A Simulation Study into
The Fundamental Laws of Synchronization

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In

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Certificate

This is to certify that the dissertation entitled **A Simulation Study Into The Fundamental Laws of Synchronization** submitted by **Arnab Chowdhury** to Indian Statistical Institute, Kolkata in partial fulfilment of requirements for the award of the degree of **Master of Technology** in **Computer Science** is a bonafide record of work carried out by him under my supervision and guidance. The dissertation has fulfilled all the requirements as per the regulation of the institution and, in my opinion, has reached the standard needed for submission.

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Kaushik Kumar Majumdar 10/7/2021

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Declaration

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Abstract

Synchronization is a ubiquitous phenomenon. Sun synchronizes everybody on the earth. A powerful leader can synchronize the masses. Here we have hypothesized that the inducer of an induced synchronization must satisfy three properties of possessing high power, low entropy and strong connection with induced. In order to test this hypothesis, we have studied the brain as a model. Epileptic seizures are hypersynchronous phenomena in the brain. We have simulated a brain functional model taking into account of synchronization during epileptic seizures that may help to verify our hypothesis.

Contents

Table of Figures

1 Chapter 1: Introduction

Modern interdisciplinary neuroscience is the greatest interdisciplinary science ever. Computational Neuroscience is a branch where mathematical modelling of the brain structure and functions are studied. Since everything in the brain cannot be observed, such modelling studies are the only way out. Epileptic seizures generate very distinctive the brain electrical signals, which offer a window to look into the functioning of the brain like the way seismological signals offer a window to study the inner composition of the earth. Modelling studies of epileptic brain is not much less older than the Computational Neuroscience itself. The latter started with the Hodgkin-Huxley model proposed in early nineteen fifties (Hodgkin and Huxley, 1952) and the work on the former was initiated in nineteen seventies (Tsuboi, 1976). A large scale abnormally simultaneous firing of neurons has been implicated in epileptic seizures. This is best described by saying that epileptic seizures are hypersynchronous phenomena, which has actually been incorporated in clinical definition of epileptic seizures (Fisher et al., 2005). So, any mathematical or computational model of epileptic seizure has to take into account of this synchronization. One such model was proposed by Wendling and co-workers (Wendling et al., 2000).

Earlier, Lopes da Silva and co-workers developed a mathematical model of cortical rhythm generation in the range of around 10 Hz, formally known of alpha wave (Lopes da Silva et al., 1976). Computational units of human brain are supposed to be cortical columns (Mountcastle, 1997). Based on da Silva's model Jansen and Rit proposed a mathematical model of electroencephalogram (EEG) signal generation in the brain by coupled cortical columns (Jansen and Rit, 1995). Later Wendling and co-workers extended the Jansen-Rit model to generate signals akin to intracranial electroencephalogram (iEEG) signals during an epileptic seizure (Wendling et al., 2000). In this work we have simulated this model with five cortical columns (Fig. 1.1). Each column is referred to as node.

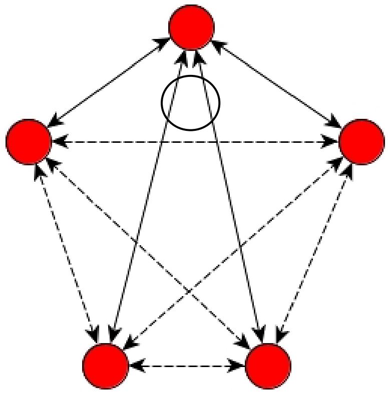

Fig 1.1. A columnar network in the the brain with five cortical columns or nodes. A dominating node has been identified by blue circle with high power, low entropy, which is also strongly coupled with the other nodes

Synchronization is a ubiquitous phenomenon. Synchronous flow of water droplets in a direction gives rise or a stream or a river. Synchronous voting by majority of voters in favour of a candidate makes the candidate winner in the election. Synchronous flow of electrons gives rise to electrical energy. Sun synchronizes everybody on the earth. A powerful leader can synchronize the masses. In the last two examples sun and leader induce synchronization on others. It has been hypothesized that the inducer of an induced synchronization must satisfy the following three properties (Majumdar, 2020). (a) The inducer (the dominant node in Fig 1.1) must have a very high power, (b) it must have low entropy, and (c) strong coupling or communication with the others.

Testing this hypothesis is important because synchronization can be of two types – self organized and induced. Dance choreography is an example of the first one, where dancers make move in synchrony without any instruction from a director (at the time of practice there may be a director, but not at the time of performance). It is a spontaneous self-organized performance which goes in synchrony among the performers. A symphony orchestra is an example of the last one. A symphony orchestra must have a conductor, under whose instructions the musicians will play in synchrony. In this case the synchrony is induced. We hypothesized that it is a necessary condition for an inducer to satisfy the above mentioned three properties (a), (b) and (c), which needed to be verified by simulating the model of Fig 1.1.

In order to test this hypothesis, we have employed the above-mentioned model. Epileptic seizures are hypersynchronous phenomena in the brain. In this simulated model power and entropy in each node and coupling strength between the nodes can be controlled. By varying the values of these parameters, we have studied the network properties of the nodes and tried to verify the hypothesis. No clear trend has emerged. However, more extensive studies are required.

In the next chapter we will describe and simulate Wendling's extension of Jansen-Rit model as configured in Fig 1.1. Chapter 3 will contain discussion on mutual information (as a notion of synchronization), entropy and correlation coefficient (as a notion for coupling) and relevant simulation results. Chapter 4 will contain our findings on how the dominant node's (Fig 1.1) entropy, power and coupling strength with the other nodes are evolving alongside the synchrony (mutual information) among the remaining four nodes. We make concluding remarks and present brief outline of future scopes of extending this work in Chapter 5, which is the final chapter.

2 Chapter 2: EEG and EP Modelling

2.1 Model of single cortical column

The mechanism of oscillations in the human brain has already been proven to be nonlinear (Watanabe and Shikita, 1981). So nonlinear model should be used to describe human cortical activities. Depending on Lopes da Silva's lumped parameter model (Lopes da Silva et al. 1974, 1976; Rotterdam et al., 1982) and the modification introduced by Wendling et al. (2000) we can have the schematic (from electrical engineering point of view) elementary cortical model as below.

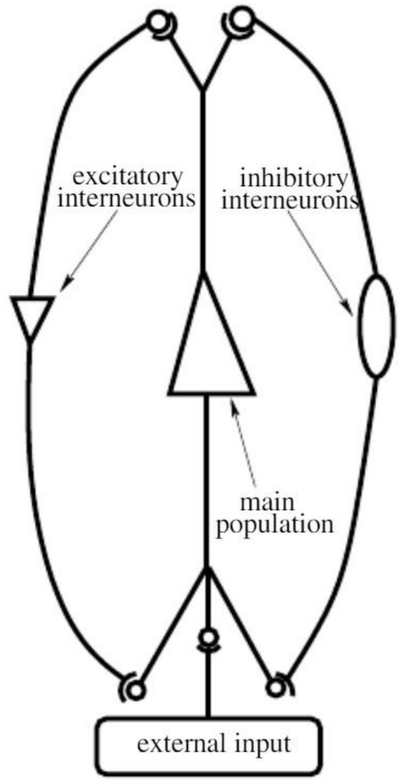

Fig 2.1Neural Mass Model of single cortical column (Grimbert et al. 2005)

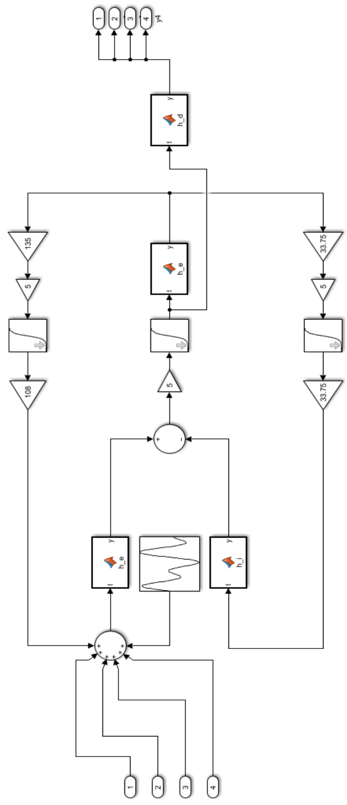

Fig 2.2. Model of a cortical column as part of multiple coupled population

Here the cortical column is modelled by population of feedforward pyramidal cells, which receive excitatory and inhibitory feedback from local interneurons i.e., other pyramidal stellate and bucket cells residing in the same column. The input from neighbours or other distant columns can be considered as noise p(t), in place of which white gaussian noise (μ=120, σ = 200) can be considered.

Each of the numerous populations can be modelled as two blocks. The first one transforms the average pass density of the action potential into an average post synaptic membrane potential which can either be called excitatory or inhibitory. This block can be represented as a linear transform with an impulse response given by

$$h_e(t) = Aate^{-at}u(t) \tag{1}$$

$$h_i(t) = Bbte^{-bt}u(t) \tag{2}$$

where $h_e(t)$ is excitatory and hi(t) is inhibitory signal. A and B determine the maximum amplitude of the excitatory and inhibitory pulse respectively, and a and b represent the last parameter of the sum of the reciprocal of the time constant of passive membrane and the delay due to all other spatially distributed dendritic network. On the other hand, the second block transforms the average membrane potential of a population of neurons into an average pulse density of action potentials fired by the neurons. This transformation is described as sigmoid function given by

$$S(v) = 2e_o/[1 + e^{r(v_o - v)}] \tag{3}$$

Here *S(v)* is a simplified version of the transformation given in Jansen et al. (1993). Here e_o represents the maximum firing rate of the neural population and v_o represents the post synaptic potential for which a 50% firing rate is achieved and *r* is the steepness of the sigmoidal transformation.

The interaction among the pyramidal cells and the excitatory add inhibitory interneurons are represented by four connectivity constants C_1 to C_4, which include the activities of the synapses established due to the connections of the axons of interneurons with dendrites of the neurons of the cortical column.

Including all previously stated conditions the transfer functions $h_e(t)$ and $h_i(t)$ produces a pair of first order ordinary differential equations as

$$\dot{z}(t) = z_1(t) \tag{4}$$

$$\dot{z}_1(t) = Ggx(t) - 2gz_1(t) - g^2z(t) \tag{5}$$

Where *G*= *A* or *B* and *g*= *a* or *b*, considering the excitatory or inhibitory case end and *x(t)* and *z(t)* are the input and output signals respectively of the linear transfer functions.

Using above equations, there can be a set of differential equations as below

$$\dot{y}_0(t) = y_3(t) \tag{6}$$

$$\dot{y}_3(t) = AaS\big(y_1(t) - y_2(t)\big) - 2ay_3(t) - a^2y_0(t) \tag{7}$$

$$\dot{y}_1(t) = y_4(t) \tag{8}$$

$$\dot{y}_4(t) = Aa\big\{p(t) + C_2S\big(C_1y_0(t)\big)\big\} - 2\,ay_4(t) - a^2y_1(t) \tag{9}$$

$$\dot{y}_2(t) = y_5(t) \tag{10}$$

$$\dot{y}_5(t) = Bb\{C_4S\big(C_3y_0(t)\big) - 2by_5(t) - b^2y_2(t) \tag{11}$$

This set of equation is solved by numerical integration methods (Runge-Kutta). Here y_0, y_1 and y_2 provides the output of the PSP block (Jansen et al., 1995).

2.2 Modelling of multiple coupled cortical columns

Jansen et al. (1993) redefined the above model by coupling the cortical columns in order to explore the hypothesis that some visual evoked potentials (EPs) are generated due to interactions between cortical columns. Depending on this hypothesis Wendling et al. (2000) modelled a set of differential equations with some changes incorporated in the Jansen-Rit model in order to fit the previous model for multiple couplings of any number greater than two. Depending on this consideration they tried to study the propagation of signals in the brain in case of epileptic activities. This modified version can account any number of connections between several cortical columns. Here gain constant K^{ij} is used today scribe the strength of coupling between population *i* and population *j* while a filter with an impulse response $h_d(t)$, *same* as $h_e(t)$ with constant $a_d \approx a/3$.

Here the model is described by a set of eight ordinary differential equations per cortical column as given below.

$$\dot{y_0}^n(t) = y_3^n(t) \tag{12}$$

$$\dot{y}_3^n(t) = AaS\big(y_1^n(t) - y_2^n(t)\big) - 2ay_3^n(t) - a^2y_0^n(t) \tag{13}$$

$$\dot{y}_1^n(t) = y_4^n(t) \tag{14}$$

$$\dot{y}_4^n(t) = Aa\left\{p^n(t) + C_2S\big(C_1y_0^n(t)\big) + \sum_{i=1, i\neq n}^{N} K^i y_6^i(t)\right\} - 2\,ay_4^n(t) - a^2y_1^n(t) \tag{15}$$

$$\dot{y_2}^n(t) = y_5^n(t) \tag{16}$$

$$\dot{y_5}^n(t) = Bb\{C_4S\big(C_3y_0^n(t)\big) - 2by_5^n(t) - b^2y_2^n(t) \tag{17}$$

$$\dot{y_6}^n(t) = y_7^n(t) \tag{18}$$

$$\dot{y}_7^n(t) = Aa_dS\big(y_1^n(t) - y_2^n(t)\big) - 2a_dy_7^n(t) - a_d^2y_6^n(t) \tag{19}$$

Here the superscript *n* indicates the cortical columns under consideration where column in receives in formation from columns $i = 1, \ldots, N, i \neq n$ along with neighbourhood or distance columns denoting as $p^n(t)$. Here $y_0^n(t)$ is the output of the interneuron EPSP transfer function h_e, and $y_1^n(t)$ and $y_2^n(t)$ are the output of the main cells' PESP and IPSP respectively. $y_6^n(t)$ is the output of EPSP transfer function h_d.

Standard values of the model parameters according to Jansen et al. 1995

$A = 3.25\ mV$	$C_3, C_4 = 0.25C$ (where $C=135$)
$B = 22mV$	$v_0 = 6mV$
$a = 100\ s^{-1}$	$e_0 = 2.5\ s^{-1}$
$b = 50\ s^{-1}$	$r = 0.56\ mV^{-1}$
$C_1 = C$	$a_d = 33\ s^{-1}$
$C_2 = 0.8C$	K^{ij} = anything to adjust coupling strength

2.3 Simulations

Using a five-node model and considering those nodes as separate cortical columns, simulating artificially using model parameters with around 8000 samples following set of plots can be obtained.

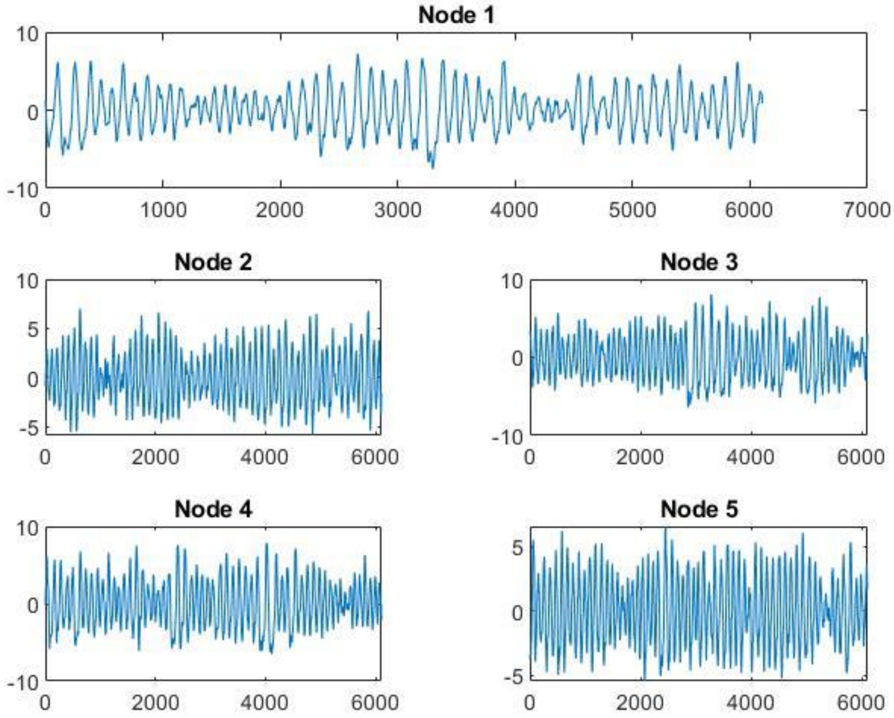

Fig 2.3. Output from the 5 separate interconnected cortical columns simulated with respect to the differential equations developed by Wendling et al., 2000

3 Chapter 3: Different measurements

3.1 Mutual Information

Consider two digital signals *X[n]* and *Y[n]* with equal number of samples in each, for a set of N samples constituting a set of different motifs (13 configurations as shown in Fig 3.2). Now Consider two-dimensional alignment of motifs between any of the signals of Fig 2.3. The frequency of occurrence of the alignment among all such two-dimensional alignments will give a frequency density, which helps to estimate the two-dimensional probability density *p(X[n], Y[n])*. Estimation of one-dimensional probability densities *p(X[n])* and *p(Y[n])* is accomplished by the frequency of occurrence of three point motifs in *X[n]* and *Y[n]* respectively. Mutual information *I(X[n], Y[n])* is then estimated within the *N* sample window by the formula (Dheer and Majumdar, 2021)

$$I(X[n], Y[n]) = \sum_{i=2}^{N-1} p(X[i], Y[i]) \log\left(\frac{p(X[n], Y[n])}{p(X[i])p(\,Y[i])}\right) \tag{20}$$

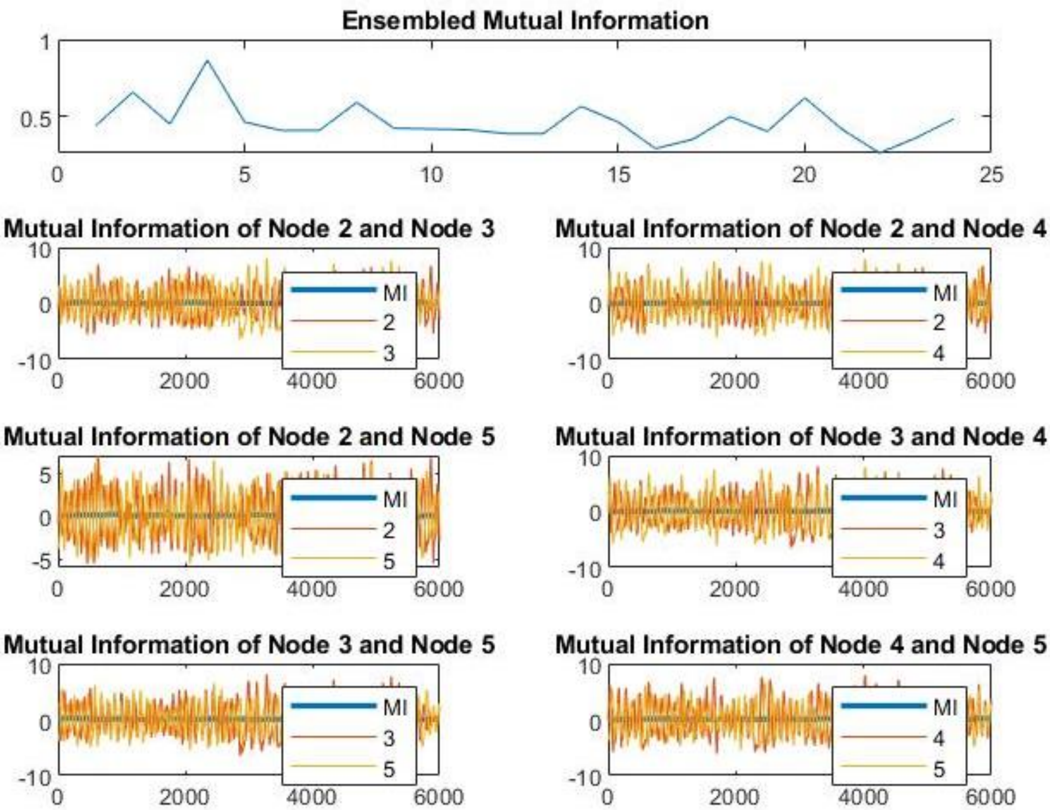

Fig 3.1. Mutual information of other nodes with respect to Node1 has been shown in six plots and the above one shows sum of these mutual information

Now considering one particular node (say *Node 1*) to be the inducer and keeping it aside we can compare other four nodes taking two at a time i.e., a total of ${}^{4}C_{2}$ combinations of nodes. Using the formula (20) for the MI between pairs of signals over a sequence of windows results in six plots as shown in Fig 3.1. Another estimation of sum of MI can be obtained from these plots of four nodes which may help to measure the influence of *Node1* over the others.

3.2 Entropy of a Signal

Measure of entropy in a time series provides a means to estimate the average information content of the time series and thus considered as an important measure of a time series. The 13 configuration decomposition of a discrete time series (Fig 3.2) readily gives a measure of entropy in terms of distribution of those configurations in the time series. Since each configuration is the semantic information about the smallest neighbourhood of a point containing that point as an interior point, the entropy based on their distribution should be called semantic entropy (Majumdar and Jayachandran, 2018).

Sign Change	s'[n]	s''[n]	s'[n+1]	3-point configuration	Configuration number	Empirical Observation
- -	-	+	-		1	Statistically more abundant
	+	-	+		2	
+ +	+	+	+		3	
	-	-	-		4	
- +	-	+	+		5	
	+	-	-		6	
0 0	+	0	+		7	Statistically less abundant
	-	0	-		8	
	0	0	0		9	
0 +	0	+	+		10	
	0	-	-		11	
- 0	+	-	0		12	
	-	+	0		13	

Fig 3.2. Configuration the neighbourhood of S[n] consisting of points (n-1), n and (n+1) along with corresponding sign changes from left product right product of P-operator

Definition: Semantic entropy of a signal of length N is given by $SE = -\sum_{i=1}^{13} p_i \, log \, p_i$ where $p_i = \frac{n_i}{N-2}$ is the frequency distribution of the *i*th configuration according to figure n_i is the number of time the *i*th configuration has occurred in the N point long signal segment.

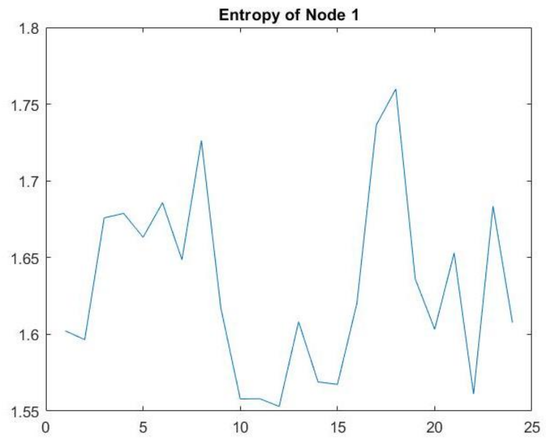

Fig 3.3. Entropy of a signal generated at a node from the simulation of a cortical column using the formula of semantic entropy at a specific sampling rate

3.3 Power of a signal

For a discrete time signal of length N i.e., the signal having N data points power P can be calculated as $P = \frac{1}{N+1}\sum_{n=1}^{N} |x(n)|^2$. After simulating for a large dataset those can easily be sampled with a specific window size to deduce the power over some small parts of a discrete time signal.

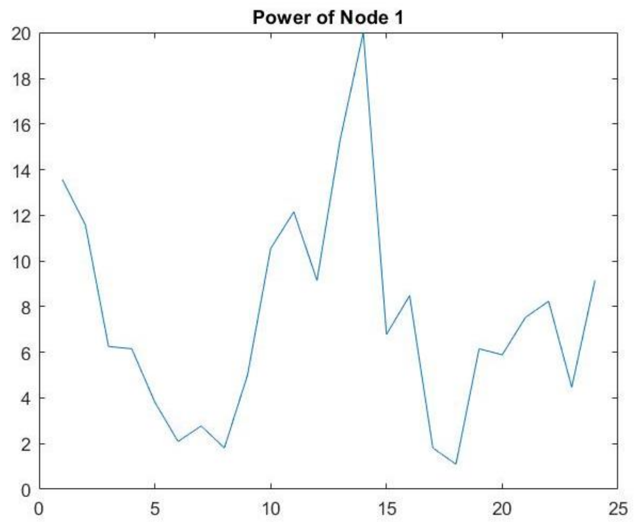

Fig 3.4. Power of a signal generated from the simulation of a cortical column using a specific window size

3.4 Correlation Coefficient

Coupling between two nodes has been calculated by taking the absolute value of correlation coefficient in windowed manner between the signals coming out of them. For two digital signals *X[n]* and *Y[n]* containing equal number of samples say *N* correlation coefficient can be deduced over some steps of calculations.

Mean of *X[n]* and *Y[n]* are $\bar{x} = \frac{1}{N}\sum_i x[i]$ and $\bar{y} = \frac{1}{N}\sum_i y[i]$ respectively.

Standard deviations are $\sigma_x = \sqrt{(\frac{1}{N}\sum_i(x[i] - \mu_x)}$ and $\sigma_y = \sqrt{(\frac{1}{N}\sum_i\left(y[i] - \mu_y\right)}$.

Covariance of *X[n]* and *Y[n]* is $cov_x = \sum_i \frac{(x[i]-\mu_x)(\,y[i]-\mu_y)}{N}$.

∴ Correlation coefficient $r = \sum_i \frac{(x[i]-\mu_x)(\,y[i]-\mu_y)}{\sigma_x.\sigma_y}$.

Using this formula *r* can easily be derived for all nodes with respect to *Node 1*.

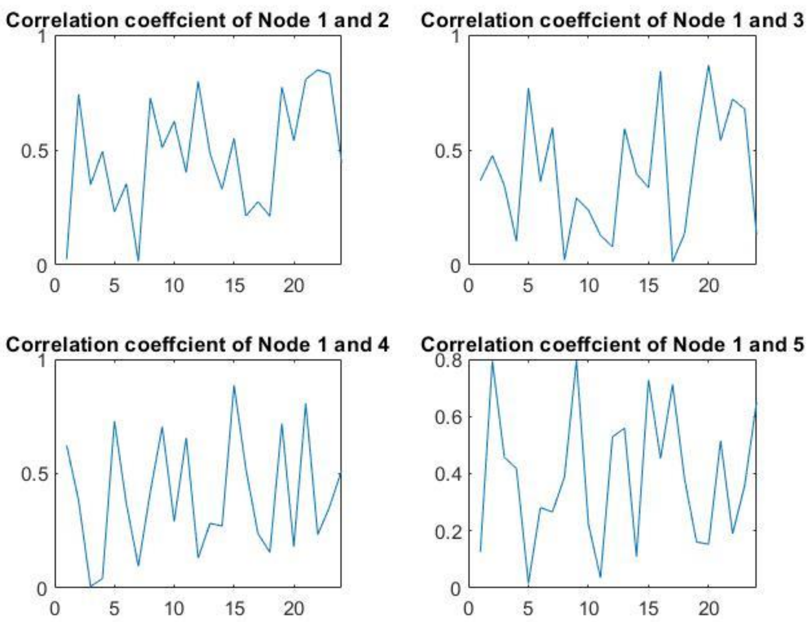

Fig 3.5. Correlation coefficients of all other nodes with respect to Node 1 are represented in clockwise manner

4 Chapter 4: Testing the Hypothesis

We started with the hypothesis that induced synchronization is influenced by a particular powerful agent i.e., the agent has an inducing effect to synchronise other nodes to which it is coupled. We assumed that the inducer must have (a) high power, as high power leads to high influence, (b) low entropy, as entropy is reciprocally proportional to the stability of the inducer, and (c) strong coupling with the other agents, because without strong coupling there cannot be any influence at all.

In order to test this hypothesis, we have studied over epileptic seizures of human brain. Because the epileptic seizures are well known hypersynchronous conditions. Thus here we have used five nodes considering them as separate cortical columns of human brain and tried to proof our assumption deducing power, entropy, and correlation coefficient of the nodes. As we know influence $\propto$ power, influence $\propto$ communication strength, influence $\propto \frac{1}{entropy}$ we assumed a measurement as below

$$\kappa = \frac{SE}{P * r} \tag{21}$$

Here we have used κ as an inducing ability index of the powerful node, which creates a hypersynchronous condition resulting epileptic seizures. In this measurement the induction will be more only when the semantic entropy of the particular node is low, the signal power is high, and the coupling strength is also high. Here the absolute value of correlation coefficient is considered as the measure of coupling strength.

Hence with low semantic entropy high powered and high correlation coefficient the measurement of influence κ will be low i.e., with low value of κ inducer node will attain higher command over other nodes.

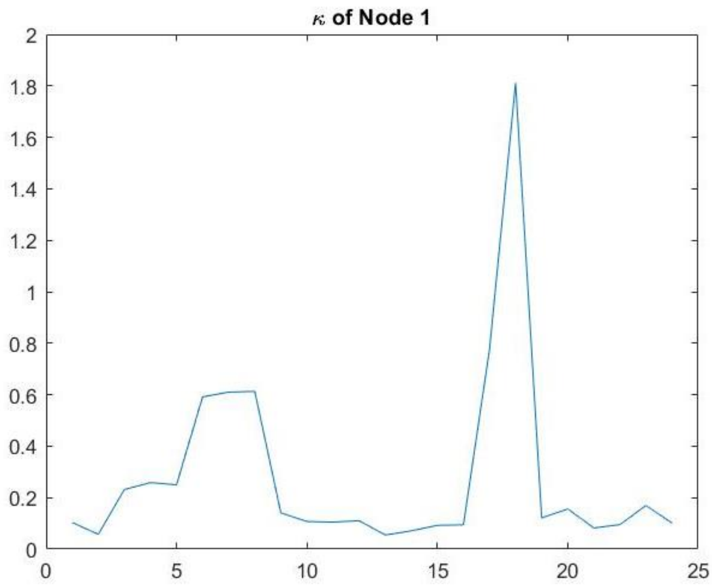

Fig 4.1. Plot of measurement of inducing power of Node 1

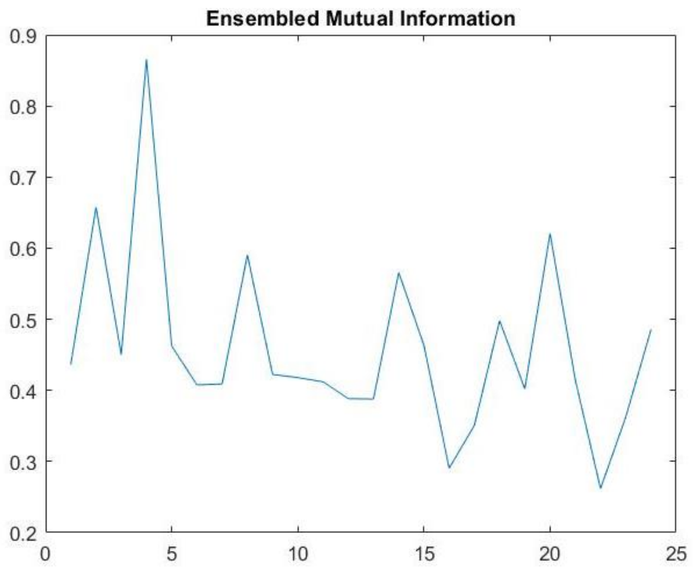

Fig 4.2. Ensembled Mutual information of all other nodes except Node 1

We did our measurement with respect to *Node 1* to study its induction power over the others. As the simulation results given for SE (Fig 3.3), Power (Fig 3.4), and correlation coefficient (Fig 3.5). To measure the inducing ability κ of *Node1* taking the sum of absolute value of the correlation coefficients of *Node1* with respect to others for the coupling strength *r* the calculation was made according to equation 21. SE, P and r must have equal number of samples to perform this measurement.

Here we can compare ensemble MI of *Node 2* through *Node 5* with κ_{Node1} in the hope of finding a relationship between them. Comparing the plots of Fig 4.1 and Fig 4.2, putting one of them right above the other, we observe generally, when the ensemble synchronization across *Node2* through *Node5* is peaking the inducing ability index κ of *Node1* is going down, which means its ability to induce synchronization is going up. Although it sounds a bit counter intuitive, this is exactly we expected. However, nothing can be concluded on one single plot. A large number of such results need to be simulated tweaking the parameters of the nodes to module their strength and statistical analysis needs to be performed on the results to reach a conclusion about our hypothesis.

5 Chapter 5: Conclusion and Future Scope

In this work we hypothesized three fundamental principles an inducer must satisfy to induce synchronization over a population of independent agents. An attempt was made to verify if the proposed hypotheses hold good. For this we chose a model of brain function, which is a network model with nodes and connections. By tweaking parameters any node can be made an inducer, which induces synchronization on the rest of the nodes. Our results remained inconclusive, albeit many more runs of the simulated model are necessary. Here we could lay the foundation of a more extensive study in search of conclusive evidence favouring or opposing our hypothesis.

We completed the computational model, where entropy/ (power x coupling strength) of the inducer node and mutual information across the remaining nodes can be calculated in windowed manner. Comparing the two values over a sequence of windows one would be able to reach a decision on the proposed hypothesis. Tweaking the parameters across wide range of values and producing a large number of simulations will give a reasonable population of results, a statistical analysis of which will help us draw a conclusion about the proposed hypothesis. This will be the future direction of the work that we initiated here.

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