A BIOPHYSICAL MODEL OF CROSS FREQUENCY COUPLING

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The National Brain Research Centre in Partial
Fulfilment of the Requirements for the Masters in Neuroscience

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DECLARATION BY THE CANDIDATE

I Anagh Pathak hereby declare that the work presented in this dissertation is carried out by me, under the guidance of Arpan Banerjee, National Brain Research Centre(Deemed University), Manesar, Haryana.

I also declare that no part of this dissertation has been previously submitted for the award of any degree or diploma at National Brain Research Centre(Deemed university) or any other University.

Anagh Pathak
MSc. final

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Date: 31 May 2018

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Lastly, I would like to thank my family for inspiring me to take up science and standing by me all throughout my journey.

Anagh Pathak

ABSTRACT

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Brain signals, as recorded by EEG/MEG/LFP show robust oscillatory activity, when filtered in appropriate frequency bands. There is a long tradition in neuroscience to think of these oscillations as indicative of neural computation. Oscillations have been implicated in diverse processes such as attention, working memory, perception and have also been involved in various pathologies such as epilepsy and schizophrenia. While previously, different oscillations were studied in isolation, recent research has hinted towards studying interactions between frequency bands. These interactions, termed as cross frequency couplings are thought to underlie many cognitive processes.

Here we present a model for cross frequency interactions in the brain, by using simulations involving a modified Wilson-Cowan model. Wilson-Cowan model is acknowledged to be a biophysically realistic neural model of macroscopic brain activity as observed in EEG.

We demonstrate phase amplitude and phase frequency coupling in neural time series. Additionally, the model can explain some recent theories of oscillatory dynamics in neurophysiological signals.

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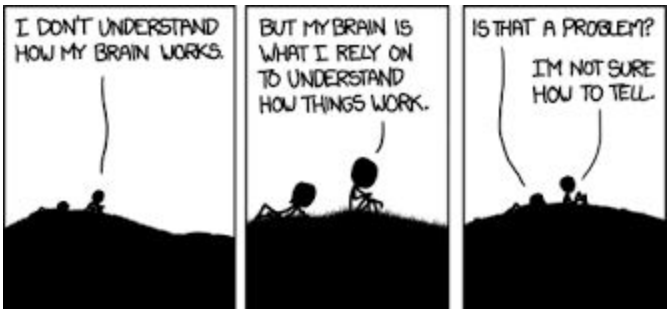


What makes neuroscience so exciting is that for the first time we are trying to understand that which makes all understanding possible.

CHAPTER 1

INTRODUCTION

Neuroscientists have known about neural oscillatory activity for close to a century. The first observations were made by Hans Berger in 1924 by using a primitive electroencephalograph. Berger observed, to his amazement, that on placing sensitive electrodes on the human scalp, one could observe robust oscillatory activity in the subsequent traces. Berger's paper titled *Uber das electrenkephalogramm des Menschen(Berger 1936)* (On the EEG in humans), published in 1929, was the first in a series of 23 articles on the subject. Berger characterised changes in oscillations due to attention, mental effort and cerebral injuries, topics that are still active subjects of modern neuroscientific research. Using his primitive setup, Berger discovered α and β rhythms, and even coined the term *electroencephalogram*.

Based on their characteristic frequency range and amplitude, endogenous neural oscillations can be broadly categorised as **delta**(0.5-4 Hz), **theta(**4-8 Hz), **alpha**(8-13 Hz), **beta**(13-30 Hz) and **gamma**(30 -80 Hz) rhythms(Wang 2006). The Delta rhythms are high amplitude waves that are associated with NREM sleep, also known as slow wave sleep. Theta rhythms have been described in the hippocampus(hippocampal theta) and in the cortex (cortical theta), and are thought to play a crucial role in memory formation and navigation. Alpha waves, also called Berger waves in honour of Hans Berger, are thought to be generated by the interaction of the thalamus and the cortex. Alpha activity is thought to be important for selective attention and working memory. A recent theory associates alpha activity with information gating in the cortex. Beta activity predominantly occurs in the motor cortex where it is associated with muscular contractions and movements. Gamma rhythms constitute the fastest rhythms in the brain(Wang 2006). Gamma waves are widely believed to be involved in visual awareness and feature binding.

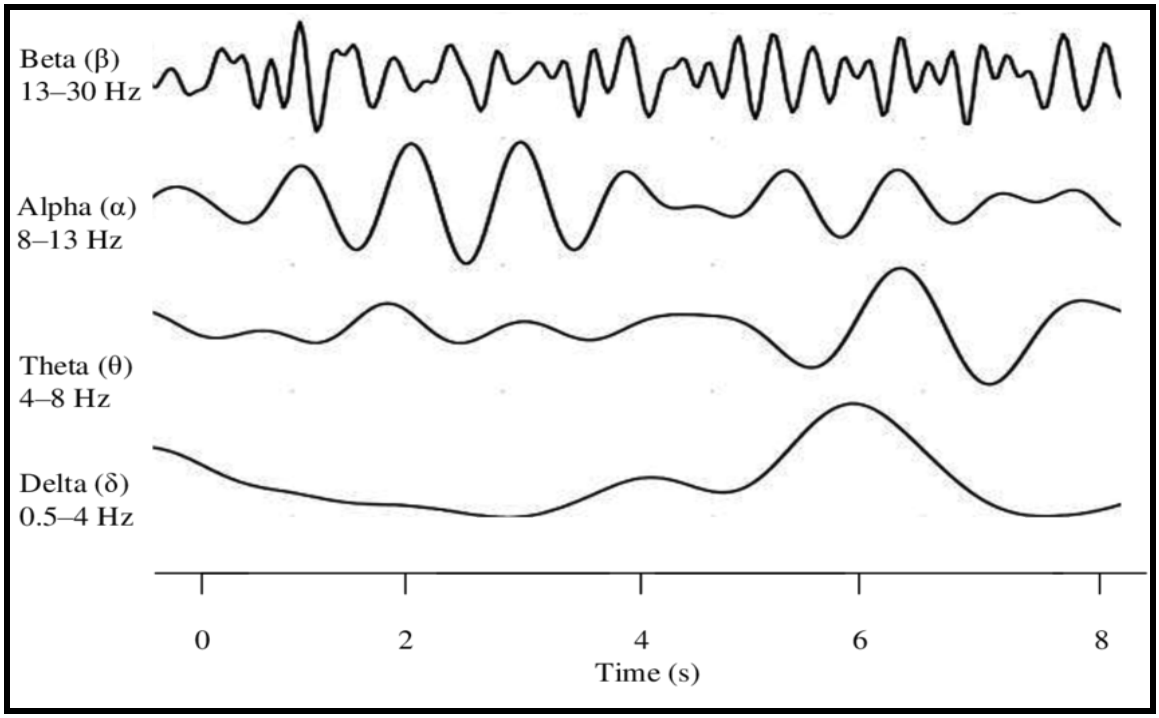


Fig 1.Oscillatory activity as seen on filtering EEG signals.

Neural oscillations, as measured in EEG/MEG are generated by the synchronized activity of neural ensembles. Synchronized activity of large number of neurons leads to the creation of a macroscopic signal that can be captured as the corresponding scalp potential(EEG) or current(MEG). Neural oscillations have been observed at all scales of neural organization- single neurons, activity of groups of neurons and activity from brain areas.

At the same time, oscillations have served as biomarkers for various brain pathologies(Schnitzler and Gross 2005).

1.1 Functional Roles of Brain Oscillations

As noted, even as early as Berger, scientists were implicating neural oscillations in brain processes such as attention, memory, brain pathologies etc. Since then, various theories have been put forward that associate oscillations with the functioning of the brain. Below, we discuss a few examples of the computational role of rhythmic activity.

The binding problem was first formulated by Von Der Malsburg, who asked how different features of the same object are bound together to form a unified percept of the object as a whole.

The oscillatory theory of feature binding posits that different features of the same object are 'bound' together through synchronization of neural assemblies that are responsible for coding the individual features of an object(von der Malsburg 2001).

Periodic motor movements like respiration, walking, running, mastication etc. are generated by oscillatory motor activity through autonomous central pattern generators. Central pattern generators have the capacity to produce rhythmic output in the absence of rhythmic inputs (Hooper 2001). Even basic bodily functions such as heartbeat and peristalsis are subserved by rhythmic oscillatory activity.

Neural oscillations have been linked to processes such as information transfer, memory and perception. Coherent neural activity has been regarded as a substrate for neuronal communication in the brain(Fries 2005). Phase synchronization has been linked to memory processes in the brain(Fell and Axmacher 2011). It has been proposed that phase synchronization between neural oscillators supports both working and long term memory by facilitating neural communication and plasticity. This hypothesis is borne out of observations of

increased phase synchronization during various memory processes such as working memory maintenance and long term memory encoding and retrieval(Fell and Axmacher 2011).

Abnormal synchronization in brain rhythms has been linked to pathologies such as Parkinson's, other movement disorders and neuropsychiatric diseases. For example, electrophysiological recordings of basal-ganglia-thalamocortical circuits in Parkinsonian primate models and patients with Parkinson's disease have provided new insights into the functional roles of oscillations and oscillatory synchronization in normal and disturbed motor behavior. Specifically, enhanced beta and reduced gamma oscillations are associated with the poverty and slowness of movement that is characteristic of Parkinson's disease. Additionally, tremor seems to arise from abnormal synchronization of oscillations in several cortical and subcortical areas(Schnitzler and Gross 2005).

1.2 Cross Frequency Coupling

As far back as 1995, Lisman and Idiart invoked cross frequency interactions to explain psychophysical measurements that indicated that human subjects can store approximately seven short term memories(Lisman and Idiart 1995). In their famous paper, titled '*Storage of 7 ± 2 short term memories in oscillatory subcycles'*, Lisman and Idiart proposed that each short term memory is stored in a different high frequency sub cycle of a low frequency oscillation. Building on this, Canolty et. al. (R. T. Canolty et al. 2006) reported robust coupling between the high- and low-frequency bands of ongoing electrical activity in the human brain. Specifically, they observed coupling between the phase of theta oscillations(4-8 Hz) and power in the high gamma (80 -150 Hz) band, recorded using electrocorticography. Axmacher et. al.(2009) used intra cortical EEG recordings in epilepsy patients while they performed multi item working memory retrieval task to show robust Cross frequency coupling in memory

maintenance(Axmacher et al. 2010). Colgin(Colgin 2015) discusses the critical role played by theta (5-10 Hz)- gamma(30-100 Hz) interactions in memory encoding and retrieval. Bonnefond et. al(Bonnefond and Jensen 2015) recorded MEG activity in healthy subjects while they performed a modified Sternberg working memory task in which distractors were presented in the retention interval. They showed that alpha(9-12Hz) - gamma(80-120Hz) phase amplitude coupling was high during the anticipatory pre-distractor period. Vaz et. al.(Vaz et al. 2017) demonstrate the role of phase amplitude coupling in encoding episodic memories in humans using intracranial electrodes. Recently, Richter et. al.(Richter et al. 2017) demonstrated robust phase amplitude coupling between the infra slow gastric oscillations(~0.05 Hz) and spontaneous brain dynamics during resting-state eyes open condition. This method extends cross frequency coupling to the realm of brain-viscera interactions(Richter et al. 2017). Phase amplitude coupling has also been implicated in pathologies like Schizophrenia and Epilepsy. Hirano.et. al (Hirano et al. 2018) report abnormal patterns of phase amplitude coupling in the EEG recordings obtained from the auditory cortex of patients suffering from Schizophrenia. Amiri et. al.(Amiri, Frauscher, and Gotman 2016) report elevated phase amplitude coupling in the onset zone of focal epileptic seizures.

1.3 Functional Roles of Cross Frequency Coupling

Various theoretical models have been put forward that aim to understand the broader computational role of cross frequency interactions(Ryan T. Canolty and Knight 2010). A recent theory has proposed the existence of oscillatory hierarchies that control neuronal excitability and stimulus processing in the auditory cortex(Lakatos et al. 2005). According to this model, EEG

oscillations reflect cyclical variations in cortical excitability across spatial scales of brain operation. Experiments based on this model suggest that EEG activity in the auditory cortex is hierarchically organized such that the phase of delta modulates theta amplitude and theta phase modulates gamma amplitude(Lakatos et al. 2005). This is an example of a theory that relies on cross frequency interactions to explain the organization of EEG spectra. Another recent theory that utilizes cross frequency interactions to explain cortical excitability is the '*gating by inhibition'* hypothesis(Jensen and Mazaheri 2010). According to this model, alpha band activity routes information to task relevant areas by inhibiting information processing in task irrelevant areas. The model posits that gamma activity, which signifies local information processing, is phasically modulated by ongoing alpha activity. Gamma activity increases during the trough of alpha oscillations and decreases when alpha reaches its peak. Accordingly, optimal task performance will be correlated with alpha activity in task irrelevant areas. Several examples have been cited for the theory of gating by inhibition. For instance, it has been demonstrated that alpha activity increases in visual areas during motor tasks and vice versa. In studies of spatial attention, it has been shown that alpha activity increases on the side that is ipsilateral to stimulus presentation, whereas there is a corresponding decrease in alpha on the contralateral side. Alpha modulation due to covert attention is so robust, that it has been used as a control signal for brain-computer interfaces. A recent study found that alpha power at parieto-occipital sites was dependent on the direction of attended speech(Jensen and Mazaheri 2010).

As is evident from the previous paragraphs, recent interest in the field has focused on characterizing the interactions between neural oscillations when the subject(human or animal) is performing certain cognitive tasks. In the following, we take a closer look at the methodological aspects of observing cross frequency interactions in real electrophysiological data.

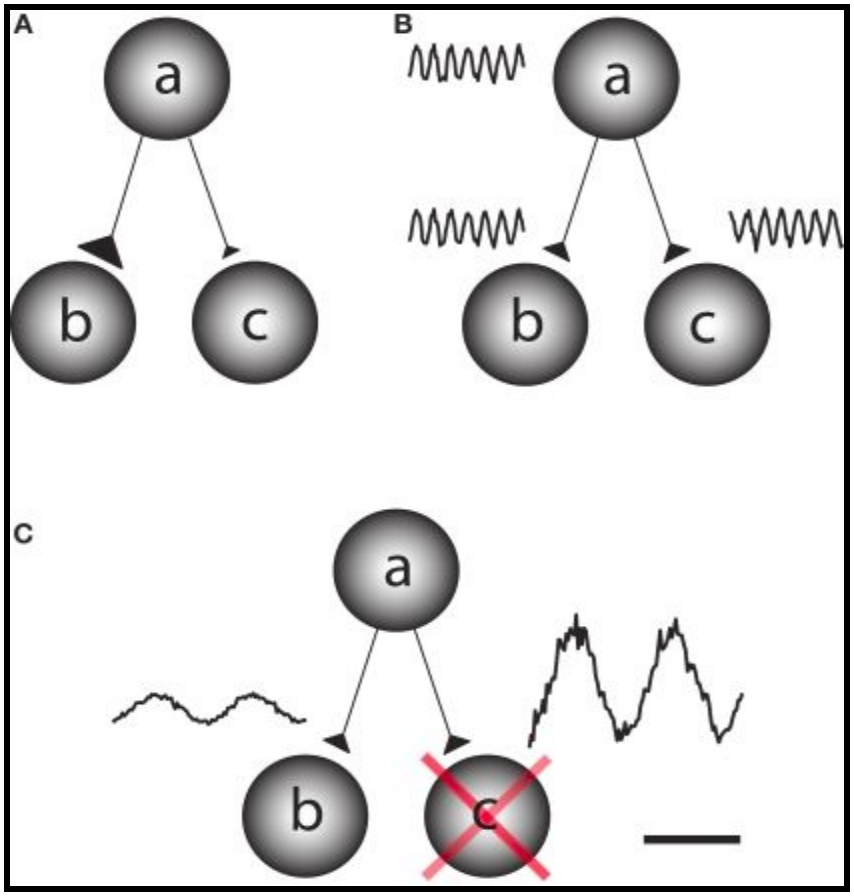


Fig 2. Possible scenarios if information is to be routed from node a to node b. A) Information is routed through synaptic inhibition of a-c connection. This would require fast synaptic time scales.B) Routing is achieved by phase synchronization between a and b and desynchronization between a and c C) Routing achieved through gating by inhibition.

1.4 Types of CFC

Any periodic activity can be characterised by three variables, namely - instantaneous phase, amplitude and frequency. Based on the nature of the interaction, we can broadly categorize CFC as either- **phase to phase, power to power, phase to power or phase to frequency** interaction(Jensen and Colgin 2007). Following is a representation of the possible forms cross frequency couplings can take.

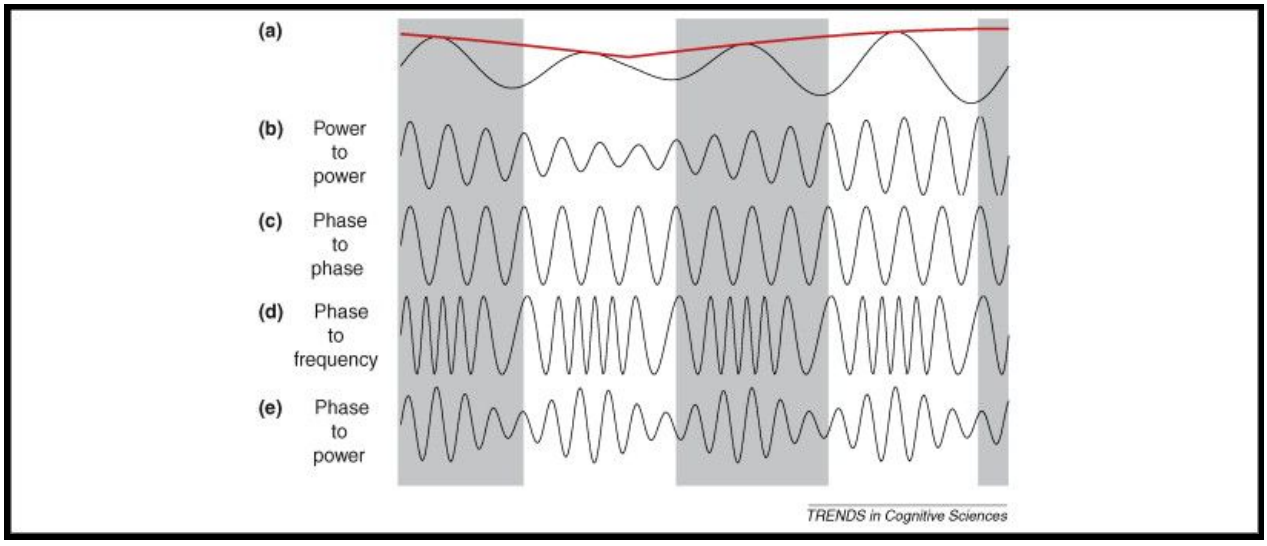


Fig 3. Possible forms of cross frequency coupling based on the power, phase and frequency of the signal

Phase phase coupling is said to exist when the phases of two oscillators are correlated. Formally speaking, the instantaneous phases of the two oscillators obey the following relationship,

$$|\Phi_{1,2}| < const., \text{ with } \Phi_{n,m} = n\Phi_1 - m\Phi_2$$

Where $\Phi_{1,2}$ are the instantaneous phases of the two oscillators and n,m are integers. Phase-phase coupling, also called n:m coupling, has been shown to exist between theta and gamma oscillations in the hippocampus(Belluscio et al. 2012).

Power- Power coupling is said to exist when the amplitude envelopes of the two oscillators are correlated. Phase to Power Coupling, referred here as phase-amplitude coupling(power corresponds to squared amplitude), is said to exist between two oscillators when the instantaneous phase of an oscillator is correlated with the phase of the instantaneous power of the second oscillator. Phase amplitude coupling naturally assumes the existence of a low frequency that modulates a higher frequency. PAC can be conceptualised as a 1:1 phase-phase coupling between the time series corresponding to low frequency and power of the higher frequency oscillator.

Phase-Frequency coupling refers to correlation of the phase of one oscillator with the spectral content(frequency) of another oscillator. Next, we consider the various methods that are used to quantify phase amplitude coupling in electrophysiological data.

CHAPTER 2

METHODS

2.1 Metrics and Pipelines to analyze phase amplitude coupling in neural data

Several methods have been proposed for detecting phase amplitude coupling. For a comprehensive review refer Penny et.al.(Penny et al. 2008)

The core of these detection methods is as under:

1. Bandpass filter the signal in the appropriate frequency ranges to obtain a slow, fast frequency signal of interest.
2. Estimate the phase of the slow oscillation using Hilbert transformations.
3. Estimate the phase of the power of the faster oscillation by using Hilbert transformation.
4. Relate the phase of the slow signal with the phase of the power of the fast signal.

Below, we describe 3 popular methods for relating the phase of the slow signal with the phase of the power of the fast signal.

2.1.1 Phase Locking Value

$$PLV = \left|\frac{1}{N}\sum_{n=1}^{N} e^{(i(\phi_{slow}[n] - \phi_{a_{fast}}[n]))}\right|$$

Where $\phi_{slow}[n]$, $\phi_{a_{fast}}[n]$ are the phase of the slower frequency, phase of the power of the fast frequency respectively at the n^{th} time point. The averaging is performed in a given temporal window of size N. PLV corresponds to the magnitude of the resultant vector obtained from the addition of the unit vectors $e^{(i(\phi_{slow}[n] - \phi_{a_{fast}}[n]))}$. As such, the value of PLV lies between 0 and 1(Cohen 2008)(Lachaux et al. 1999).

2.1.2 Modulation Index

$$z[n] = a_{fast}[n]e^{(i\Phi_{slow}[n])}$$

$$M = |\frac{1}{N}\sum_{n=1}^{N} z[n]|$$

The modulation index is the resultant vector obtained by adding the unit vectors corresponding to the product of the phase of the slow oscillations and the amplitude of the fast oscillation. MI can take any positive value. As such, MI should be scaled using surrogate statistics(Penny et al. 2008)

2.1.3 Correlation

$$r = Corr_n(a_{slow}[n], a_{fast}[n])$$

Correlation metric corresponds to the linear correlation between the amplitudes of the slow and the fast oscillations. Since correlation is linear, the metric suffers from an inability at estimating fractional correlations, as would be the case if PAC occurs at quarter cycles(Penny et al. 2008).

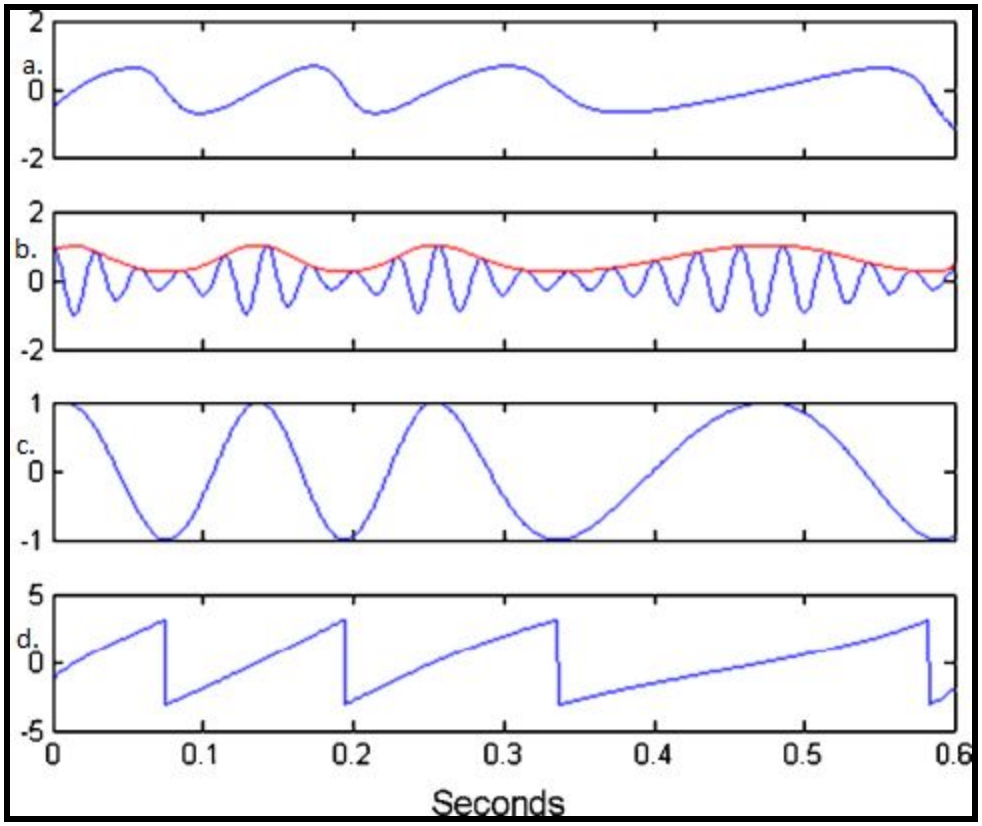


Fig.4 Schematic representation of signals a.)Phase of amplitude of fast oscillation $\phi_{a_{fast}}$ b.)raw trace and amplitude of fast oscillation x_{fast}, a_{fast} c.)raw trace of slow oscillation x_{slow} d.)phase of slow oscillation ϕ_{slow}

2.2 Mathematical Models of Cross Frequency Coupling

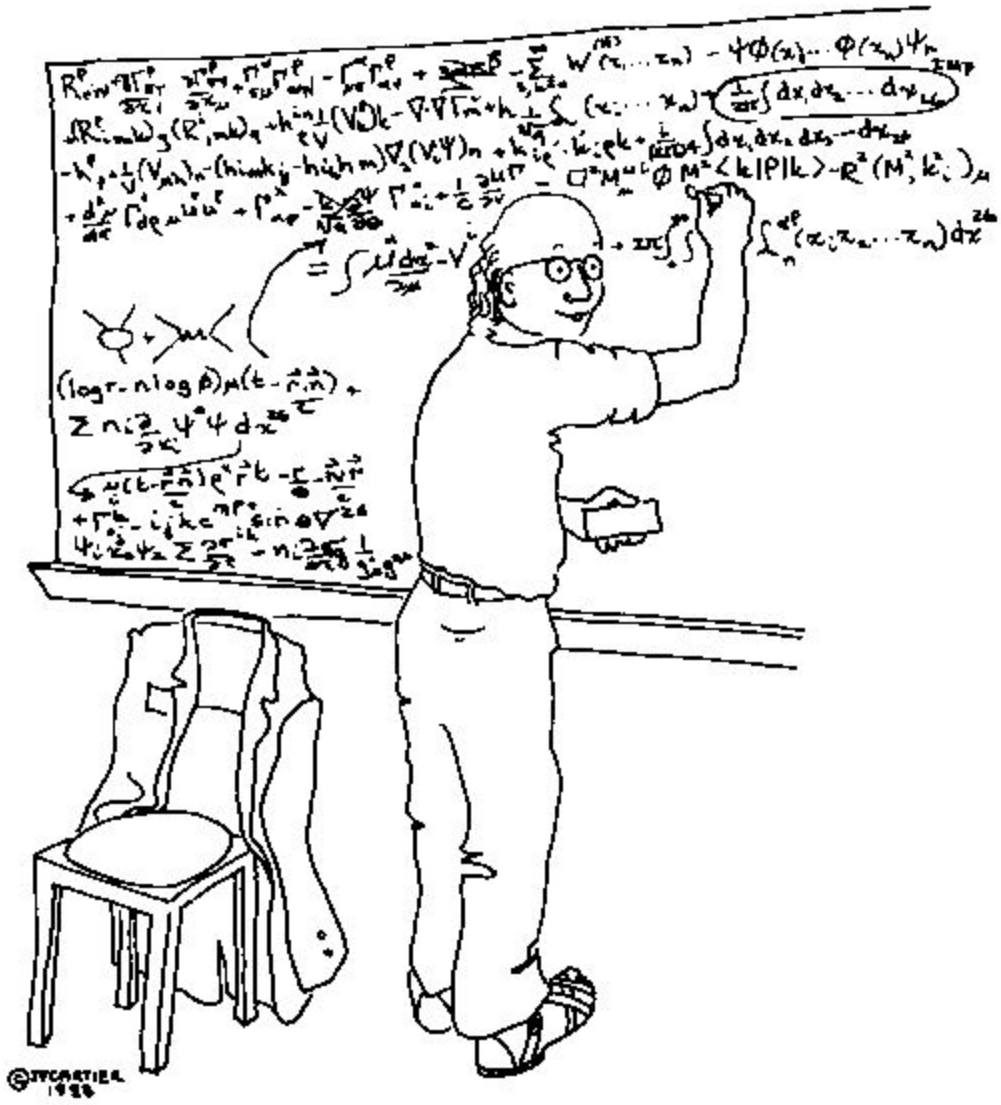
Mathematical modelling of neuronal dynamics can be performed using detailed or mass models. Detailed modelling involves modelling each and every cell in in the network, with separate equations for soma, dendrite and axons. Spiking neural networks are examples of detailed models.

While this approach is more biophysically realistic, it suffers from certain drawbacks. Firstly, solving a high dimensional system of equations, such as those arising from detailed models, is

computationally expensive. Secondly, biological detailing leads to an explosion in model parameters which can lead to model overfitting. To circumvent these issues, we resort to the second approach, namely, mass modelling(Sotero 2015). Mass Modelling reduces the dimensionality of the system by assuming that neural population dynamics can be appropriately summarized using the average activity. Examples of mass models include the Wilson-Cowan oscillator and the Jansen Ritt(Sotero 2015). Mass models have been used to simulate seizures, cognitive phenomenon, anaesthetic action etc. Sotero et. al. (Sotero 2015) argues that NMMs are an appropriate mathematical framework to study PAC because of the small number of parameters and variables involved and the richness of the dynamics they can generate.

Here we briefly review some of the models that have been proposed for phase amplitude coupling. Chehelcheraghi et. al. (Chehelcheraghi et al. 2017) studied phase amplitude coupling using a modified version of the Wendling neural mass model.Sotero et. al. (Sotero 2015) goes on to propose a detailed cortical column model comprising 4 layers and 14 neuronal populations to account for PAC. Onslow et. al.(Onslow, Jones, and Bogacz 2014) proposed a model for Phase Amplitude Coupling which is similar to the one considered here. Excitatory and Inhibitory neural populations are coupled to each other in a recurrent fashion and external current to the individual populations is sinusoidally modulated to perturb the system across a bifurcation point.

2.3 Model



"At this point we notice that this equation is beautifully simplified if we assume that space–time has 92 dimensions."

As mentioned earlier, neural oscillations are produced when large number of neurons(ensembles) fire synchronously, leading to the generation of a macroscopic signal. The Wilson-Cowan model treats the summed activity of excitatory and inhibitory networks as the state variable that evolves in time, due to its intrinsic connectivity and external inputs(Destexhe and Sejnowski 2009). The WC model consists of an excitatory population connected to an inhibitory population in a recurrent fashion. The dynamics of the system is governed by a system of coupled differential equations(Cowan, Neuman, and van Drongelen 2016). The synaptic connections between the two populations, the intrinsic connectivity within the two populations and the constants within the rectification functions serve as the model parameters.

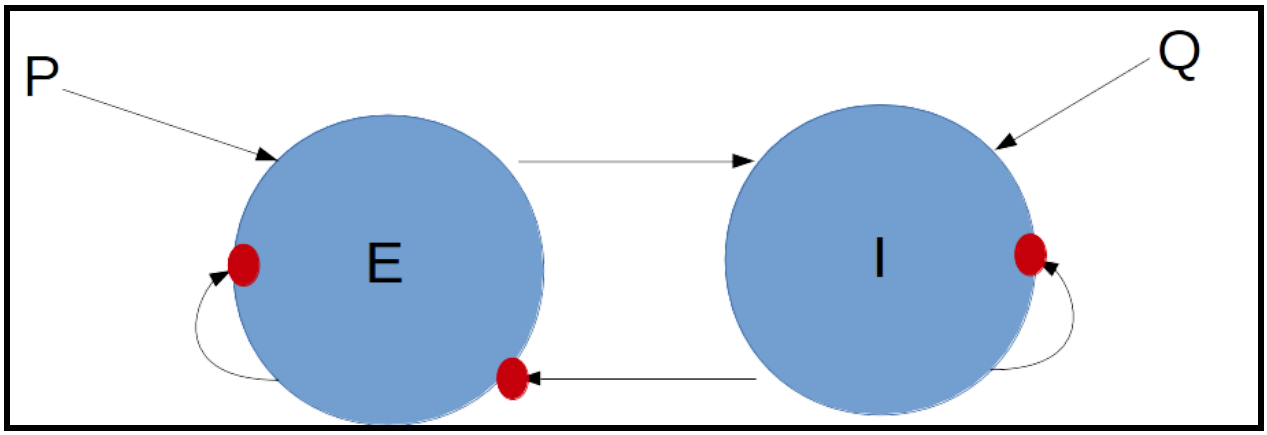


Fig 5. Representation of Wilson Cowan Oscillator. E and I are excitatory and inhibitory populations respectively. P and Q are external inputs. Red dots indicate inhibitory connections.

$$\tau_e \frac{dE}{dT} = -E + (1 - r_e E) S_e(c_1 E - c_2 I + P)$$

$$\tau_i \frac{dI}{dT} = -I + (1 - r_i I) S_i(c_3 E - c_4 I + Q)$$

E and I are the averaged summed activities of the excitatory and inhibitory populations respectively. S_e and S_i represent sigmoidal functions. The argument of the sigmoidal functions is the summation of excitatory/inhibitory populations and external inputs. c_1, c_2, c_3 and c_4 are the respective coupling constants. P and Q are the external inputs to the population(Cowan, Neuman, and van Drongelen 2016).

CHAPTER 3

RESULTS

The aim of the study was to explore the possibility of obtaining regimes of phase amplitude coupling that are independent of any phase frequency modulations and likewise, regimes of phase frequency coupling that are independent of any phase amplitude modulations. While, one previous study has utilized a wilson-cowan oscillator model to explain PAC, it does so by forcing the oscillators around the bifurcation point of the system(Fig 7,Fig 8). Sinusoidal forcing along the critical points leads to robust oscillatory activity in specific phases of the external input but leads to a dampening of frequency(along with Amplitude) in other phases of the input. This should be considered as an instance of phase-amplitude-frequency modulation, where the phase of the low frequency not only modulates the amplitude, but also the spectral content of the higher frequency. Estimation methodologies that rely on bandpass filtering in order to decompose signals in appropriate frequency bands are apt to fail in detecting PAC where the higher frequency shows phasic broad spectrum modulations. To account for this, we performed bifurcation analysis to explore regimes where pure phase amplitude couplings could be obtained. Fig 7. shows the frequency-amplitude characteristic of the Wilson-Cowan Oscillator for a given value of parameters. The shaded areas correspond to regimes where the amplitude of oscillatory response changes significantly while there is relatively narrow band modulation in the frequency response. If the population is forced by external input in this regime, we expect phasic modulation of the power spectra of response with little change in the frequency response. Therefore, this regime corresponds to PAC between the input drive and population response. Next, we generated the population response time series along with the external input (Fig 9). An examination of Fig 8. reveals areas where there is little change in amplitude for relatively broad spectrum changes in frequency. This would correspond to a phase frequency coupled regime . Interestingly, the PAC/PFC regimes occur at either sides of the region of hopf bifurcation, near the critical point. Any phasic modulation in the intervening area would lead to a

scenario reminiscent of phase-amplitude-frequency coupling as discussed in Onslow et. al.(Onslow, Jones, and Bogacz 2014). Next, we used 9 popular metrics from literature to quantify the extent of PAC present in the signal Fig 9. 7 of the 9 metrics were able to detect PAC, while 2 methods Dupra La Tour et. al. and Tort et. al were unable to detect PAC(Dupre la Tour et al. 2017)(Fig 10.).

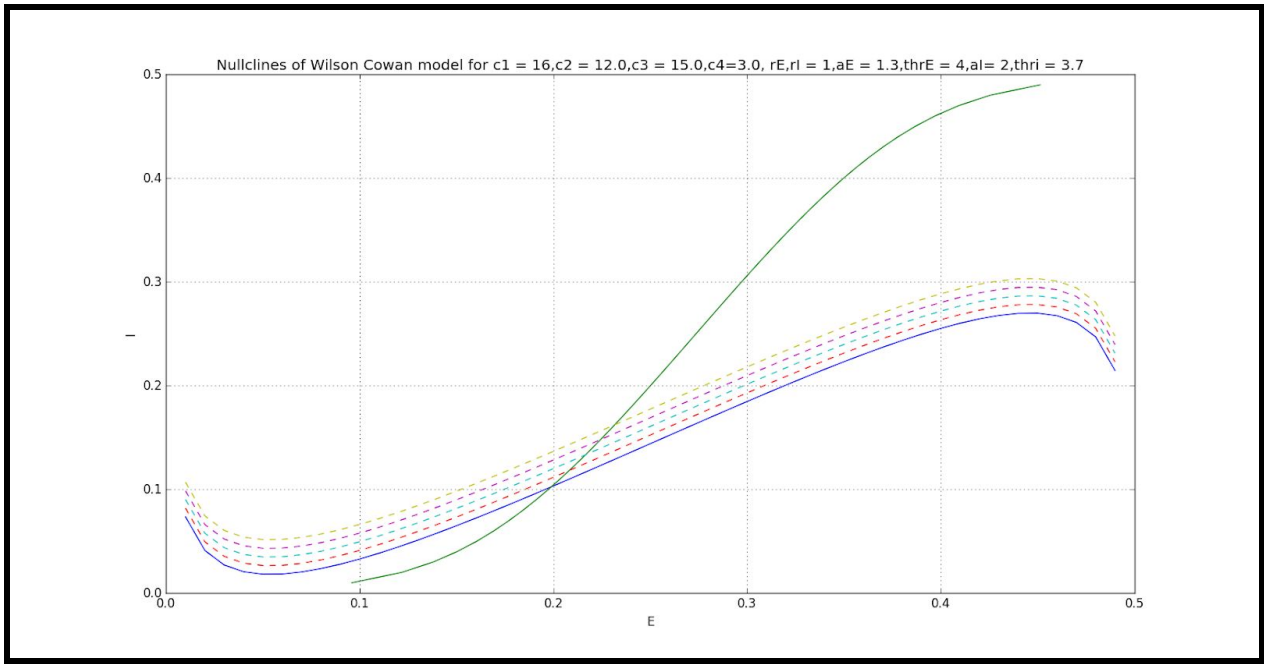


Fig 6. Nullclines for the Wilson Cowan model for

$c_1 = 16.0,\ c_2 = 12.0,\ c_3 = 15.0,\ c_4 = 2.0,\ r_E = 1,\ r_I = 1\ ,\ a_E = 1.3, a_I = 2.0, E_{thr} = 4.0, I_{thr} = 3.7$

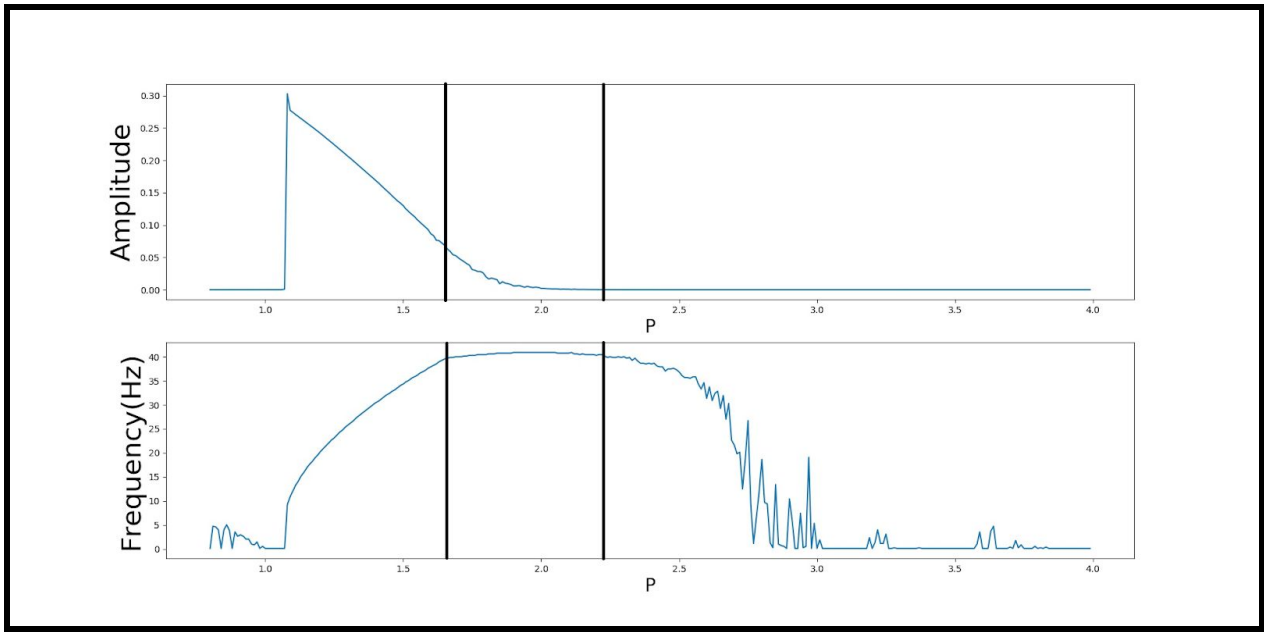


Fig 7. Amplitude and frequency plots as a function of varying the bifurcation parameter(P). Areas enclosed within black lines correspond to regions where there is appreciable change in amplitude without corresponding change in frequency.

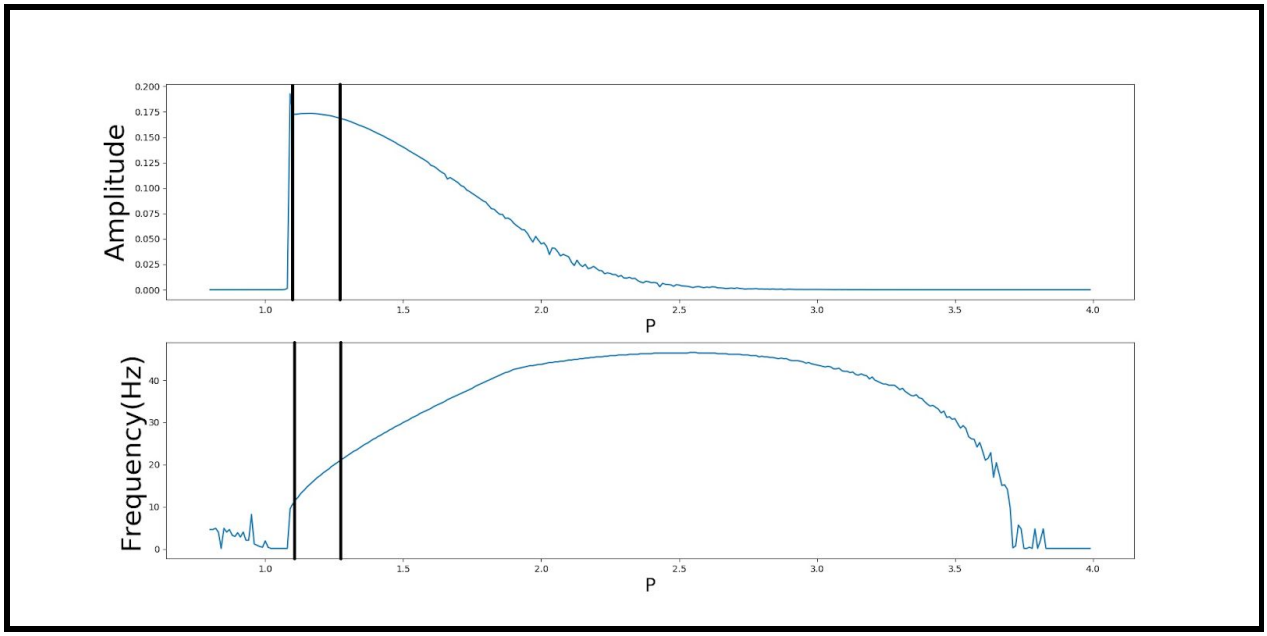


Fig 8. Amplitude and frequency plots as a function of varying the bifurcation parameter(P). Areas enclosed within black lines correspond to regions where there is appreciable change in frequency without corresponding change in amplitude.

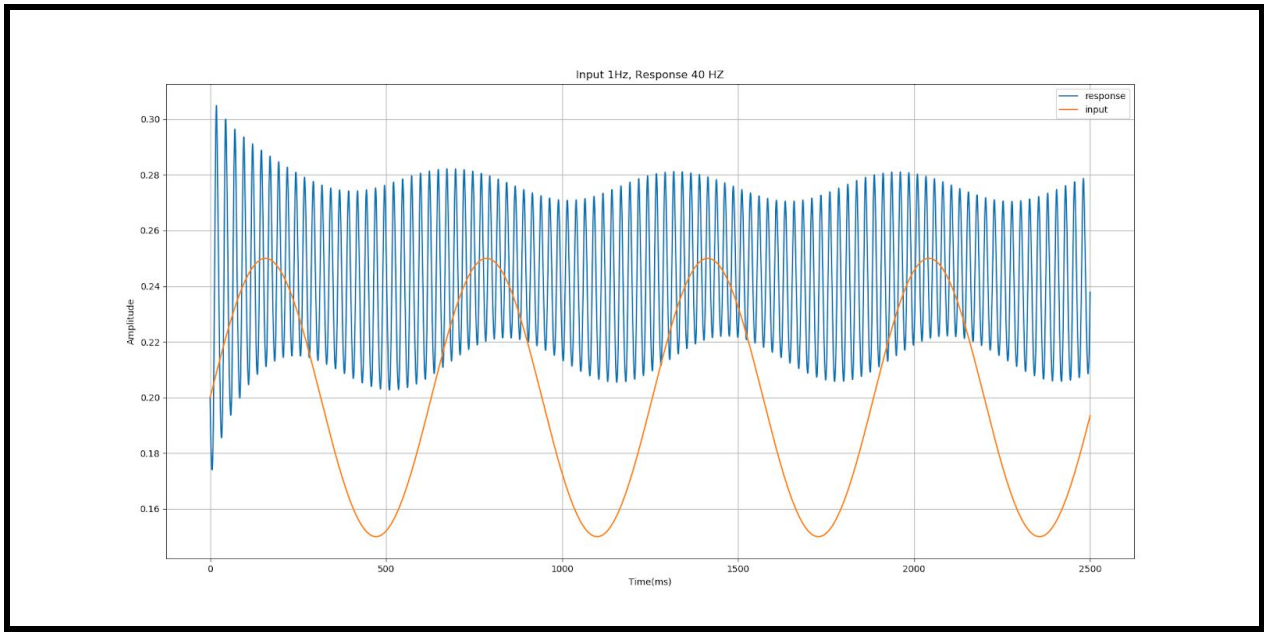


Fig 9. Population Response showing phase amplitude coupling between the input(red) and response(blue)

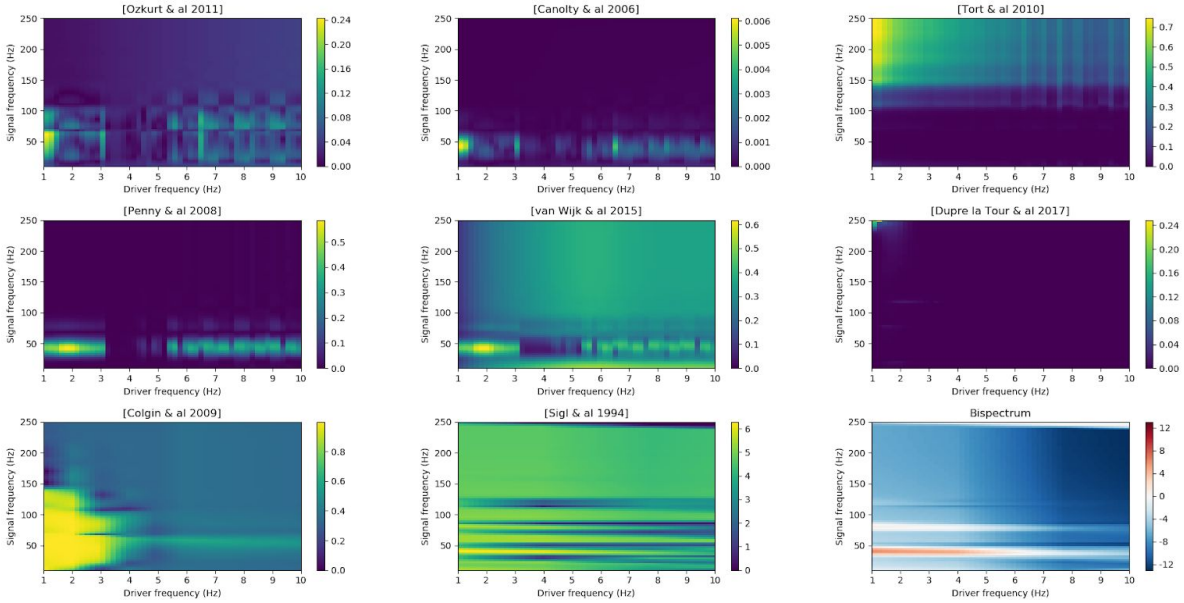


Fig 10. Estimating PAC for signal in Fig.9 by using 9 measures

"You are completely free to carry out whatever research you want, so long as you come to these conclusions."

CHAPTER 4

DISCUSSIONS AND CONCLUSIONS

4.1 Gating by inhibition

According to a recent theory, cortical excitability is regulated by alpha oscillations. Alpha oscillations control the flow of information to task relevant areas by shutting down task irrelevant regions(Jensen and Mazaheri 2010). Several studies have demonstrated a robust increase in alpha power with memory load during the retention interval. According to GBI, alpha increases in magnitude in the posterior regions to shut down areas not involved in encoding the specific memory(Jensen and Mazaheri 2010). Similarly, it has been shown that alpha activity over visual areas increases in motor tasks and vice versa. The phasic modulation in alpha rhythms and therefore, cortical excitability is referred to as pulsed inhibition. The following figure explains how the alpha activity disengages a given region by means of ‘pulsed inhibition’.

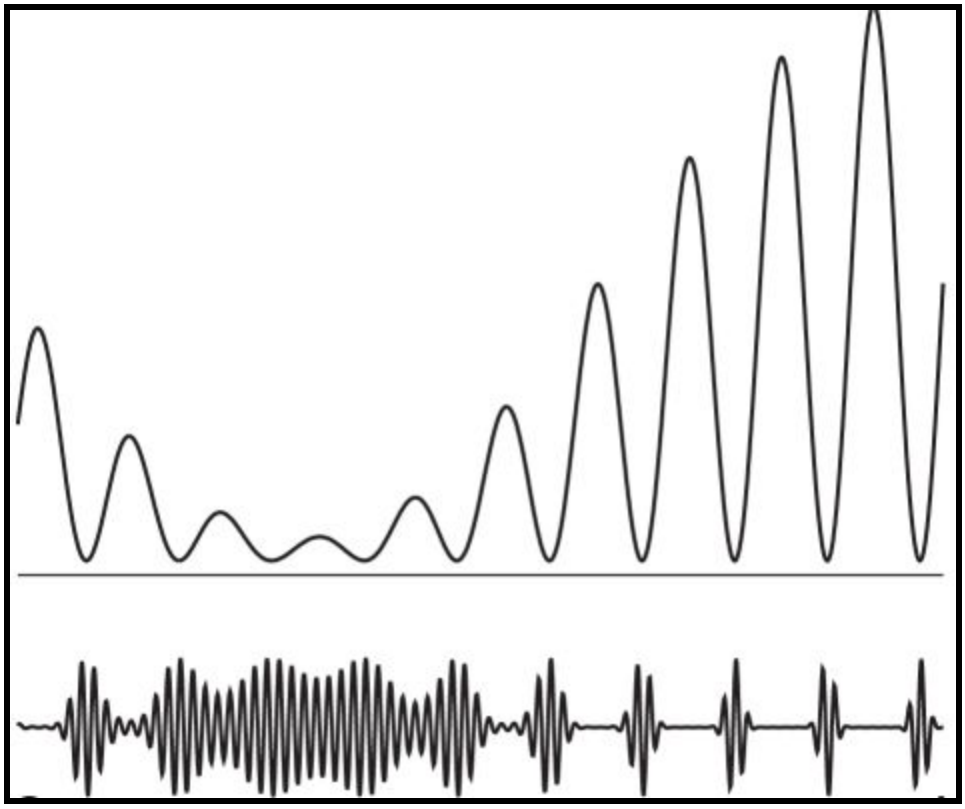


Fig 11. A schematic to show pulsed inhibition between alpha(above) and gamma(below) signal. There is a reduction in the duty cycle of gamma oscillations as the amplitude asymmetry of alpha oscillations is increased .

The upper trace represents an amplitude asymmetric input. An amplitude asymmetric signal is one where the mean of the signal is biased by its magnitude. This corresponds to a rhythmic pulsing(Jensen and Mazaheri 2010).

We explored the possibility of simulating the above scenario using the wilson cowan model. By forcing the system along the hopf bifurcation by an amplitude asymmetric signal yields a scenario similar to the above figure. As the amplitude of the external input increases, the effective ‘duty cycle’ of the population response(gamma) is suppressed, thus representing a

pulsed inhibition. Notice, a relatively small phase shift between the peak input and population response.

Through this we demonstrate that it is possible to simulate pulsed inhibition using the simple Wilson-Cowan model where the fast local activity(gamma) corresponds to the response of the neural population and the slow modulation(alpha) is provided by the external pulse. Moreover, we show that cross frequency interactions arise very naturally from simple oscillatory models involving just two neural populations.

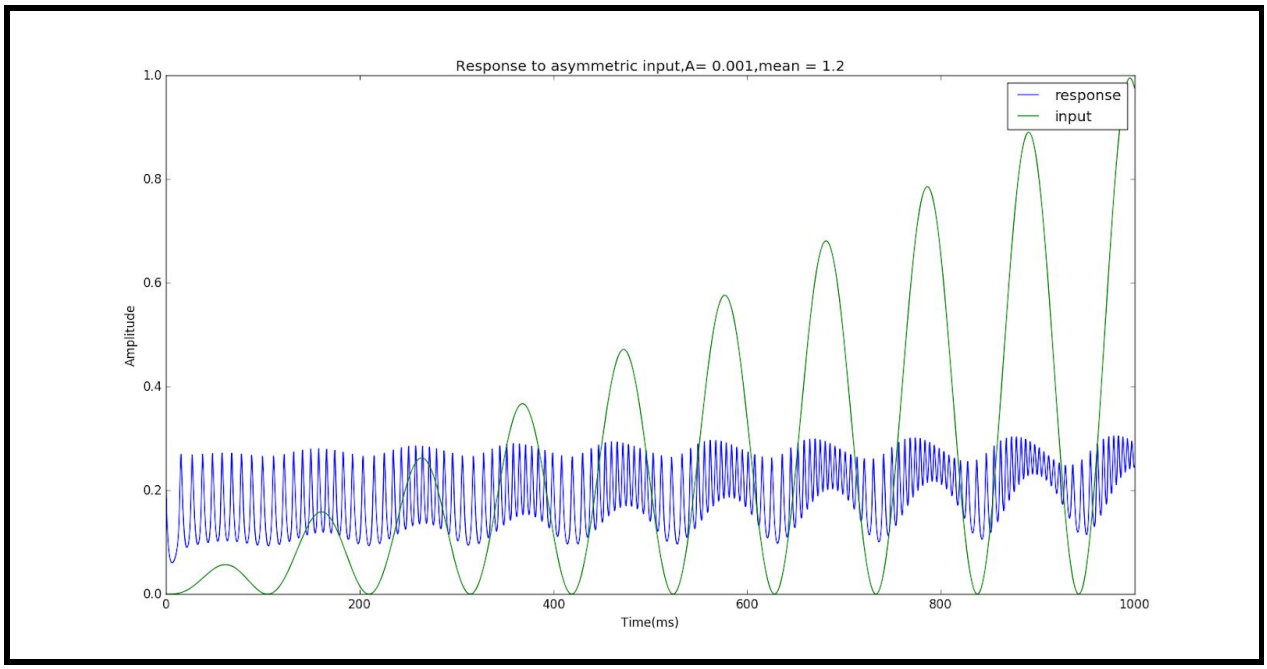


Fig 12. Pulsed Inhibition modelled using Wilson Cowan model

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SUPPLEMENTARY MATERIAL

All simulations were performed using python programming language(v. 2.7.14). PAC estimation was done by using the PAC tools library developed by Dupre la Tour et. al. (Dupre la Tour et al. 2017). Following is the code to obtain Fig 8.

```
"""
@author: Anagh Pathak
"""
import numpy as np
import matplotlib.pyplot as plt
from scipy.integrate import odeint
from scipy import signal
import multiprocessing as mp
import time
import random
import pickle

#Parameters
c1 = 16.0
c2 = 12.0
c3 = 15.0
c4 = 3.0

# refractory periods
rE = 1
rI = 1
''' Functions that define the sigmoids'''
def sigmoid(x, a, thr):
    return 1 / (1 + np.exp(-a * (x - thr)))

def Se(x):
    aE = 1.3
    thrE = 4
    return sigmoid(x, aE,thrE) - sigmoid(0, aE,thrE)

def Si(x):
    aI = 2
    thrI = 3.7
```

```
    return sigmoid(x,aI,thrI) - sigmoid(0, aI,thrI)

''' Function that defines the external forcing'''
def I_mod(t,A,freq):
    return 1.185 + A*np.sin(freq*t)

''' Wilson Cowan Solver'''
def WilsonCowanStatic(y,t,P):
    E = y[0]
    I = y[1]
    y1 = 0.1*(-E + (1.0 - rE * E) * Se(c1 * E - c2 * I + P ))
    y2 = 0.1*(-I + (1.0 - rI * I) * Si(c3 * E - c4 * I ))
    return [y1, y2]

def odesolverWC(P):
    t = np.arange(0,10000,0.01)

    init = [random.random(),random.random()]
    sol = odeint(WilsonCowanStatic,init,t,args = (P,))
    rep_sig = sol[:,0][30000:700000]
    freq,power = signal.periodogram(rep_sig, 100000)
    frq = freq[np.where(power == max(power))]
    amp = max(rep_sig) - min(rep_sig)
    return [amp,frq]

# Write parallel code
# Save data as pickle

if __name__ == '__main__':

    pool = mp.Pool()
    PP = list(np.arange(0.8,4.0,0.01))
    results = pool.map(odesolverWC,PP)
    with open('odesolve.pkl','wb') as f:
        pickle.dump(results,f)

#Open the pickled data
import pickle
import numpy as np
import matplotlib.pyplot as plt

with open('odesolve.pkl','rb') as f:
    res = pickle.load(f)
```

```
PP = list(np.arange(0.8,4.0,0.01))

plt.subplot(211)
plt.plot(PP[:],[i[0] for i in res])
plt.xlabel('P', fontsize = 20)
plt.ylabel('Amplitude', fontsize = 30)
plt.subplot(212)
plt.plot(PP[:],[i[1] for i in res])
plt.xlabel('P', fontsize = 20)
plt.ylabel('Frequency(Hz)', fontsize = 30)
```