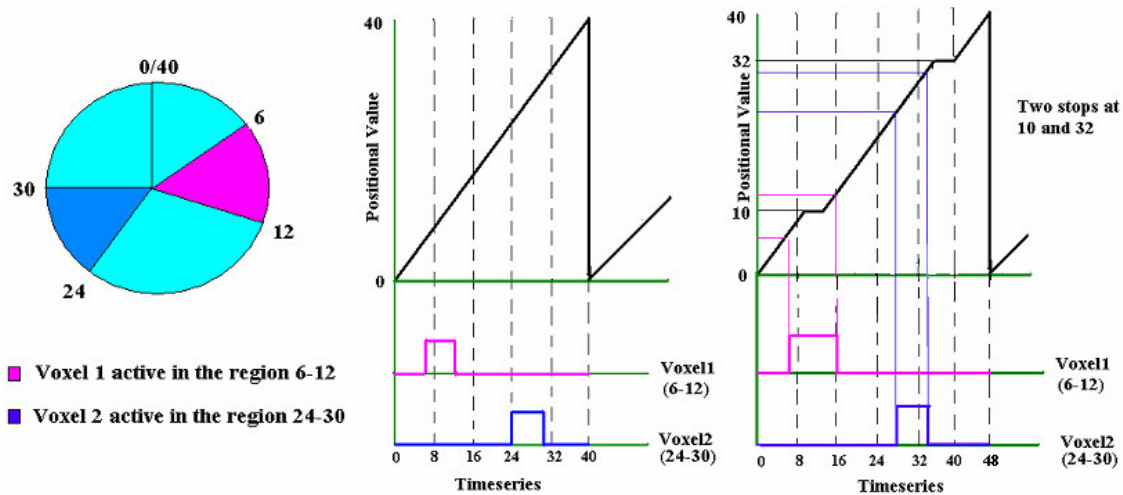


Fig 2. This figure explains the overall experiment and the simulation of the data. The human is asked to stop at two positions (at 10 and at 32). Two voxel time series are generated. One voxel is active in the region 6-12 and another at 24-30.

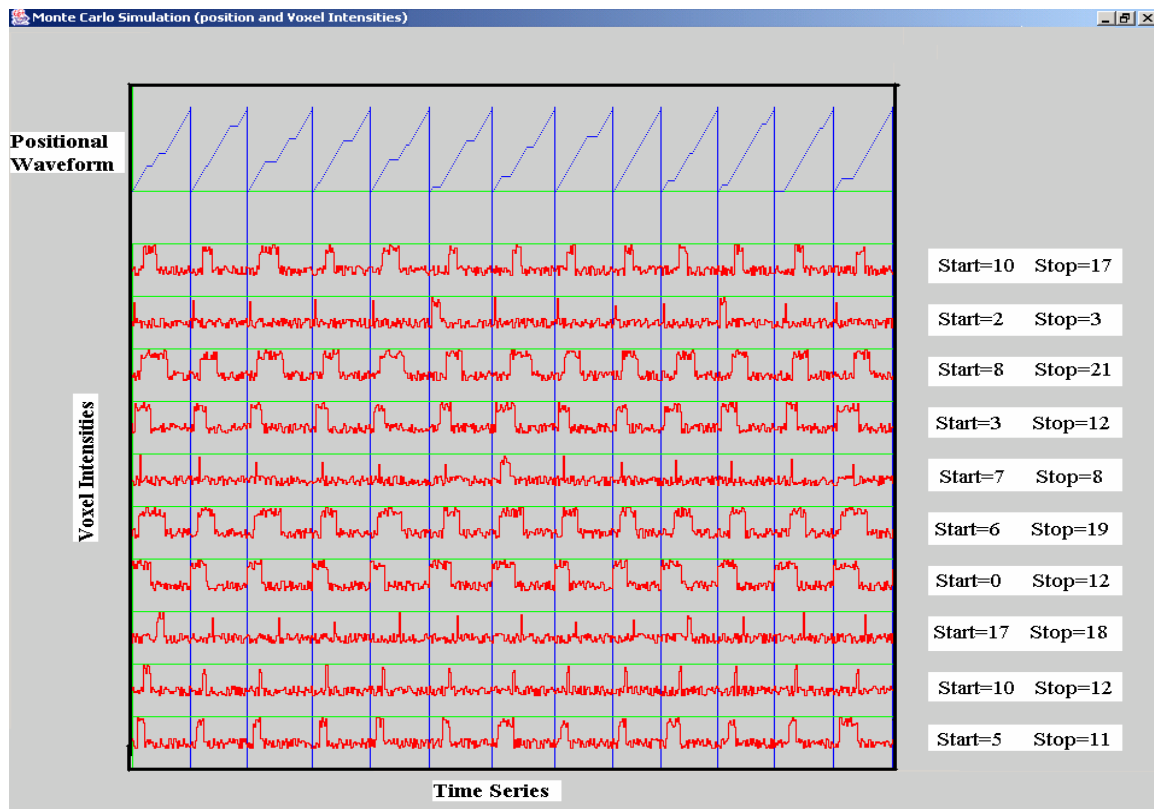


Fig 3. Simultaneous generation of position value and 10 voxel time series. The figure demonstrates how the fMRI data had been simulated based on the real data time series. The corresponding start and stop values for each values are given at the right. The top row represents the simulated movement of the subject through the virtual environment (in deg). Each row represents the activity of a simulated voxel that is active in a particular place (place voxel).

5. RESULTS

The two stage algorithm was confirmed with simulated data (figure 8). The effects of noise have been studied (figure 6). We were able to discover optimal required stop times for future experimental designs based on the results we have obtained (figure 7). Additionally, a distribution of mutual information responses was obtained using randomized real data. For this dataset, a 95% confidence interval was established at 3.1 bits (figure 5).

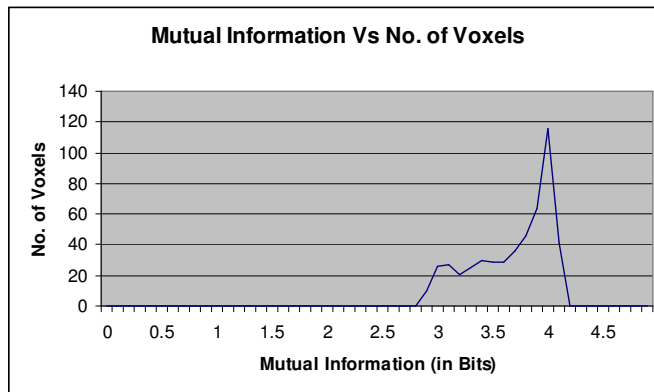


Fig 4. Effects of mutual information on simulated data. No. of voxels Vs Mutual Information.

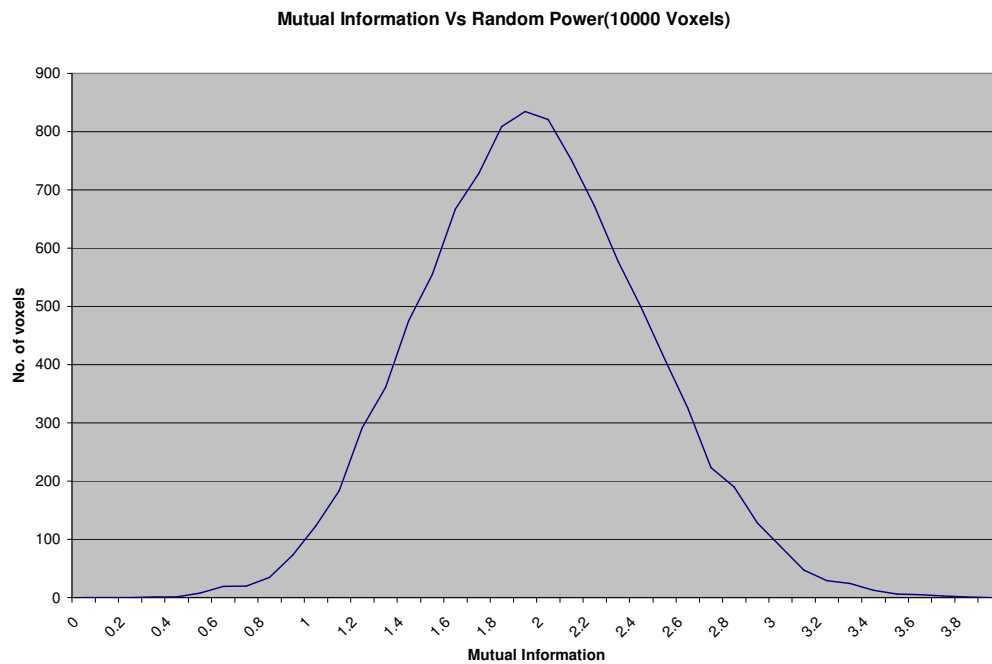


Fig 5. Study of mutual information between real voxel time series and positional waveform - power analysis by randomization of a single voxel series. The study with 10000 voxels. Taking a real data series and performing randomization and generating 10000 voxel series appears to be a Gaussian distribution with 95% confidence interval at 3.1 bits.

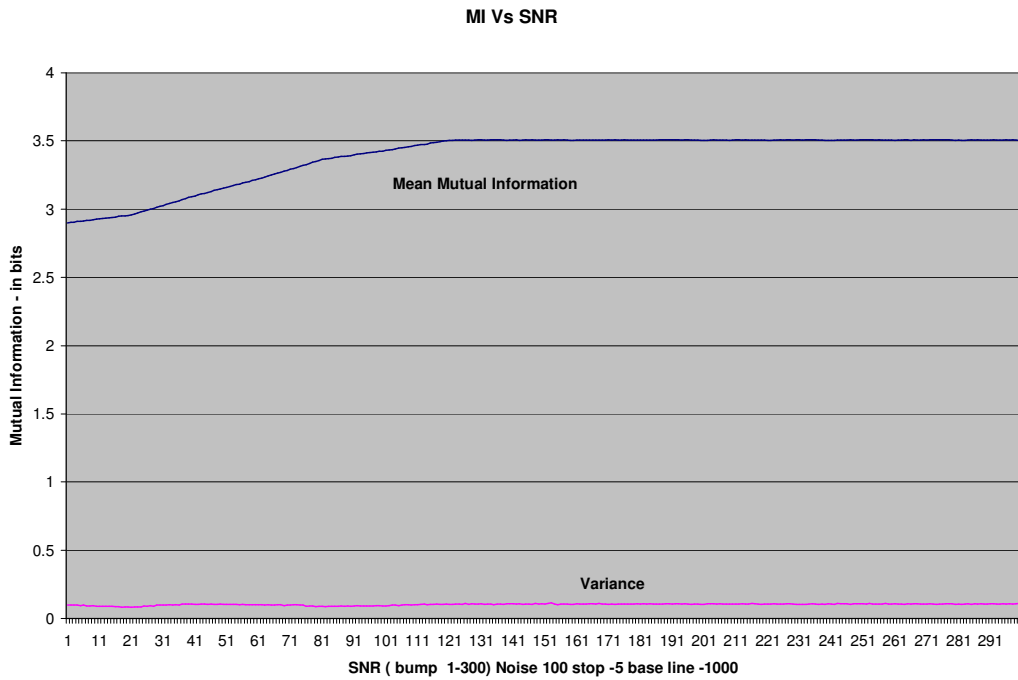


Fig 6. This figure explains the effects of mutual information with the changes in the signal to noise ratio of the time series. We can see the mutual information is not affected after the bump size reaches a particular level.

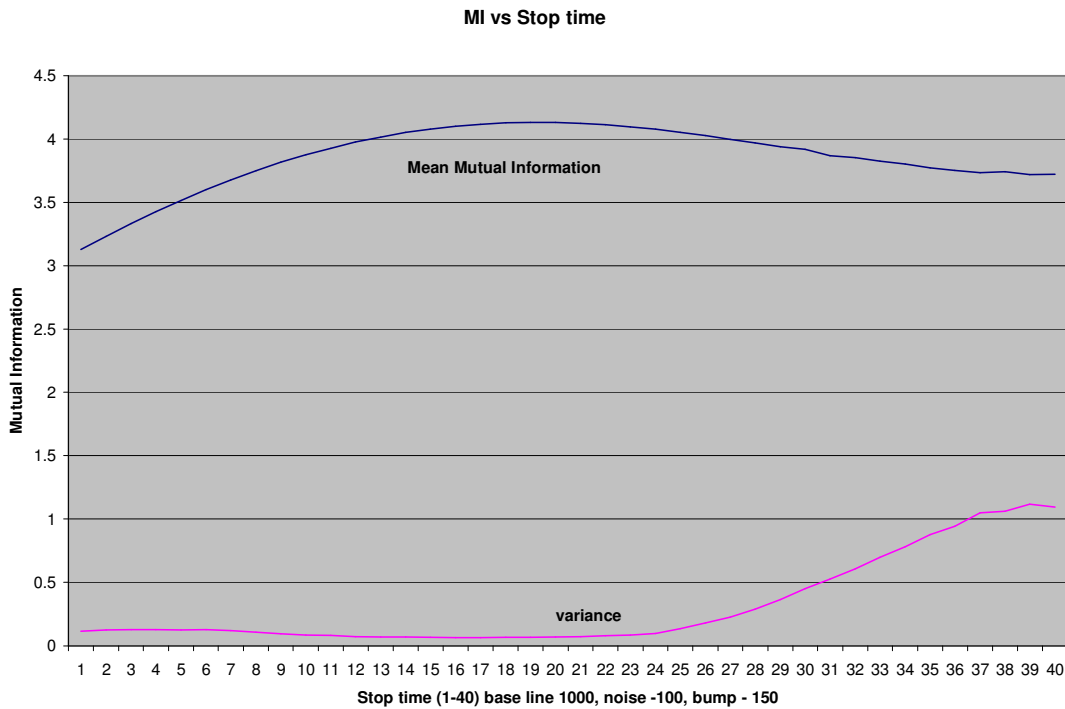


Fig 7. This figure explains the effects of stop on mutual information of the time series. We can observe from the graph that as the person stops for more time the mutual information with the positional values keeps increasing (provided other factors like base line, bump size and noise level remains the same). After a while there is a slow deterioration in the increase and it reduces gradually at the end. We can also observe that, at the end the confidence is very less because the variance is more.

**Predicted Vs Actual Position
(with no noise)**

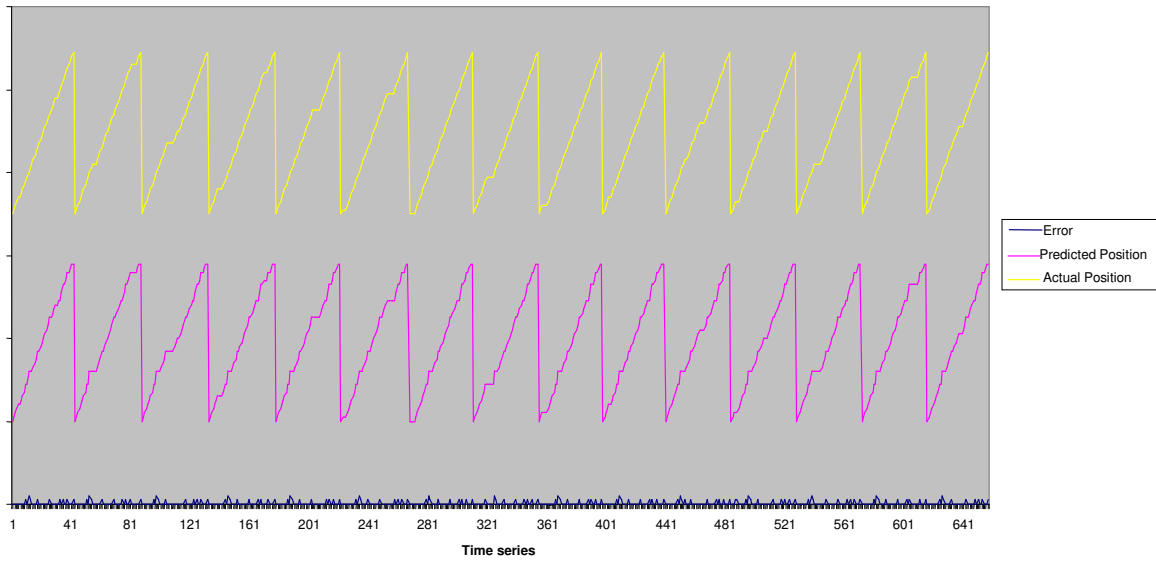


Fig 8.a.

**Predicted position Vs Actual Position
(with Noise=100)**

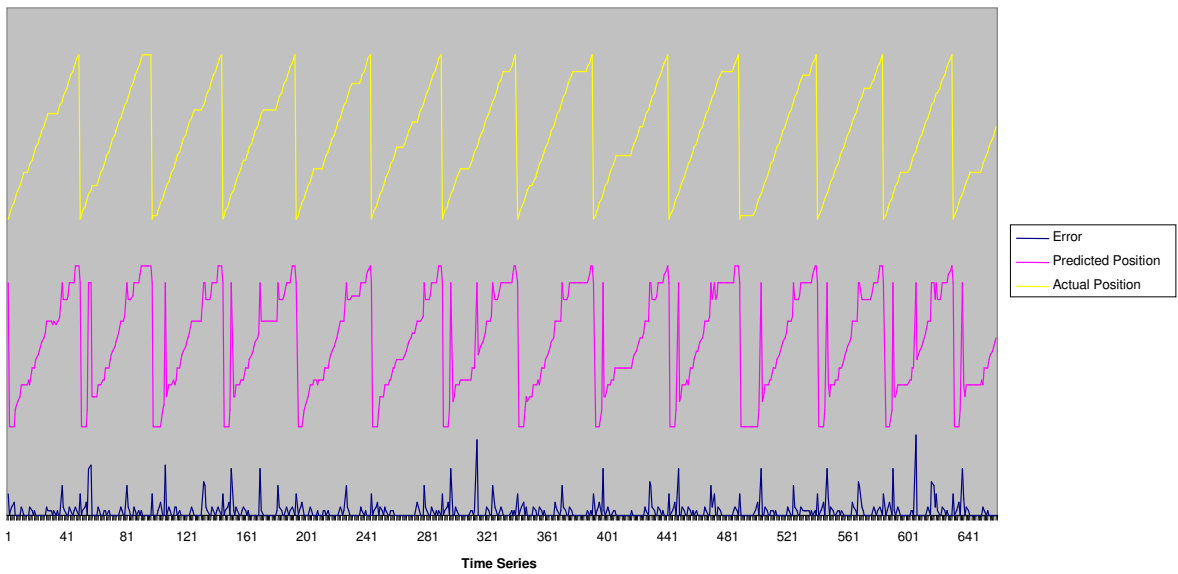


Fig 8.b.

Fig 8. Prediction of Position values based on generated voxel series (simulated data) (a) with no noise (b) with noise=100. The values at the bottom indicate the prediction error from the estimated value and the original value.

6. CONCLUSION

We were able to simulate the fMRI data and the corresponding positional values as a continuous variable. The results demonstrate the feasibility of using this novel information theoretic method for the prediction of behavior based on acquired fMRI data. Estimates of the statistical power of the mutual information were derived from a Monte Carlo simulation. Because of the noise inherent in fMRI data, a voxel must convey 3.1 bits of information to be considered statistically significant. Typical values for hippocampal pyramidal cells are typically in the range of 1.5 bits/spike. Efforts are underway to consider how smoothing and other preprocessing steps can reduce the threshold for fMRI voxel data. Mutual information offers many advantages over traditional fMRI analysis methods for voxel extraction. Once meaningful voxels are extracted then reconstruction is a viable method for prediction of the behavior based on the neural response. The ability to predict the location of a subject in the virtual environment based on brain signals will be useful in developing a physiological understanding of many applications involving navigation in virtual environments. Although developed for experiments involving spatial location, the technique can be used generally, for example, to predict eye movements.

7. REFERENCES

1. Thomas M. Cover and Joy A. Thomas, *elements of Information Theory*, John Wiley & Sons, 1991.
2. A. Tsai, J. Fisher, C. Wible, W. Wells, J. Kim, A. Willsky, "Analysis of Functional MRI Data Using Mutual Information", *Proceedings of the second international conference on Medical Image Computing and Computer Assisted Intervention*, Cambridge, England, 1999.
3. O'Keefe J. and Nadel L. *The hippocampus as a cognitive map*", Oxford university press, UK, 1978.
4. Java Advanced Imaging tutorial available on the web at <http://java.sun.com>
5. Zhang, K. C., Ginzburg, I., McNaughton, B. L. and Sejnowski, T. J., "Interpreting neuronal population activity by reconstruction: Unified framework with application to hippocampal place cells", *Journal of Neurophysiology*, 79: 1017-1044, 1998.
6. Lazar, N. A., Eddy, W. F., Genovese, C. R. and Welling, J., "Statistical Issues in fMRI for Brain Imaging", *International Statistical Review*, 69:105-127, 2001.
7. Henriksen, Larrson, Ring, E. Rostrup, A. Stensgaard, M. Stubgaard, F. Stahlberg, L. Sondergaard, C. Thomsen and P. Toft, "Functional MR Imaging at 1.5T", *Acta Radiologica*, 34:101-103,1993.
8. Bandettini PA, Jesmanowicz AJ, Wong EC, Hyde JS, "Processing strategies for time-course data sets in functional MRI of the human brain" *Magnetic Resonance in Medicine*;30:161-173, 1993.
9. Georgopoulos AP. Schwartz AB. Kettner R, "Neuronal population coding of movement direction. *Science*", 233(4771):1416-1419, 1986.
10. Salinas E. and Abbott L.F., "Vector reconstruction from firing rates", *Journal of Computational Neuroscience* 1:89-107, 1994.
11. A tutorial on JAVA 3D available at <http://java.sun.com>.
12. J. L. Ostuni, A. K. S. Santha, V. S. Mattay, D. R. Weinberger, R. L. Levin, and J. A. Frank, "Analysis of interpolation effects in the reslicing of functional MR images", *Journal of Computer Assisted Tomography*, vol. 21: 803-810, 1997.
13. P. A. Bandettini, A. Jesmanowicz, E.C. Wong and J.S. Hyde, "Processing strategies for time-course data sets in functional MRI of the human brain", *Magnetic Resonance in medicine*, 30:161-170, 1993.
14. K. J. Friston, P. Jezzard, and R. Turner, "Analysis of functional MRI time-series", *Human Brain Mapping*, 1:153-171, 1994.
15. O. Henriksen, H.B.W.Larrson, P.Ring, E. Rostrup, A. Stensgaard, M. Stubgaard, F. Stahlberg, L. Sondergaard, C. Thomsen and P. Toft, "Functional MR Imaging at 1.5 T", *Acta Radiologica*, 34:101-103, 1993.
16. Wood G.K., Berkowitz B.A., Wilson C.A., "Visualization of subtle contrast related intensity changes using temporal correlation", *Magnetic Resonance Imaging*, 12:1013- 20, 1994.
17. Wilson M.A. and McNaughton B.L. , "Dynamics of the hippocampal ensemble code for space" , *Science*, 261: 1055-1058, 1993.