MATHEMATICAL MODELING RELATING PSYCHOSOCIAL THERAPY AS A VERITABLE PANACEA FOR BIPOLAR II DISORDER PATIENT

BY

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DECLARATION

I hereby declare that this thesis is my original work and has not been previously presented wholly or in part, for the award of any degree.

……

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CERTIFICATION

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The board of examiners certifies as follows; that to the best of our knowledge, this is the original work of the candidate. That the thesis is accepted in partial fulfillment of the requirements for the award of the degree of Doctor of Philosophy (Ph.D) in Mathematics

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External Examiner	Signature	Date

DEDICATION

To the Holy Spirit my best friend and to all mentally challenged.

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PUBLICATIONS

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ABSTRACT

This study applies mathematical models to emotional variation in patients with bipolar II disorder using dynamical oscillator. Three models of the mood swing are studied and solved using multiple scale perturbation and some numerical simulation. We first incorporated the psychosocial therapy in the forcing function which reveals that if Family and Friends Therapy (FFT) is constructively administered the patient recuperate speedily. The second model studies the effect of HPA axis secretions to the emotional variation of bipolar II disorder patient; it is observed that the increase or decrease of the HPA hormone from the basal level in the body system affects the mood variation of bipolar II disorder patients but should not be used as an etiology maker. Finally, Fractional – ordered oscillator is used to model the mood variation of bipolar II disorder patient to absorb the continuous stressors in the environment that triggers the illness; it is observed that the fractional model brings out a better explaination of the medication parameter (pharmacotherapy and psychotherapy) effect on the amplitude (magnitude) of the mood of the patient with the stressors variation. Generally, it is observed that FFT is of great importance for the recuperation of the patient when combined with administered psychotic drugs both for in the onset of the disorder and the diagnosed patient.

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ABBREVIATIONS

WHO – World Health Organisation

APA – American Psychiatric Association

BD – Bipolar Disorder

BD II – Bipolar II disorder

BD I – Bipolar I disorder

DSM – Diagnostic and Statistical Manual of APA

ICD – International Statistical Classification of Diseases

UNTH – University of Nigeria Teaching Hospital

BC – Before Christ

TR – Text Revision

QID – SR – Quick Inventory of Depressive symptomatology – Self Report scale

ASRM – Altman Self – Rating Mania Scale

CBT – Cognitive Behavior Therapy

ISRT – Interpersonal and Social Rhythm Therapy

FFT – Family and Friends Therapy

CBZ – Carbamazepine

CNS – Central Nervous System

CRH – Corticotropin – Releasing – Hormone.

ACTH – Adrenocorticotropic Hormone

SCN – Suprachiasmatic Nuclei

LG – Longitudinal Analyses

TS – Time Series Analysis

TAU – Treatment As Usual

SCIT – Social Cognition and Interaction Training

HPA – Hypothalamic – Pituitary – Adrenal Axis

TSH – Thyroid Stimulating Hormone

GR – Glucocortisolic Receptors

QoL – Quality of Life

PSR – Physicians for Social Responsibility

CHAPTER ONE

INTRODUCTION

1.1 Background

Often times when mental disorder is mentioned in Nigeria, what comes to mind is the picture of insane men and women with particular spectrum of behaviour not in conformity with ordinary living. It is believed that typical naked and dirty person on the street who picks un-useful things in sight and talks periodically to himself is the ideal person with mental disorder. Several indications show that over 60 million Nigerians have one form of mental disorder or the other with only about 20 per cent of persons in such category are seen to have the obvious forms of it, which includes what the ordinary Nigerian refers to madness, schizophrenia, and perhaps extreme case of drug or alcohol addiction; a reason that has largely made mental disorder in the remaining 80 per cent or 48 million Nigerians ignored or poorly understood (Punch Newspaper, Nov 2018). The World Health Organisation (WHO) in its 2017 World Health Day message says 7,079,815 Nigerians suffer from one of the most ignored and misunderstood form of mental disorder in the country – depression. This represents 3.9 per cent of the entire population; making Nigeria, according to the current prevalence rate [WHO, 2017], the most depressed country in Africa. Unfortunately, this is the worst part of it because the depressed often suffer the ailment alone without a clear signal of help from either the society or even health providers. And when the depression has reached a certain level where they have concluded no one will ever understand them, the next thing is to commit suicide or harm themselves.

Statistics show that Nigeria has only about 150 Psychiatrists to care for over 194 million Nigerians. That is one psychiatrist to 1.2 million Nigerians. It also shows that there are five mental health nurses to 100,000 Nigerians (THISDAY Newspaper, 3rd April, 2017).

Bipolar disorder is a chronic recurrent mental illness (American Psychiatric Association, 2013). The universal health problem of bipolar disorder is alarming: $1-4\%$ of adults live with the condition and present projection suggest that this mental illness accounts for up to 10% of the burden of other mental and substance use disorder (Whiteford, 2013). Bipolar disorder is associated with pathological mood variation including episodes of both elevated mood called mania and extreme low mood called depression, interspersed with less severe but still problematic mood fluctuations or, in some people, relative mood stability (Geddes and Miklowitz, 2013). Mania is a condition in which the patient probably experience racing thoughts, grandiose ideas, delusions and impulsive actions. Under these circumstances, individuals are predisposed to indulge in activities which can be damaging both to themselves and to those around them (Moore et al., 2012). Depression is peculiar with low mood, poor concentration, insomnia; suicidal attempt etc. the annual years of healthy life lost per 100,000 people from bipolar disorder in Nigeria has increased by 2.5% since1990, an average of 0.1% a year [Global Burden of Disease, 2016]. For men, the health burden of bipolar disorder in Nigeria, as measured in years of healthy life lost per 100,000 men peaks at age $18-29$. Women are harmed at the highest rate from bipolar disorder in Nigeria at age $16-29$. In 2013 the peak rate for women was higher than that of men (300.3 per 100,000 women against 233.8 per 100,000 men) (Global Burden of Disease, 2016). Younger age of disease onset is associated with higher suicidal risk, with lifetime suicide attempt rates estimated between $20-47\%$ (Goldstein et al., 2017). The prevailing alarming rate is as such that bipolar disorder has the highest rate of suicide across all psychiatric disorders (Hawton et al., 2005).

The neurobiology of bipolar disorder understanding is greatly underpinned/low, and the long – term pharmacological interventions which are standard treatment always result to poor clinical responses (Geddes and Miklowitz, 2013; Goodwin, 2014). There have been no

significant clinical advances since the use of Lithum in the $1950s$ (Bonsall et al., 2015). Fortunately, the good news is; bipolar disorder can be treated, and people with this illness can lead full and productive lives (Sachs and Thase, 2000; Huxley et al., 2000). Observation has shown that bipolar can be rather erratic, there exist patterns of recurrence to the episodes. Progress has been made on the explanation of the mechanism and the development of treatments, the molecular and cellular bases of bipolar disorders remain unknown (Soares and Young, 2007, Barnett and Smoller, 2009). Many studies explained the involvement of neural circuits located in the prefrontal cortex with connections in the thalamus (Blumberg et al.; 2017, Chepenik and Blumberg, 2010; Womer et al., 2009). These psychopathological patterns are accompanied but apparently not correlated with variations of concentration of biological parameters such as the blood plasma cortisol level: the mood of depressive patients is better in the evening whereas cortisol usually exhibits a diurnal rhythm with a higher level in the morning than in the evening hours.

This affective instability or disorder poses peculiar problems to temporal clinical practitioners; ranging from difficulty in diagnosing, stigma of mental illness, patient non – compliance to treatment and/or medication, and the toxicity of most of the drugs if taken individually (Frank et al., 2000). Consequently, there is a deficiency in data pertaining bipolar disorder, in part because of a lack in concordance on well – suited trial design. Hence, bipolar disorder is very difficult to study using clinical trials only (Robert and David, 2009). For a patient with this affective disorder, there is a periodicity which governs the manic and depressive episodes (Strakowski and Delbello, 2003). Understanding of the complex and dynamics of temporal mood variability in bipolar disorder leads to the use of quantitative methods. The variability in mood provides a basis for developing mathematical approaches based on limit cycle oscillators (Nana, 2009; Daugherty et al., 2009, Goldbeter, 2011, 2013; Wirkus and Porter, 2009) to appreciate the dynamics of this mental health disorder.

1.2 AIM AND OBJECTIVES

Our aim is basically to propose mathematical models that attempt to represent the qualitative dynamics of bipolar disorder patients and analyze then quantitatively. To actualize this veritable goal we

i. Propose dynamic models for bipolar II disorder,
ii. Solve the proposed models analytically,
iii. Show the dynamics of the mood swings assuming the existence of an oscillator (Cortisol Secretion) that is capable of explaining the observed behavior of bipolar patient,
iv. Study the mood variation of bipolar patient using fractional derivative and
v. Examine the efficacy of psychosocial therapy to bipolar II disorder patient.

1.3 THE SIGNIFICANCE OF THE STUDY

The significance of this study can never be over emphasized; it creates a new dimension of research consideration of the mood variation of the bipolar II disorder patients. It explores the leverage between the clinical practices and analytical methods that is a leeway to the complexities of human compositions. The results of this research can be used by the clinicians and pharmacist for pharmacotherapy of patients of bipolar II disorder, which shall bring back the ever illuminating interpersonal relationship of extended families. This work also explores the management of affective disorder as it relates to the environment and the society as a greater factor for the onset and exasperating factor.

1.4 SCOPE OF STUDY

Biological models for this medical condition is in existence, however mathematical equations have not been employed majorly to study of bipolar individuals; except handy researchers like ((Nana, 2009; Daughertty et al., 2009, Goldbeter, 2013). In this work, mathematical models of bipolar II disorder is proposed and analyzed, focusing basically on the dynamics of our models under the proposed treatment strategy, which is understood to involve a combination of psychopharmacological and/or psychotherapeutic (American Psychiatric Association, 2013, Daughertty et al., 2009); neglecting diagnostic approach which is a difficult clinical problem. The Diagnostic and Statistical Manual of the American Psychiatric Association DSM – IV – TR and ICD – 10 provide the keys for diagnostic guidance. The cause of the affective disorder is uncertain; widely believed that it results from many factors, which includes genetics, environment, abnormality in the endocrine secretion in the basal regime and circadian rhythm abnormality. In the course of our study the genetic causative which has about 35% chance of the offspring of people with bipolar II disorder being afflicted is relaxed (Daughertty et al., 2009, Duffy et al., 2000). Minimalist models of this sort are not intended to suggest the mechanisms especially in situations, like this, one with unknown or poor understanding.

1.5 THESIS STRUCTURE

Chapter 1 introduces the thesis and sets the motivation of the research. Chapter 2 is a literature review of bipolar disorder, the works on time series analysis of the disorder and the mathematical models of bipolar disorder proposed by different researchers.

Chapter 3 is about the mood modeling of chaotic intermittency exhibited by the patient's mood using Duffing oscillator that is the extension of the paper *Mathematical model of bipolar diosorder* (Daughertty et al., 2009). The introduction of psychosocial parameter as

one of the parameter in the forcing function is considered to accommodate Family and Friend Therapy (FFT) as a treatment option.

Chapter 4 addresses the question of whether Hypothalamic – Pituitary – Adrenal (HPA) axis activities can be used as a state maker for the onset of bipolar II disorder. It is an application of the paper *Modeling the HPA axis: a review and extension* (Hessemchimch et al., 2015) to bipolar disorder. Our result was validated by (Belvederi et al., 2016) published in Psychoneuroendocrinology.

Chapter 5 applies fractional calculus to modeling of mood variation of bipolar II disorder patient. It is the application of the paper *Forced vibrations of a nonlinear oscillation with weak fractional damping* (Rossiklin et al., 2009) to bipolar disorder patient. The paper (McIntyre et al., 2013) was used to validate our claims.

Chapter 6 is a general discussion of our findings and Chapter 7 is the summary and conclusion of the entire study.

CHAPTER 2

2.0 LITERATURE REVIEW

2.1 BIPOLAR DISORDER

Bipolar disorder (BD), also known as manic depression, is classified as a type of affective disorder or mood disorder that goes beyond the day's ordinary ups and downs, and is a serious medical condition and important health concern in the country (UNTH, 2017). BD is a condition affecting mood and featuring recurrent episodes of mania and depression which can be severe in intensity. Mania is a condition in which the sufferer might experience overly inflated self – esteem, decreased need for rest and sleep, increased distractibility and irritability, increased physical agitation, increased talkativeness, excessive euphoric feelings, increased sex drive, increased energy level, uncharacteristically poor judgment etc. Depression is characterized by persistent sad, anxious or empty mood; loss of interest in activities once previously enjoyed, excessive crying, increased restlessness and irritability, decreased energy, thoughts of death or suicide, or suicide attempts, increased feeling of guilt, changes in sleep pattern and social withdrawal. Both states are characterized by conspicuous changes in energy and activity levels which are increased in mania and decreased in depression (Moore et al., 2012).

The severity of mood swings is individually based. Using clinical data, it is shown that many people with BD have long periods of normal mood when they are unaffected by their illness while others experience rapidly changing moods or persistent low moods that adversely affect their quality of life (Judd, 2012). Sometimes, the patient experiences mixed episode which occur if the person experiences symptoms of mania and depression at the same time or at close intervals. The patient may also experience under developed mania called hypomania which is characterized by an increase in activity and little need for sleep. Hypomania is

generally less harmful than mania and individuals undergoing a hypomanic episode may still be able to function effectively.

2.1.1 TYPES OF BIPOLAR DISORDER

The classification of mental illness dates back to the Greeks. The initial taxonomies, for instance the Ayur Veda (Jamison, 1996), a system of medicine current in India around 1400 BC, were grounded on a supernatural world interpretation. Hippocrates (460-377 BC) was the first to provide naturalistic categories (Geddes, 2013). He identified both mania and melancholia, concepts which are related to, though extensive than the contemporary day equivalents. The modern system of nosology is based on the work of the German psychiatrist Emil Kraepelin (1856-1926). His approach was to group illnesses by their course and then find the permutation of symptoms that are concommitant. The first attempt at an international classification system was made in 1948 when the World Health Organisation added a section on mental disorders to the Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death (ICD – 6). This section was not widely adopted and the United States in particular did not use it officially. An alternative was published in the US, the first edition of The Diagnostic and Statistical Manual of Mental Disorders *(DSM – 1)*. Development of the ICD section on mental disorder continued under the guidance of the British psychiatrist Erwin Stengel, and this later became the basis for the second revision of the DSM. Both texts continue to be developed, and while the latest revision of the ICD section *(ICD-10)* is more frequently used and more valued in a clinical setting, DSM-IV is more valued for research (Vladimir and Raison, 2014). Having been through five revisions, the most commonly used version of the DSM was published in 2000, and is referred to as DSM-IV Text Revision (DSM-IV-TR). A more recent version, DSM-V, was published in 2013.

The DSM – IV – TR provides a framework for assessment by organizing mental disorders along five axes or domains.

DSM – IV – TR Axis	DISORDER
Axis I	Clinical Disorder
Axis II	Developmental and personality disorders
Axis III	General medical condition
Axis IV	Psychosocial and environmental factors
Axis V	Global Assessment of functioning

Table 2.1 Diagnostic Axes from the DSM – IV – TR framework (American Pyschiatric Association (APA), 2000).

Axis IV lists psychological stressors or stressful life events that the individual has recently faced: individuals with personality or developmental disorders are likely to be more sensitive to such events; they form the background to the disorder under discussion. DSM – IV – TR defines four subtypes of bipolar disorder and these are summarized in Table 2 . 2

SUBTYPE	CHARACTERISTICS
Bipolar I Disorder	At least one manic episode which lasts at least seven days, or manic symptoms that are so severe that the person needs immediate hospital care. Usually, the person also has depressive episodes, typically lasting at least two weeks.
Bipolar II Disorder	Characterized by a pattern of at least one major depressive episode with accompanying hypomania. Mania does not occur with this type.
Cyclothymia	Characterized by a history of hypomania and non – major depression over at least two years. People who have cyclothymia have episodes of hypomania that shift back and forth with mild depression for at least two years. Has few intervening euthymia.
Bipolar NOS	A classification for symptoms of mania and depression which do not fit into the categories above.

Table 2 . 2: DSM – IV – TR Bipolar disorder subtypes (APA, 2000).

2.2 Rating Scales

Rating scales may be premeditated either to yield a diagnostic judgment of a mood disorder or to make available a measure of severity. The former categorical methodology tends to adhere to a current nosology such as documented in DSM-TR-IV and consists of examinations administered by the clinician or schedules. Such diagnostic tools are imperative for determining eligibility for treatment and help from social services. Measurements of severity are important for management of a condition, and for research. Dimensional instruments may be administered by the clinician or the patient and are designed or adapted for either use. The two scales used in this study are described next, one measuring depression and the other mania.

A rating scale used for depression is the Quick Inventory of Depressive Symptomatology - Self Report *(QIDS-SR*16*)* (Rush, 2003) which comprises 16 questions. This self – rated instrument has acceptable psychometric qualities including a high validity (Rush, 2003). Its scale assesses the nine DSM-IV symptom domains for a major depressive episode, as shown in Table 2.3. Each inventory category can contribute up to 3 points and the maximum score for each of the 9 domains is totaled, giving a total possible score of 27 on the scale. Most scales for mania have been designed for rating by the clinician rather than for self – rating because it was thought that the condition would vitiate accurate self-assessment. However, some self – rated scales for mania have been assessed for reliability (self-consistency) and validity (effectiveness at measurement) (American Association of Psychiatrist, 2013). The Altman Self-Rating Mania Scale (ASRM) is comprised of 5 items, each of which may contribute up to 4 points, giving a total possible score of 20 on the scale. For both depression and mania ratings, a score of 0 corresponds to a healthy condition and higher scores correspond to worse symptoms. The schema for mania and depression are shown below

QIDS Category (Depression)	ASRM Category (Mania)
Sleep (4 Questions)	Feeling happier or more cheerful than usual
Feeling Sad	Feeling more self – confident than usual
Appetite/Weight (4 Questions)	Needing less sleep than usual
Concentration	Talking more than usual
Self – View	Being more active than usual
Death/Suicide	
General Level	
Energy Level	
Slowed down/Restless (2 Questions)	

Table 2.3: Rating scales for depression and mania.

2 . 3 NEUROBIOLOGY OF BIPOLAR DISORDER AND TREATMENT

BD is a complex medical condition whose etiology involves genetic and epigenetic factors acting alongside environment stresses in causing expression of the disease (Pregelj, 2011). Despite significant advances in the understanding of the underlying neurobiology of BD, its timely diagnosis and efficient treatment remain daunting clinical challenges (Vladimir and Raison, 2014). In addition to progressive risk of suicide, BD is also associated with considerable medical comorbidities, including cardio and cerebrovascular disease, and metabolic and endocrine disorders, which, when combined with neuropsychiatric morbidity and suicidality, have been found to cut life expectancy by an average of 11 years in female and 10 years in male afflicted with bipolarity (McIntyre, 2004; Chang et al., 2011). There is convincing evidence of crosstalk between different biological systems that act in a deleterious manner causing expression of the disease in genetically predisposed individuals (Muneer,

2016). Treatment of BD includes both psychological therapy – cognitive behavior therapy (CBT), interpersonal and social rhythm therapy (IPSRT), Family focused therapy (FFT), group psychoeducation and medication to stabilize mood. Drugs usually used to treat BD are antimanic and antidepressant. Antipsychotic or anticonvulsants (olanzapine, quetiapine, risperidone, ziprasidone etc.), Lithium, valproate, carbamazepine (CBZ) are prescribed to treat episodes of mania or hypomania (National Institute for health, 2006, APA, 2013, Smith et al., 2007). Conventional antidepressants (imipramine, fluoxetine, tranylcypromine) and atypical antipsychotic agents like olanzapine, quetiapine, lamtrigine are used for depression episode (APA, 2013; Castberg et al., 2007; Suppes e. al., 2008). All medication must be taken on the prescription of a physician; some of the antipsychotics are monotherapeutic.

2. 4 HPA AXIS

Bipolar disorder is associated with abnormalities of hypothalamic – pituitary – adrenal axis activity, with unclear pathophysiological role (Dadan et al., 2005; Martino et al., 2016). The HPA axis is one of the main biological systems responsible for stress. Its main byproduct, cortisol, exerts fundamental homeostatic and allostatic effects on cognitive and affective processes in responses to environmental stimuli, ultimately shaping the central nervous system (CNS) structures along the lifespan (Martino et al., 2016; McEven, 2007). The hyperproduction of cortisol in Cushing's disease leads to depressive, manic symptoms and neurocognitive deficits (Marques et al., 2009; Andela and Halen, 2015; Martino et al., 2016). During stressed situations, the HPA axis plays an essential part in increasing the concentration of the HPA axis hormones: Corticotropin – Releasing – Hormone (CRH), Adrenocorticortropic Hormone (ACTH) and cortisol, which leads to energy being directed to the organism. The hormonal concentration has been correlated to depression when it is in the state of hypercortisolism (Anderson et al., 2013; Peter et al., 2004). The cortisol concentration has a circadian rhythm. It is observably low between 8: 00 pm and 2:00 am;

and peaks in the period 6:00 – 10: 00 am (Carroll et al., 2007; Griffin and Ojeda, 2004). Hence there is a possibility of oscillations that cause successive production of hormones with self – regulatory cortisol.

2.5 CIRCADIAN RHYTHMS

Circadian rhythms are physical, mental, and behavioral changes that follow a daily cycle which are greatly photosensitive. Physiological and behavioral circadian rhythms are maintained by a biological timekeeping capability that evolved in most of life on earth (Li et al., 2013). Circadian rhythm and mood fluctuation are stable against perturbations in the healthy state because of its ability of adjusting to alter internal cues or ongoing changes in external conditions. BD patients describe sleep – wake disturbance across episodes of both mania and depression. Long – term monitoring of BD patients behavior describes changes to sleep and daily rhythms that appear as part of a characteristic prodrome of BD (Zeschel et al., 2013; Brietzke et al., 2012). The premises suggest that sleep – wake or circadian rhythms disruption may be comorbid in the aetiology and development of mood episodes. The standard view is that the circadian clock is a hierarchically organized system, governed by the suprachiasmatic nuclei (SCN) in the hypothalamus. SCN consists of about 20,000 neurons that are coupled to each other and are entrained by light to oscillate in synchrony to the 24 hours earth rotation (Westermark et al., 2009)

2.5.1 CIRCADIAN AS MOOD CONTROLLER

Clinical findings on affective disorders highlight a great connection to circadian rhythm disruption alongside potential genetic and neurobiological mechanisms that contribute to the pathophysiology and aetiology of BD (Moore et al., 2012). The misalignment of circadian rhythms through sleep deprivation, shift work and jetlag can have a negative impact on mood,

with increased risk of depression and low mood states (Srinivasan, 2009; Levandovski, 2011).

2.6 MATHEMATICAL MODELS

Mathematical models deals with the mathematical description of biological process but not limited, that can offer frames of understanding that reconcile opposed points of view in diagnostics, or they can establish the key notions in understanding particular processes. These mathematical models can provide insights into the dynamics of bipolar disorder with assimilating data.

2.6.1 NONLINEAR OSCILLATORS

Daugherty et al. (2009) use a theoretical model based on low dimensional limit cycle oscillator to describe mood in bipolar II disorder patients. They were interested in the dynamics of bipolar II disorder rather than to model real data. Daugherty et al. model the mood of a treated individual with a Van der Pol oscillator

$$y'' - \alpha y' + \omega^2 y - \beta y^2 y' = g\left(y, y'\right) \tag{2.1}$$

where y represent the patient's mood rating, y' is the rate of change of mood rating with time, β determines amplitude and α, ω determine damping and frequency respectively. Treatment is modeled as autonomous forcing function $g\left(y, y'\right) = \gamma y^4 y'$ which represents all treatment, including mood stabilizers, antidepressants and psychological therapies. In an untreated individual $g\left(y, y'\right) = 0$. The existence of limit cycles is analyzed with respect to parameter values α, β and γ and the biologically relevant situation of two limit cycles is found when $\beta/\gamma < 0$ and $\beta^2 > 8\alpha\gamma > 0$. Daughterry and his co-authors propose generalizations of their limit cycle modeling of bipolar disorder, including an analysis of the

bifurcations that occur in their models and an improvement to model the delay in treatment taking effect. They suggest that employing their modeling framework along with clinical data will lead to a significantly improved understanding of bipolar disorder. Mohan (2007) studied the model of bipolar mood disorder, using

$$y'' - b\left(a - y^2\right)y' + cy = sy + dy'. \tag{2.2}$$

Daughterry et al. (2009) also introduced Lienard oscillator which is of the form

$$y'' + f\left(y\right)y' + h\left(y\right) = g\left(y, y'\right). \tag{2.3}$$

The forcing function $g\left(y, y'\right)$ is configured according to whether a patient is treated or untreated.

2.6.2 TIME SERIES ANALYSES

Many researchers have studied the dynamics of depression in bipolar disorder using time series analysis techniques. Bonsall et al. (2012) applied this method at the Department of Psychiatry in Oxford for 220 weeks, on which they divided the patients into two groups: stable and unstable. They found out that there were underlying deterministic patterns in the mood dynamics and suggested that the models could characterize mood variability in patients.

The paper by Gottschalk *et al.* (1995) dealt with 7 patients having a rapid-cycling course. Data was sampled on a daily basis in contrast to this study and to Bonsall *et al.* (2015) where weekly data is used. Gottschalk *et al.* (1995). used a surrogate data approach with nonlinear time series techniques to study the dynamics of depression. They also examined mood power spectra for patients and controls. They found a difference between the power spectral decay with frequency for patients and controls. They also found a difference in the correlation

dimension for these two groups. From these findings, they inferred the presence of chaotic dynamics in the time series from bipolar patients.

2.6.3 COMPUTATIONAL PSYCHIATRY

Computational psychiatry is area of psychiatry that attempts to apply computational modeling to phenomena in psychology and neuroscience. This area of study includes reinforcement learning (Dynamic programming (Sutton and Barto, 1998), Markov decision process (Bellman , 1957); value functions etc.

2.6.4 DATA ANALYSES

Most of analyses of mood in bipolar disorder have been qualitative: Individuals under study are likely to be outpatients; their general functioning most often are variable and heterogeneous across the cohort, hence resulting to a difficult quantitative data collection. The task involved in collecting mood data from patients with bipolar disorder has influenced the kinds of study that have been published. The table below shows some data analyses survey

Authors	Subjects	Analysis	Scale	Mood Metrics
Wehr (1979) et al.	BP1/2 (n = 5)	LG	Bunney – Hanburg	None
Gottschalk (1995) et al.	BP1 (n = 7)	TS	100 Point Analogue	Linear/ Nonlinear
Judd (2002)	BP1 (n = 146)	LG	PSR Scales	Weeks at level
Judd (2003) et al.	BP2 (n = 86)	LG	PSR Scales	Weeks at Level
Glenn (2006) et al.	BP1 (n = 45)	TS	100 Point Analogue	Approximate entropy
Bonsall (2012) et al.	BP1/2 (n=23)	TS	QIDS – SR	Linear, Nonlinear
Moore (2012) et al.	BP1/2 (n = 100)	TS	QIDS – SR	Linear, Nonlinear
Moore (2014) et al.	BP1/2 (n = 100)	TS	QIDS – SR	Linear, Nonlinear

Table 2.4: Analyses of mood in bipolar disorder.

The article by Wehr and Godwin uses twice daily mood ratings for five patients. Judd (2003) and Judd *et al.* (2002) measure patients' mood using the proportion of weeks in the year when symptoms are present. This kind of measurement lacks the frequency and the resolution for time series analysis. The scarcity of suitable data has also constrained the kinds of measure used for analysis of mood. Until recently the primary measures used have been the mean and standard deviation of the ratings from questionnaires (Pincus, 2003), although other measures have been used. Pincus (2003) has introduced approximate entropy which is a technique used to quantify the amount of regularity and the predictability of fluctuations in time-series data. It is useful for relatively small datasets and has since been applied to both mood data generally (Yeragani et al., 2003) and to mood in bipolar disorder (Glenn et al., 2006); in the latter case, 60 days of mood data from 45 patients was used for the analysis. Gottschalk *et al.* (1995) analysed daily mood records from 7 rapid cycling patients with

bipolar disorder and 28 normal controls. The participants in this study kept mood histories on a daily basis over a period of 1 to 2.5 years. The mood charts were gaged for periodicity and correlation dimension and they inferred the presence of nonlinear dynamics, a claim that was later challenged by (Krystal, 1998) and defended in (Gottschalk et al., 1998).

2.7 PSYCHOSOCIAL THERAPY

It has been solidly shown that BD has an uncomplimentary outcome in a considerable number of patients, in spite of the recent advances in its pharmacological treatment (Fountoulakis et al. 2012 ; Grunze et al. 2013). Many BD patients eventually suffer from chronic mood symptoms with significant global disability and burden, not only for themselves but also for their family and the society (Murray et al. 2012; Rosa et al. 2010). The overall functional outcome can be captured mainly by two dimensions representing clinical severity and cognitive dysfunction (Reinares et al. 2013). Unfortunately, symptomatic remission does not imply functional recovery which is absent in a significant number of clinically and symptomatically remitted patients (Tohen, 2017 ; Rosa et al. 2011). Pharmacological treatment often fails to address all the patients' needs and there is a growing need for the development and implementation of effective and affordable interventions, tailored to the individual patient (Catala-Lopez et al. 2013). Early successful treatment, with full recovery if possible, is of prime importance for the long-term outcome. It has been clearly shown that subsyndromal symptoms together with psychosocial stress at baseline are factors predicting earlier relapse (De Barros et al. 2013). Longitudinal studies show that poor adherence is also predictive of a poorer long-term outcome (Berk et al. 2010). There are several specific adjunctive psychotherapies which have been developed with the aim to fill the above gaps and eventually to improve the illness outcome (Geddes and Miklowitz 2013). It is still unclear which psychotherapies truly work and which patients are eligible. The time

of intervention is also an open question (De Barros et al. 2013; Reinares et al. 2014). Acute depression and the maintenance phase but not acute mania are at the centre of research. Concerning the quality of the data available, the studies in BD patients suffer from the same limitations and methodological problems all psychotherapy trials do. There is no universally accepted standardized method to conduct this kind of studies and blindness and the nature of the control intervention are unresolved limitations.

2.7.1 Cognitive-Behavioural Therapy (CBT)

CBT for BD includes education about BD as a diathesis – stress illness, enhances the cognitive-behavioural skills to cope with prodromes, stresses the importance of routine excersise and sleep. CBT deals with cognitive and behavioural barriers to treatment adherence and guides the patient towards the identification of triggering factors and the dealing with long-term vulnerabilities. It also challenges dysfunctional thoughts and underlying maladaptive assumptions. There are a small number of studies which investigate the usefulness of CBT in BD. All of them utilize CBT as adjunct treatment on pharmacotherapy and all have inadequate placebo conditions as control.

The first study on CBT in bipolar depression included 103 BD-I patients and randomized them to 14 sessions of CBT or a control group which however did not include any placebo condition. During a 12-month period, fewer patients in the CBT group relapsed in comparison to controls (44 % vs. 75 %). Also, patients in the control group had shorter duration in an episode, less admissions and mood symptoms and higher social functioning (Lam et al. 2003). However, the report of an extension (18-month follow-up) reported no effect of CBT on the relapse rate (Lam et al. 2005b).

Another study on 52 BD patients confirmed this loss of efficacy during the follow- up in a study which compared CBT plus additional emotive techniques vs. treatment as usual

(TAU) (Ball et al. 2006). The comparison of CBT plus psychoeducation vs. TAU in 40 BD patients reported a beneficial effect even after 5 years in terms of symptoms and social–occupational functioning, but rate of recurrences and time to recurrence were not reported (Gonzalez – Isasi et al. 2012). CBT plus psychoeducation has been proven superior to psychoeducation alone in a study of 79 BD patients (52 BD-I and 27 BD-II). In that study, the combined treatment group had 50 % fewer depressed days per month, while at the same time the psychoeducation alone group had more antidepressant use (Zaretsky et al. 2008). Similar results were reported from a study in 41 BD patients randomized to CBT vs. TAU. The results suggested an improvement in symptoms, frequency and duration of episodes (Costa et al. 2011).

2.7.2 Psychoeducation

Psychoeducation for BD includes training of patients regarding the overall consciousness of the disorder, the treatment adherence, the ducking of substance abuse as well as the early detection of new episodes. It also focuses on regular habits and stress management. One of the first studies concerning the teaching of patients to recognize and identify the components of their disease and especially early symptoms of relapse and recurrence and to seek professional help as early as possible followed 69 patients for 18 months and compared psychoeducation to TAU and reported important prolongation of the time to first manic relapse ($p = 0.008$) and significant reductions in the number of manic relapses over 18 months ($30\ \% \ vs. 52\ \%;\ p = 0.013$). The experimental treatment had no effect on time to first relapse or number of relapses with depression, but it significantly improved overall social functioning. It is important to note that the psychoeducation method included a limited number of sessions (7–12) (Perry et al. 1999).

2.7.3 Interpersonal and Social Rhythm Therapy (IPSRT)

IPSRT is based on the proposition that traumatic life events and disrupted daily routines can lead to circadian rhythm instability and, in exposed individuals, to affective episodes (Reinares et al. 2014). It includes the management of affective symptoms through improvement of adherence to medication and stabilizing social rhythms and the resolution of interpersonal problems (political instability, unresolved grief, social role transitions, interpersonal role disputes, interpersonal deficits, grief for the lost healthy self etc).

There are only limited data concerning its usefulness. The first study included 175 acutely ill BD patients and followed them for 2 years. The trial involved four treatment groups depending on the combination of treatment and phase, that is, IPSRT vs. intensive clinical management during the acute and the maintenance phase. Overall, the data suggested there was no difference between IPSRT and intensive clinical management in terms of time to remission and in the proportion of patients achieving remission (70 % vs. 72 %). A positive finding was that those patients who received IPSRT during the acute treatment phase survived longer without an episode and show higher regularity of social rhythms (Frank et al. 2005). Regarding psychosocial functioning, the results suggested that those who initially received IPSRT especially women showed faster improvement in occupational functioning, but again there were no differences between groups at the end of the follow-up (Frank et al. 2008). More recently (Swartz et al. 2012), a 12-week study in which unmedicated depressed BD-II patients were randomized to IPSRT ($N = 14$) vs. treatment with quetiapine (up to 300 mg/day; $N = 11$) showed that both groups experienced significant reduction in symptoms over time, but there were no group – by – time interactions. Response and dropout rates were similar.

2.7.4 Family and Friends Therapy.

Family intervention for BD includes psychoeducation, communication enhancement and problem-solving skills training, as well as support and self-care training for caregivers. Family intervention targets the whole family and not only the patient. There are significantly more studies on the possible usefulness of family intervention in BD patients. The importance of involving the whole family in the treatment intervention was highlighted in a study of 81 BD patients and 33 family dyads, which reported that the odds ratio for hospitalization at 1-year follow-up was related with high perceived criticism (by the patients from their relatives), poor adherence and the relatives' lack of knowledge concerning BD (OR 3.3; 95 % CI: 1.3 - 8.6) (Scott et al. 2012).

Several studies support the use of adjunctive family-focused treatment. One intervention design consists of 21 one-hour sessions which combine psychoeducation, communication skills training and problem-solving training. The sessions take place at home and include both the patient and his/her family during the post episode period. The treatment has shown its efficacy vs. crisis management in 101 BD patients in reducing relapses ($35\ \%\ vs.\ 54\ \%$) and increasing time to relapse (53 vs. 73 weeks, respectively) (Miklowitz et al. 2000 , 2003) and to reduce hospitalization risk compared with individual treatment ($12\ \%\ vs.\ 60\ \%$).

2.7.5 Cognitive Remediation and Functional Remediation

Functional remediation tailored for the needs of BD patients includes education on neurocognitive deficits, communication, autonomy and stress management. So far a similar picture seems to be in place concerning BD as well, with the limited research data that exist, failing to provide solid support to this kind of intervention.

The combination of neurocognitive techniques with psychoeducation and problem-solving within an ecological framework was tested in a multicentre trial in 239 euthymic BD patients with a moderate–severe degree of functional impairment ($N = 77$) vs. psychoeducation ($N = 82$) and vs. TAU ($N = 80$). At endpoint the combined programme was superior to TAU but not to psychoeducation alone (Martinez-Aran et al. 2011 ; Torrent et al. 2013). A small study in 37 BD and schizoaffective patients tested Social Cognition and Interaction Training (SCIT) as adjunctive to TAU ($N = 21$) vs. TAU alone ($N = 16$). This showed that there was no difference between groups concerning social functioning, but there was a superiority of the combination group in the improvement of emotion perception, theory of mind, hostile attribution bias and depressive symptoms (Lahera et al. 2013).

This work advocates greatly on the family and friends' therapy that includes psychoeducation, efficient communication gap bridges, support and self care training for caregivers, that will fill – in the trust gaps, basically in Nigeria. Generally, we need to go back to days of family and friends cohension not neglecting the efficacy and importance of appropriate prescribed medication to the recuperation of bipolar disorder patient.

CHAPTER 3

MOOD VARIATION MODEL FOR BIPOLAR II DISORDER WITH CHAOTIC INTERMITTANCY

3.1 INTRODUCTION

Our objective in this work is to understand better the dynamics of mood variation and the effect of psychosocial therapy on the mood swings; with the assumption that the observed behavior of bipolar disorder patient can be modeled as an oscillator. We assume that the treatment with the psychosocial therapy as the main consideration can be modeled using parametric polynomial forcing function. We use multiscale perturbation method to determine the effect of psychosocial therapy to a bipolar II disorder patient.

3.2 Governing Equation Formulation

We shall make some necessary assumptions for the purpose of proposing a model for bipolar II disorder. The manic and depressive episodes are governed by periodic patterns and it is assumed that the disorder will escalate greatly if left untreated. Patients are more prone to rapid cycling especially if initially treated only with antidepressant (Nana, 2009). In addition, (Daugherty et al., 2009) suggests that the behavior of the single bipolar patient they studied can be described qualitatively as a limit cycle oscillator. We then model the periodic mood variations of a bipolar II patient with a negatively damped oscillator. The model can be written thus

$$u'' - \delta u' + a_0 u = 0 \tag{3.1}$$

where δ is the damping coefficient, u is the emotional state of the patient, and a_0 is the natural frequency of the oscillator. Eqn. (3.1) is the episodes of the untreated patient. We suppose that treatment can be modeled using

$$f\left(\bar{t},u\right)=\sum_{m=0}^{M}\left(P_m\cos w\bar{t}+Q_m\sin w\bar{t}\right)-\sum_{n=1}^{N}a_n u^{2n+1} \tag{3.2}$$

where P_m, Q_m, w and a are parameters. The treatment of bipolar II disorder is always the combination of mood stabilizers, antidepressant, antipsychotic or tranquilizers and psychotherapy. Treatments of bipolar II disorder are basically dependent upon the severity of the emotional state which explains why we choose the parametric function for the medication. The Damped Duffing Oscillator with multiple driving force is generally expressed as

$$u''-\delta u'+\sum_{n=0}^{N}a_n u^{2n+1}=\sum_{m=0}^{M}\left(P_m\cos w\bar{t}+Q_m\sin w\bar{t}\right) \tag{3.3}$$

where δ is the immune system and other physiological damping coefficient, a_n, P_m, Q_m are arbitrary constant that translate to the restoring forces and the periodic driving forces (day and night, HPA, Circadian rhythms). We consider the Duffing equation for $N=3$ and $M=3$. We have

$$u''-\delta u'+a_0u+a_1u^3+a_2u^5+a_3u^7=P\cos w\bar{t}+Q\sin w\bar{t} \tag{3.4}$$

where $P_0+P_1+P_2+P_3=P,\ Q_0+Q_1+Q_2+Q_3=Q$.

Then we have

$$u''-\delta u'+a_0u+a_1u^3+a_2u^5+a_3u^7=\varepsilon K\sin\left(w\bar{t}+\beta\right), \tag{3.5}$$

where

$$P=\varepsilon P_\alpha \text{ and } Q=\varepsilon Q_\alpha,\ \varepsilon K=\sqrt{P_\alpha{}^2+Q_\alpha{}^2} \text{ and } \tan\beta=\frac{P_\alpha}{Q_\alpha},\ \bar{t}>0,\ 0<\delta\ll 1. \tag{3.6a}$$

$u'=$ Rate of change of mood,
$a_0=$ Natural frequency of the mood variation,
$a_1=$ Medication parameter that is a measure of medication adeherence,
$a_2=$ Psycosocial parameter (FFT),

$a_3 =$ Other psycho - therapy parameter,
$K =$ Resultant of external and internal forces that is capable of affecting the mood swing,
$\beta =$ Oscillation lag.

Assuming initial condition

$$u(0) = 0,\ u'(0) = 0. \tag{3.6b}$$

Equation $(3.6b)$ represents the healthy state of an individual. The emotional state of the individual does not exhibit any noticeable variation.

3.3 ANALYTICAL APPROACH

We now introduce a slow time scale τ such that

$$\tau = \delta t \tag{3.6c}$$

and

$$\hat{t} = t + \frac{1}{\delta}\left(\varepsilon\mu_1 + \varepsilon^2\mu_2 + \varepsilon^3\mu_3 + \cdots\right), \tag{3.7}$$

$$\overline{t} = t, \tag{3.8}$$

$$\mu_i = \mu_i(\tau),\ \mu_i(0) = 0, \tag{3.9}$$

and

$$u(t,\tau) = v\left(\hat{t},\tau,;\varepsilon,\delta\right). \tag{3.10}$$

Thus

$$\frac{du}{dt} = \frac{\partial v}{\partial t} = \frac{\partial v}{\partial \hat{t}}\cdot\frac{\partial \hat{t}}{\partial t} + \frac{\partial v}{\partial \hat{t}}\cdot\frac{\partial \hat{t}}{\partial \tau}\cdot\frac{d\tau}{dt} + \frac{\partial v}{\partial \tau}\frac{d\tau}{dt}. \tag{3.11}$$

Substituting appropriately the values of the derivatives in (3.11) we have

$$\begin{aligned}\frac{du}{dt} &= \frac{\partial v}{\partial \hat{t}} + \delta\cdot\frac{1}{\delta}\left(\varepsilon\mu_1' + \varepsilon^2\mu_2' + \varepsilon^3\mu_3' + \cdots\right)\frac{dv}{d\hat{t}} + \delta\frac{dv}{d\tau} \\ &= \frac{\partial v}{\partial \hat{t}} + \left(\varepsilon\mu_1' + \varepsilon^2\mu_2' + \varepsilon^3\mu_3' + \cdots\right)\frac{\partial v}{\partial \hat{t}} + \delta\frac{\partial v}{\partial \tau},\end{aligned} \tag{3.12}$$

$$\frac{d^2u}{dt^2}=\frac{d}{dt}\left(\frac{du}{dt}\right)=\frac{d}{dt}\left(\frac{\partial v}{\partial \hat{t}}+\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)\frac{\partial v}{\partial \hat{t}}+\delta\frac{\partial v}{\partial \tau}\right)$$
$$=\frac{\partial v'}{\partial \hat{t}}+\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)\frac{\partial v'}{\partial \hat{t}}+\delta\frac{\partial v'}{\partial \tau}. \tag{3.13}$$

Substituting (3.10) into (3.11)

$$\frac{d^2u}{dt^2}=\frac{\partial}{\partial \hat{t}}\left(\frac{\partial v}{\partial \hat{t}}+\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3+\cdots\right)\frac{\partial v}{\partial \hat{t}}+\delta\frac{\partial v}{\partial \tau}\right)$$
$$+\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)\frac{\partial}{\partial \hat{t}}\left(\frac{\partial v}{\partial \hat{t}}+\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)\frac{\partial v}{\partial \hat{t}}+\delta\frac{\partial v}{\partial \tau}\right)$$
$$+\delta\frac{\partial}{\partial \tau}\left(\frac{\partial v}{\partial \hat{t}}+\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)\frac{\partial v}{\partial \hat{t}}+\delta\frac{\partial v}{\partial \tau}\right)$$

$$=\frac{\partial^2 v}{\partial \hat{t}^2}+\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)\frac{\partial^2 v}{\partial \hat{t}^2}+\delta\frac{\partial^2 v}{\partial \hat{t}\partial \tau}+\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)\frac{\partial^2 v}{\partial \hat{t}^2}$$
$$+\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)^2\frac{\partial^2 v}{\partial \hat{t}^2}+\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)\delta\frac{\partial^2 v}{\partial \hat{t}\partial \tau}$$
$$+\delta\frac{\partial^2 v}{\partial \hat{t}\partial \tau}+\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)\delta\frac{\partial^2 v}{\partial \hat{t}\partial \tau}+\delta^2\frac{\partial^2 v}{\partial \tau^2}.$$

$$\frac{d^2u}{dt^2}=\frac{\partial^2 v}{\partial \hat{t}^2}+2\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)\frac{\partial^2 v}{\partial \hat{t}^2}+2\delta\frac{\partial^2 v}{\partial \hat{t}\partial \tau}+\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)^2\frac{\partial^2 v}{\partial \hat{t}^2}$$
$$+2\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)\delta\frac{\partial^2 v}{\partial \hat{t}\partial \tau}+\delta^2\frac{\partial^2 v}{\partial \tau^2}.$$

(3.14)

Substituting (3.12) and (3.14) into (3.4), we have

$$\frac{\partial^2 v}{\partial \hat{t}^2}+2\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)\frac{\partial^2 v}{\partial \hat{t}^2}+2\delta\frac{\partial^2 v}{\partial \hat{t}\partial \tau}+\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)^2\frac{\partial^2 v}{\partial \hat{t}^2}$$
$$+2\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)\delta\frac{\partial^2 v}{\partial \hat{t}\partial \tau}+\delta^2\frac{\partial^2 v}{\partial \tau^2}+\delta\left(\frac{\partial v}{\partial \hat{t}}+\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)\frac{\partial v}{\partial \hat{t}}+\delta\frac{\partial v}{\partial \tau}\right)$$
$$+a_0u+a_1u^3+a_2u^5+a_3u^7=P\cos wt+Q\sin wt.$$

$$\frac{\partial^2 v}{\partial \hat{t}^2}+2\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)\frac{\partial^2 v}{\partial \hat{t}^2}+2\delta\frac{\partial^2 v}{\partial \hat{t}\partial \tau}+\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)^2\frac{\partial^2 v}{\partial \hat{t}^2}$$
$$+2\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)\delta\frac{\partial^2 v}{\partial \hat{t}\partial \tau}+\delta^2\frac{\partial^2 v}{\partial \tau^2}+\delta\frac{\partial v}{\partial \hat{t}}+\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)\delta\frac{\partial v}{\partial \hat{t}} \tag{3.15}$$
$$+\delta^2\frac{\partial v}{\partial \tau}+a_0u+a_1u^3+a_2u^5+a_3u^7=\varepsilon K\sin\left(wt+\beta\right).$$

We now let

$$v\left(\hat{t},\tau\right)=\sum_{i=0}^{\infty}\sum_{j=0}^{\infty}v^{ij}\left(\hat{t},\tau,\varepsilon,\delta\right)\varepsilon^{i}\delta^{j} \tag{3.16}$$

where ij on v^{ij} denotes superscript and on ε,δ denotes powers. Hence

$$\begin{aligned}v\left(\hat{t},\tau,\varepsilon,\delta\right)=\varepsilon\left(v^{10}+\delta u^{11}+\delta^{2}u^{12}+\cdots\right)+\varepsilon^{2}\left(v^{20}+\delta u^{21}+\delta^{2}u^{22}+\cdots\right)\\+\varepsilon^{3}\left(v^{30}+\delta u^{31}+\delta^{2}u^{32}+\cdots\right)+\cdots\end{aligned} \tag{3.17}$$

Substituting (3.17) into (3.15), and equate coefficients of $\varepsilon^{i}\delta^{j}$ we get

$$\begin{aligned}&\frac{\partial^{2}}{\partial\hat{t}^{2}}\left[\varepsilon\left(v^{10}+\delta u^{11}+\delta^{2}u^{12}+\cdots\right)+\varepsilon^{2}\left(v^{20}+\delta u^{21}+\delta^{2}u^{22}+\cdots\right)+\varepsilon^{3}\left(v^{30}+\delta u^{31}+\delta^{2}u^{32}+\cdots\right)+\cdots\right]\\&+2\left(\varepsilon\mu_{1}'+\varepsilon^{2}\mu_{2}'+\varepsilon^{3}\mu_{3}'+\cdots\right)\frac{\partial^{2}}{\partial\hat{t}^{2}}\left[\varepsilon\left(v^{10}+\delta u^{11}+\delta^{2}u^{12}+\cdots\right)+\varepsilon^{2}\left(v^{20}+\delta u^{21}+\delta^{2}u^{22}+\cdots\right)+\cdots\right]\\&+2\delta\frac{\partial^{2}}{\partial\hat{t}\partial\tau}\left[\varepsilon\left(v^{10}+\delta u^{11}+\delta^{2}u^{12}+\cdots\right)+\varepsilon^{2}\left(v^{20}+\delta u^{21}+\delta^{2}u^{22}+\cdots\right)+\varepsilon^{3}\left(v^{30}+\delta u^{31}+\cdots\right)+\cdots\right]\\&+\left(\varepsilon\mu_{1}'+\varepsilon^{2}\mu_{2}'+\varepsilon^{3}\mu_{3}'+\cdots\right)^{2}\frac{\partial^{2}}{\partial\hat{t}^{2}}\left[\varepsilon\left(v^{10}+\delta u^{11}+\delta^{2}u^{12}+\cdots\right)+\varepsilon^{2}\left(v^{20}+\delta u^{21}+\delta^{2}u^{22}+\cdots\right)+\cdots\right]\\&+2\left(\varepsilon\mu_{1}'+\varepsilon^{2}\mu_{2}'+\varepsilon^{3}\mu_{3}'+\cdots\right)\delta\frac{\partial^{2}}{\partial\hat{t}\partial\tau}\left[\varepsilon\left(v^{10}+\delta u^{11}+\delta^{2}u^{12}+\cdots\right)+\varepsilon^{2}\left(v^{20}+\delta u^{21}+\cdots\right)+\cdots\right]\\&+\delta^{2}\frac{\partial^{2}}{\partial\tau^{2}}\left[\varepsilon\left(v^{10}+\delta u^{11}+\delta^{2}u^{12}+\cdots\right)+\varepsilon^{2}\left(v^{20}+\delta u^{21}+\delta^{2}u^{22}+\cdots\right)+\varepsilon^{3}\left(v^{30}+\delta u^{31}+\cdots\right)+\cdots\right]\\&-\delta\frac{\partial}{\partial\hat{t}}\left[\varepsilon\left(v^{10}+\delta u^{11}+\delta^{2}u^{12}+\cdots\right)+\varepsilon^{2}\left(v^{20}+\delta u^{21}+\delta^{2}u^{22}+\cdots\right)+\varepsilon^{3}\left(v^{30}+\delta u^{31}+\cdots\right)+\cdots\right]\\&+\left(\varepsilon\mu_{1}'+\varepsilon^{2}\mu_{2}'+\varepsilon^{3}\mu_{3}'+\cdots\right)\delta\frac{\partial}{\partial\hat{t}}\left[\varepsilon\left(v^{10}+\delta u^{11}+\delta^{2}u^{12}+\cdots\right)+\varepsilon^{2}\left(v^{20}+\delta u^{21}+\delta^{2}u^{22}+\cdots\right)+\cdots\right]\\&+\delta^{2}\frac{\partial}{\partial\tau}\left[\varepsilon\left(v^{10}+\delta u^{11}+\delta^{2}u^{12}+\cdots\right)+\varepsilon^{2}\left(v^{20}+\delta u^{21}+\delta^{2}u^{22}+\cdots\right)+\varepsilon^{3}\left(v^{30}+\delta u^{31}+\cdots\right)+\cdots\right]\\&+a_{0}\left(\varepsilon\left(v^{10}+\delta u^{11}+\delta^{2}u^{12}+\cdots\right)+\varepsilon^{2}\left(v^{20}+\delta u^{21}+\delta^{2}u^{22}+\cdots\right)+\varepsilon^{3}\left(v^{30}+\delta u^{31}+\cdots\right)+\cdots\right)\\&+a_{1}\left[\varepsilon\left(v^{10}+\delta u^{11}+\delta^{2}u^{12}+\cdots\right)+\varepsilon^{2}\left(v^{20}+\delta u^{21}+\delta^{2}u^{22}+\cdots\right)+\varepsilon^{3}\left(v^{30}+\delta u^{31}+\cdots\right)+\cdots\right]^{3}\\&+a_{2}\left[\varepsilon\left(v^{10}+\delta u^{11}+\delta^{2}u^{12}+\cdots\right)+\varepsilon^{2}\left(v^{20}+\delta u^{21}+\delta^{2}u^{22}+\cdots\right)+\varepsilon^{3}\left(v^{30}+\delta u^{31}+\cdots\right)+\cdots\right]^{5}\\&+a_{3}\left[\varepsilon\left(v^{10}+\delta u^{11}+\delta^{2}u^{12}+\cdots\right)+\varepsilon^{2}\left(v^{20}+\delta u^{21}+\delta^{2}u^{22}+\cdots\right)+\varepsilon^{3}\left(v^{30}+\delta u^{31}+\cdots\right)+\cdots\right]^{7}\\&=\varepsilon K\sin\left(wt+\beta\right).\end{aligned} \tag{3.18}$$

Let

$$a_0 = \Omega^2. \tag{3.19a}$$

To solve (3.18) using perturbation method, we obtain a system of differential equations by equating the terms of different orders of $\varepsilon^i \delta^j$ for $i = 0,1,2,...$ and $j = 0,1,2,....$

Terms of order ε:

$$\frac{\partial^2 v^{10}}{\partial \hat{t}^2} + \Omega^2 v^{10} = k \sin\left(wt + \beta\right). \tag{3.19b}$$

Terms of order $\varepsilon\delta$:

$$\frac{\partial^2 v^{11}}{\partial \hat{t}^2} + \Omega^2 v^{11} = -2\frac{\partial^2 v^{10}}{\partial \hat{t}\partial \tau} - \frac{\partial v^{10}}{\partial \hat{t}}. \tag{3.20}$$

Terms of Order $\varepsilon\delta^2$:

$$\frac{\partial^2 v^{12}}{\partial \hat{t}^2} + \Omega^2 v^{12} = -2\frac{\partial^2 v^{11}}{\partial \hat{t}\partial \tau} - \frac{\partial v^{11}}{\partial \hat{t}} - \frac{\partial^2 v^{10}}{\partial \tau^2}. \tag{3.21}$$

Terms of order ε^2:

$$\frac{\partial^2 v^{20}}{\partial \hat{t}^2} + \Omega^2 v^{20} = -2\mu_1' \frac{\partial^2 v^{10}}{\partial \hat{t}^2}. \tag{3.22}$$

Terms of order $\varepsilon^2\delta$:

$$\frac{\partial^2 v^{21}}{\partial \hat{t}^2} + \Omega^2 v^{21} = -2\mu_1' \frac{\partial^2 v^{11}}{\partial \hat{t}^2} - 2\mu_1' \frac{\partial^2 v^{10}}{\partial \hat{t}\partial \tau} - 2\frac{\partial^2 v^{20}}{\partial \hat{t}\partial \tau} - 2\frac{\partial v^{20}}{\partial \hat{t}} - \mu_1' \frac{\partial v^{10}}{\partial \hat{t}}. \tag{3.23}$$

Terms of order $\varepsilon^2\delta^2$:

$$\frac{\partial^2 v^{22}}{\partial \hat{t}^2} + \Omega^2 v^{22} = -2\mu_1' \frac{\partial^2 v^{12}}{\partial \hat{t}^2} - 2\mu_1' \frac{\partial^2 v^{11}}{\partial \hat{t}\partial \tau} - 2\frac{\partial^2 v^{21}}{\partial \hat{t}\partial \tau} - \frac{\partial v^{21}}{\partial \hat{t}} - \mu_1' \frac{\partial v^{11}}{\partial \hat{t}} - \frac{\partial v^{20}}{\partial \tau} - \frac{\partial^2 v^{20}}{\partial \tau^2}. \tag{3.24}$$

Terms of order ε^3:

$$\frac{\partial^2 v^{30}}{\partial \hat{t}^2} + \Omega^2 v^{30} = -\left(\mu_1'\right)^2 \frac{\partial^2 v^{10}}{\partial \hat{t}^2} - 2\mu_1' \frac{\partial^2 v^{20}}{\partial \hat{t}^2} - \mu_2' \frac{\partial v^{10}}{\partial \hat{t}^2} - \Omega^2 \left(v^{10}\right)^3. \tag{3.25}$$

Terms of order $\varepsilon^3\delta$:

$$\begin{aligned}\frac{\partial^2 v^{31}}{\partial \hat{t}^2}+\Omega^2 v^{31} &= -2\left(\mu_1'\frac{\partial^2 v^{21}}{\partial \hat{t}^2}+\mu_2'\frac{\partial^2 v^{11}}{\partial \hat{t}^2}\right)-\left(\mu_1'\right)^2\frac{\partial^2 v^{11}}{\partial \hat{t}^2}-2\left(\mu_1'\frac{\partial^2 v^{20}}{\partial \hat{t}\partial\tau}+\mu_2'\frac{\partial^2 v^{10}}{\partial \hat{t}\partial\tau}\right)-2\frac{\partial^2 v^{30}}{\partial \hat{t}\partial\tau}\\ &-\left(\mu_1'\frac{\partial v^{20}}{\partial \hat{t}}+\mu_2'\frac{\partial v^{10}}{\partial \hat{t}}\right)-\left(\frac{\partial v^{30}}{\partial \hat{t}}+\mu_1'\frac{\partial v^{20}}{\partial \hat{t}}+\mu_2'\frac{\partial v^{10}}{\partial \hat{t}}\right)-3\Omega^2\left(v^{10}\right)^2 v^{11}.\end{aligned} \tag{3.26}$$

Terms of order $\varepsilon^3\delta^2$:

$$\begin{aligned}\frac{\partial^2 v^{32}}{\partial \hat{t}^2}+\Omega^2 v^{32} &= -\left(\mu_1'\right)^2\frac{\partial^2 v^{12}}{\partial \hat{t}^2}-2\frac{\partial^2 v^{30}}{\partial \tau^2}-2\left(\mu_1'\frac{\partial^2 v^{22}}{\partial \hat{t}^2}+\mu_2'\frac{\partial^2 v^{12}}{\partial \hat{t}^2}\right)\\ &-2\left(\mu_1'\frac{\partial^2 v^{22}}{\partial \hat{t}^2}+\mu_2'\frac{\partial^2 v^{12}}{\partial \hat{t}^2}\right)-2\frac{\partial^2 v^{31}}{\partial \hat{t}\partial\tau}\\ &-2\left(\frac{\partial v^{31}}{\partial \hat{t}}+\mu_1'\frac{\partial v^{21}}{\partial \hat{t}}+\mu_2'\frac{\partial v^{11}}{\partial \hat{t}}+\frac{\partial v^{30}}{\partial \hat{t}}\right)\\ &-a_1\left(3\left(v^{10}\right)^2 v^{12}+\left(v^{11}\right)^2 v^{10}\right).\end{aligned} \tag{3.27}$$

The associated initial conditions can obtained by evaluating (3.12) and (3.17) at (0,0)

$$v^{ij}(0,0)=0. \tag{3.28}$$

$$\begin{aligned}&\frac{\partial}{\partial \hat{t}}(\varepsilon\left(v^{10}(0,0)+\delta u^{11}(0,0)+\delta^2 u^{12}(0,0)+\cdots\right)+\varepsilon^2\left(v^{20}(0,0)+\delta u^{21}(0,0)+\cdots\right)\\ &+\varepsilon^3\left(v^{30}(0,0)+\delta u^{31}(0,0)+\delta^2 u^{32}(0,0)+\cdots\right)+\cdots)\\ &+\left(\varepsilon\mu_1'+\varepsilon^2\mu_2'+\varepsilon^3\mu_3'+\cdots\right)\frac{\partial}{\partial \hat{t}}(\varepsilon\left(v^{10}(0,0)+\delta u^{11}(0,0)+\delta^2 u^{12}(0,0)+\cdots\right)\\ &+\varepsilon^2\left(v^{20}(0,0)+\delta u^{21}(0,0)+\delta^2 u^{22}(0,0)+\cdots\right)+\varepsilon^3\left(v^{30}(0,0)+\delta u^{31}(0,0)+\cdots\right)+\cdots)\\ &+\delta\frac{\partial}{\partial \tau}(\varepsilon\left(v^{10}(0,0)+\delta u^{11}(0,0)+\delta^2 u^{12}(0,0)+\cdots\right)+\varepsilon^2\left(v^{20}(0,0)+\delta u^{21}(0,0)+\cdots\right)\\ &+\varepsilon^3\left(v^{30}(0,0)+\delta u^{31}(0,0)+\delta^2 u^{32}(0,0)+\cdots\right)+\cdots)=0\end{aligned} \tag{3.29}$$

.

Equating the coefficient of

$$O(\varepsilon):\frac{\partial v^{10}}{\partial \hat{t}}(0,0)=0. \tag{3.30}$$

terms of $\varepsilon\delta$

$$O(\varepsilon\delta):\frac{\partial v^{11}}{\partial \hat{t}}(0,0)+\frac{\partial v^{10}}{\partial \tau}(0,0)=0. \tag{3.31}$$

$$O\left(\varepsilon\delta^2\right): \frac{\partial v^{12}}{\partial \hat{t}}(0,0) + \frac{\partial v^{11}}{\partial \tau}(0,0) = 0. \tag{3.32}$$

$$O\left(\varepsilon^2\right): \frac{\partial v^{20}}{\partial \hat{t}}(0,0) + \mu_1'(0)\frac{\partial v^{10}}{\partial \hat{t}}(0,0) = 0. \tag{3.33}$$

$$O\left(\varepsilon^2\delta\right): \frac{\partial v^{21}}{\partial \hat{t}}(0,0) + \mu_1'(0)\frac{\partial v^{11}}{\partial \hat{t}}(0,0) + \frac{\partial v^{20}}{\partial \tau}(0,0) = 0. \tag{3.34}$$

$$O\left(\varepsilon^2\delta^2\right): \frac{\partial v^{22}}{\partial \hat{t}}(0,0) + \mu_1'(0)\frac{\partial v^{12}}{\partial \hat{t}}(0,0) + \frac{\partial v^{21}}{\partial \tau}(0,0) = 0. \tag{3.35}$$

$$O\left(\varepsilon^3\right): \frac{\partial v^{30}}{\partial \hat{t}}(0,0) + \mu_1'(0)\frac{\partial v^{20}}{\partial \hat{t}}(0,0) + \mu_2'(0)\frac{\partial v^{10}}{\partial \hat{t}}(0,0) = 0. \tag{3.36}$$

$$O\left(\varepsilon^3\delta\right): \frac{\partial v^{31}}{\partial \hat{t}}(0,0) + \mu_1'(0)\frac{\partial v^{21}}{\partial \hat{t}}(0,0) + \mu_2'(0)\frac{\partial v^{11}}{\partial \hat{t}}(0,0) + \frac{\partial v^{30}}{\partial \tau}(0,0) = 0. \tag{3.37}$$

$$O\left(\varepsilon^3\delta^2\right): \frac{\partial v^{32}}{\partial \hat{t}}(0,0) + \mu_1'(0)\frac{\partial v^{22}}{\partial \hat{t}}(0,0) + \mu_2'(0)\frac{\partial v^{12}}{\partial \hat{t}}(0,0) + \frac{\partial v^{31}}{\partial \tau}(0,0) = 0. \tag{3.38}$$

We then solve $(3.19b)$ using the initial conditions, (3.28) and (3.30); recasting, we have

$$\frac{\partial^2 v^{10}}{\partial \hat{t}^2} + \Omega^2 v^{10} = h_1(\tau) \tag{3.39}$$

where

$$h_1(\tau) = k\sin(wt + \beta). \tag{3.40}$$

Solving (3.39), we get

$$v^{10}(\hat{t}, \tau) = \alpha_{10}\cos\Omega\hat{t} + \beta_{10}\sin\Omega\hat{t} + h_1(\tau). \tag{3.41}$$

Applying (3.28) to (3.41) we get

$$\alpha_{10}(0) + h_1(0) = 0,$$

$$\alpha_{10}(0) = -h_1(0). \tag{3.42}$$

Using (3.30) on (3.41), we get

$$\beta_{10}(0) = 0.$$

$$\therefore\ v^{10}\left(\hat{t},\tau\right)=\alpha_{10}\cos\Omega t+h_1\left(\tau\right). \tag{3.43}$$

To solve (3.20) we make appropriate substitution, we get

$$\frac{\partial^2 v^{11}}{\partial\hat{t}^2}+v^{11}=-2\frac{\partial^2 v^{10}}{\partial\hat{t}\partial\tau}-\frac{\partial v^{10}}{\partial\hat{t}}=-2\frac{\partial}{\partial\hat{t}}\left(\alpha_{10}'\cos\Omega\hat{t}+\beta_{10}'\sin\Omega\hat{t}-h_1'\left(\tau\right)\right)$$
$$+\alpha_{10}\Omega\sin\Omega\hat{t}+\beta_{10}\Omega\cos\Omega\hat{t},$$

$$\frac{\partial^2 v^{11}}{\partial\hat{t}^2}+v^{11}=2\alpha_{10}'\Omega\sin\Omega\hat{t}-2\beta_{10}'\Omega\cos\Omega\hat{t}+\alpha_{10}\Omega\sin\Omega\hat{t}+\beta_{10}\Omega\cos\Omega\hat{t}. \tag{3.44}$$

To ensure uniformly valid asymptotic solution in $\hat{t}$, we equate to zero the coefficients of $\cos\Omega\hat{t}$ and $\sin\Omega\hat{t}$ in (3.44).

Coefficients of $\cos\Omega\hat{t}$:

$$2\alpha_{10}'+\alpha_{10}=0$$
$$\Rightarrow\qquad \alpha_{10}\left(\tau\right)=\alpha_{10}\left(0\right)e^{-\frac{\tau}{2}}$$
$$\alpha_{10}\left(\tau\right)=-h_1\left(0\right)e^{-\frac{\tau}{2}}. \tag{3.45}$$

Coefficients of $\sin\Omega\hat{t}$:

$$-2\beta_{10}'+\beta_{10}=0$$
$$\Rightarrow\qquad \beta_{10}\left(\tau\right)=\beta_{10}\left(0\right)e^{\frac{\tau}{2}}$$
$$\beta_{10}\left(\tau\right)=0. \tag{3.46}$$

Therefore

$$v^{10}\left(\hat{t},\tau\right)=-h_1\left(0\right)e^{-\frac{\tau}{2}}\cos\Omega\hat{t}+h_1\left(\tau\right). \tag{3.47}$$

The remaining terms in (3.44) is

$$\frac{\partial^2 v^{11}}{\partial\hat{t}^2}+\Omega^2 v^{11}=0. \tag{3.48}$$

Solving (3.48) we have

$$v^{11}=\alpha_{11}\cos\Omega\hat{t}+\beta_{11}\sin\Omega\hat{t}. \tag{3.49}$$

Applying (3.28) to (3.49) we get

$$\alpha_{11}(0)=0. \tag{3.50}$$

Applying (3.31) to (3.49) we get

$$\beta_{11}(0)=-h_1'(0). \tag{3.51}$$

$$\therefore \qquad v^{11}(\hat{t},\tau)=\beta_{11}(0)\sin\Omega\hat{t}. \tag{3.52}$$

To solve (3.21), we make proper substitutions to get

$$\begin{aligned}\frac{\partial^2 v^{12}}{\partial\hat{t}^2}+\Omega^2 v^{12} &= -2\left(-\alpha_{11}'\Omega\sin\Omega\hat{t}+\beta_{11}'\Omega\cos\Omega\hat{t}\right)+\alpha_{11}\Omega\sin\Omega\hat{t}-\beta_{11}\Omega\cos\Omega\hat{t}\\ &\quad -\alpha_{10}''\Omega\cos\Omega\hat{t}-h_1''\\ &= \Omega\left(2\alpha_{11}'+\alpha_{11}\right)\sin\Omega\hat{t}-\Omega\left(2\beta_{11}'+\beta_{11}+\alpha_{10}''\right)\cos\Omega\hat{t}-h_1''.\end{aligned} \tag{3.53}$$

To ensure uniformly valid asymptotic solution in $\hat{t}$, we equate to zero the coefficients of $\cos\Omega\hat{t}$ and $\sin\Omega\hat{t}$ in (3.53).

Coefficients of $\cos\Omega\hat{t}$:

$$\Omega\left(2\beta_{11}'+\beta_{11}+\alpha_{10}''\right)=0$$

$$2\beta_{11}'+\beta_{11}=-\alpha_{10}''. \tag{3.54}$$

$$\beta_{11}(\tau)=e^{-\frac{\tau}{2}}\left(\int_0^{\tau}e^{\frac{s}{2}}\alpha_{10}''(s)\,ds+\beta_{11}(0)\right),$$

$$\Rightarrow \qquad \beta_{11}(\tau)=e^{-\frac{\tau}{2}}\left(\int_0^{\tau}e^{\frac{s}{2}}\alpha_{10}''(s)\,ds-h_1'(0)\right). \tag{3.55}$$

Coefficients of $\sin\Omega\hat{t}$:

$$2\alpha_{11}'+\alpha_{11}=0.$$

$$\Rightarrow \qquad \alpha_{11}(\tau)=\alpha_{11}(0)e^{-\frac{\tau}{2}}=0. \tag{3.56}$$

$$\therefore \quad v^{11}(\hat{t},\tau)=\beta_{11}(\tau)e^{-\frac{\tau}{2}}\sin\Omega\hat{t}. \tag{3.57}$$

The remaining terms in (3.53) are

$$\frac{\partial^2 v^{12}}{\partial \hat{t}^2} + \Omega^2 v^{12} = h_1''. \tag{3.58}$$

Solving (3.58), we get

$$v^{12} = \alpha_{12} \cos \Omega \hat{t} + \beta_{12} \sin \Omega \hat{t} + h_1''. \tag{3.59}$$

Applying the initial value condition, (3.28), we have

$$\alpha_{12}(0) = h_1''(0). \tag{3.60}$$

Using the condition in (3.32) we get

$$\left(-\alpha_{12}\Omega \sin \Omega \hat{t} + \beta_{12}\Omega \cos \Omega \hat{t} + \alpha_{11}' \cos \Omega \hat{t} + \beta_{11}' \sin \Omega \hat{t}\right)\Big|_{(0,0)} = 0 \tag{3.61}$$

$$\beta_{12}(0) = 0. \tag{3.62}$$

$$\therefore \; v^{12}(\hat{t}, \tau) = h_1''(0) \cos \Omega \hat{t} - h_1''(\tau). \tag{3.63}$$

To solve (3.22), we make necessary substitutions that results to

$$\frac{\partial^2 v^{20}}{\partial \hat{t}^2} + \Omega^2 v^{20} = -2\mu_1' \frac{\partial^2 v^{10}}{\partial \hat{t}^2} = -2\mu_1' \alpha_{10} \Omega^2 \cos \Omega \hat{t}.$$

To ensure uniformly valid asymptotic solution in $\hat{t}$, we equate to zero the coefficients of $\cos \Omega \hat{t}$ in (3.63)

$$2\mu_1' \alpha_{10} = 0.$$

$$\Rightarrow \mu_1' = 0 \text{ and } \mu_1 = k(\text{constant}). \tag{3.64}$$

The remaining equation in (3.63) is

$$\frac{\partial^2 v^{20}}{\partial \hat{t}^2} + \Omega^2 v^{20} = 0. \tag{3.65}$$

Solving (3.65), we get

$$v^{20} = \alpha_{20} \cos \Omega \hat{t} + \beta_{20} \sin \Omega \hat{t}. \tag{3.66}$$

Using the initial condition in (3.28) on (3.66) we have

$$\alpha_{20}(0) = 0. \tag{3.67}$$

and on using the initial value condition in (3.33), we get

$$\beta_{20}(0) = 0. \tag{3.68}$$

$$\therefore\ v^{20}(\hat{t}, \tau) = 0. \tag{3.69}$$

We solve (3.23), having (3.64) and (3.69) in mind; it reduces to

$$\frac{\partial^2 v^{21}}{\partial \hat{t}^2} + \Omega^2 v^{21} = 0, \tag{3.70}$$

whose solution is

$$v^{21} = \alpha_{21} \cos \Omega \hat{t} + \beta_{21} \sin \Omega \hat{t}. \tag{3.71}$$

Using the initial condition (3.28) on (3.71), we get

$$\alpha_{21}(0) = 0, \tag{3.72}$$

and using (3.35) on (3.71) having in mind (3.64) and (3.69), we get

$$\beta_{21}(0) = 0. \tag{3.73}$$

$$\therefore\ \ v^{21}(\hat{t}, \tau) = 0. \tag{3.74}$$

To solve (3.24), having in view (3.64), (3.69) and (3.74); it reduces to

$$\frac{\partial^2 v^{22}}{\partial \hat{t}^2} + \Omega^2 v^{22} = 0, \tag{3.75}$$

whose solution is

$$v^{22} = \alpha_{22} \cos \Omega \hat{t} + \beta_{22} \sin \Omega \hat{t}. \tag{3.76}$$

Using the initial condition (3.28) on (3.76), we get

$$\alpha_{22}(0) = 0, \tag{3.77}$$

and using (3.36) on (3.76) having in mind (3.64), (3.69) and (3.74) we get

$$\beta_{22}(0) = 0. \tag{3.78}$$

$$\therefore \; v^{22}\left(\hat{t},\tau\right)=0. \tag{3.79}$$

To solve (3.25), having (3.64) and (3.69) in mind it can be reduced to

$$\frac{\partial^2 v^{30}}{\partial \hat{t}^2}+\Omega^2 v^{30}=-\mu_2'\frac{\partial^2 v^{10}}{\partial \hat{t}^2}-a_1\left(v^{10}\right)^3. \tag{3.80}$$

$$\frac{\partial^2 v^{30}}{\partial \hat{t}^2}+\Omega^2 v^{30}=-\mu_2'\alpha_{10}\Omega^2\cos\Omega\hat{t}-a_1\left(\alpha_{10}\cos\Omega\hat{t}+h_1\left(\tau\right)\right)^3.$$

Using binomial expansion, we get

$$\begin{aligned}\frac{\partial^2 v^{30}}{\partial \hat{t}^2}+\Omega^2 v^{30} &= 2\mu_2'\alpha_{10}\Omega^2\cos\Omega\hat{t}\\ &\quad -a_1\left(\alpha_{10}^3\left(\cos\Omega\hat{t}\right)^3+3\alpha_{10}^2\left(\cos\Omega\hat{t}\right)^2 h_1+3\alpha_{10}\cos\Omega\hat{t}\,h_1^2+h_1^3\right)\\ &= 2\mu_2'\alpha_{10}\Omega^2\cos\Omega\hat{t}\\ &\quad -a_1\left[\left(h_1^3+\frac{3\alpha_{10}^2 h_1}{2}\right)+\left(\frac{3\alpha_{10}^2}{4}+3\alpha_{10}^2 h_1^2\right)\cos\Omega\hat{t}+\frac{3\alpha_{10}^2 h_1}{2}\cos 2\Omega\hat{t}+\frac{\alpha_{10}^3}{4}\cos 3\Omega\hat{t}\right].\end{aligned} \tag{3.81}$$

To ensure uniformly valid asymptotic solution in $\hat{t}$, we equate to zero the coefficients of $\cos\Omega\hat{t}$ in (3.81), we get

$$2\mu_2'\Omega^2\alpha_{10}-a_1\left(\frac{3\alpha_{10}^3}{4}+3\alpha_{10}h_1^2\right)=0.$$

$$2\mu_2'\Omega^2\alpha_{10}=a_1\left(\frac{3\alpha_{10}^3}{4}+3\alpha_{10}h_1^2\right).$$

$$\begin{aligned}\mu_2'\left(0\right) &= \frac{3a_1}{2\Omega^2}\left(\frac{\left(\alpha_{10}\left(0\right)\right)^2}{4}+\left(h_1\left(0\right)\right)^2\right)\\ &= \frac{3a_1}{2\Omega^2}\left(\frac{\left(h_1\left(0\right)\right)^2}{4}+\left(h_1\left(0\right)\right)^2\right)\end{aligned}$$

$$\mu_2'\left(0\right)=\frac{15a_1\left(h_1\left(0\right)\right)^2}{8\Omega^2}. \tag{3.82}$$

The remaining equation in (3.81) is

$$\frac{\partial^2 v^{30}}{\partial \hat{t}^2}+\Omega^2 v^{30}=-a_1\left[\left(h_1^3+\frac{3h_1\alpha_{10}}{2}\right)+\frac{3h_1\alpha_{10}^2}{2}\cos 2\Omega\hat{t}+\frac{\alpha_{10}^3}{4}\cos 3\Omega\hat{t}\right]. \tag{3.83}$$

Let

$$l_1(\tau)=-\left(h_1^3+\frac{3h_1\alpha_{10}}{2}\right)a_1. \tag{3.84}$$

$$l_2(\tau)=-\frac{3h_1\alpha_{10}^2}{2}a_1, \tag{3.85a}$$

$$l_3(\tau)=-\frac{\alpha_{10}^3}{4}a_1, \tag{3.85b}$$

and

$$l_1(0)=-\left(\left(h_1(0)\right)^3+\frac{3\left(h_1(0)\right)^2 h_1(0)}{2}\right)a_1=-\frac{5\left(h_1(0)\right)^3}{2}a_1. \tag{3.86a}$$

$$l_2(0)=-\frac{3\left(h_1(0)\right)^2 h_1(0)}{2}a_1=-\frac{3\left(h_1(0)\right)^3}{2}. \tag{3.86b}$$

$$l_3(0)=-\frac{\alpha_{10}^3}{4}a_1=-\frac{\left(h_1(0)\right)^3}{4}a_1. \tag{3.86c}$$

Therefore (3.84) becomes

$$\frac{\partial^2 v^{30}}{\partial \hat{t}^2}+\Omega^2 v^{30}=l_1+l_2\cos 2\Omega\hat{t}+l_3\cos 3\Omega\hat{t}. \tag{3.87}$$

Solving (3.87) by variation of parameter, we get

$$v^{30}=\alpha_{30}\cos\Omega\hat{t}+\beta_{30}\sin\Omega\hat{t}+l_1-\frac{l_2}{2}\cos 2\Omega\hat{t}-\frac{l_3}{8}\cos 3\Omega\hat{t}. \tag{3.88}$$

Using the initial condition in (3.28) we have

$$\alpha_{30}(0)+l_1(0)-\frac{l_2(0)}{3}-\frac{l_3(0)}{8}=0.$$

$$\alpha_{30}(0)-\frac{5\left(h_1(0)\right)^3}{2}a_1+\frac{\left(h_1(0)\right)^3}{2}a_1-\frac{\left(h_1(0)\right)^3}{32}a_1=0.$$

$$\alpha_{30}(0)=\frac{5\left(h_1(0)\right)^3}{2}a_1+\frac{\left(h_1(0)\right)^3}{32}a_1-\frac{\left(h_1(0)\right)^3}{2}.$$

$$\alpha_{30}(0)=\frac{65\left(h_1(0)\right)^3}{32}a_1. \tag{3.89}$$

Using the initial condition (3.35) having (3.64) and (3.69) in view, we get

$$\beta_{30}(0)=0. \tag{3.90}$$

Moving further, (3.26) can be reduced to

$$\frac{\partial^2 v^{31}}{\partial \hat{t}^2}+v^{31}=-2\mu_2'\frac{\partial^2 v^{11}}{\partial \hat{t}^2}-2\mu_2'\frac{\partial^2 v^{10}}{\partial \hat{t}\partial\tau}-2\frac{\partial^2 v^{30}}{\partial \hat{t}\partial\tau}-2\mu_2'\frac{\partial v^{10}}{\partial \hat{t}}-\frac{\partial v^{30}}{\partial \hat{t}}-3\left(v^{10}\right)^2 v^{11}. \tag{3.91}$$

Simplification of terms

$$\begin{aligned}\left(v^{10}\right)^2 v^{11}&=\left(\alpha_{10}\cos\Omega\hat{t}+h_1\right)^2\left(\beta_{11}\sin\Omega\hat{t}\right)\\&=\left[\left(\frac{\alpha_{10}^2}{2}+h_1^2\right)+2h_1\alpha_{10}\cos\Omega\hat{t}+\frac{\alpha_{10}^2}{2}\cos 2\Omega\hat{t}\right]\beta_{11}\sin\Omega\hat{t}.\end{aligned} \tag{3.92}$$

$$\left(v^{10}\right)^2 v^{11}=\left(\frac{\alpha_{10}^2}{4}+h_1^2\right)\beta_{11}\sin\Omega\hat{t}+h_1\alpha_{10}\beta_{11}\sin 2\Omega\hat{t}+\frac{\alpha_{10}^2}{4}\beta_{11}\sin 3\Omega\hat{t}. \tag{3.93}$$

On proper substitution of (3.93) and related derivatives in (3.91) we get

$$\begin{aligned}\frac{\partial^2 v^{31}}{\partial \hat{t}^2}+\Omega^2 v^{31}&=2\Omega^2\mu_2'\beta_{11}\sin\Omega\hat{t}-2\Omega\mu_2'\alpha_{10}'\sin\Omega\hat{t}+2\Omega\alpha_{30}'\sin\Omega\hat{t}+2\Omega\beta_{11}\cos\Omega\hat{t}\\&+\frac{4l_2'}{3}\Omega\sin 2\Omega\hat{t}+\frac{3l_3'\Omega}{4}\sin 3\Omega\hat{t}+2\mu_2'\Omega\alpha_{10}\sin\Omega\hat{t}+\alpha_{30}\Omega\sin\Omega\hat{t}\\&+\beta_{30}\Omega\cos\Omega\hat{t}+\frac{2l_2\Omega}{3}\sin\Omega\hat{t}+\frac{3\Omega l_3}{8}\sin 3\Omega\hat{t}\\&-3a_1\left[\left(\frac{\alpha_{10}^2}{4}+h_1^2\right)\beta_{11}\sin\Omega\hat{t}+h_1\alpha_{10}\beta_{11}\sin\Omega\hat{t}+\frac{\alpha_{10}^2\beta_{11}}{4}\sin 3\Omega\hat{t}\right].\end{aligned} \tag{3.94}$$

To ensure uniformly valid asymptotic solution in $\hat{t}$, we equate to zero the coefficients of $\cos\Omega\hat{t}$ and $\sin\Omega\hat{t}$ in (3.94)

Coefficients of $\cos\Omega\hat{t}$:

$$2\beta_{30}'+\beta_{30}=0.$$

$$\Rightarrow \beta_{30}(\tau)=\beta_{30}(0)e^{-\frac{\tau}{2}}=0. \tag{3.95}$$

Coefficients of $\sin\Omega\hat{t}$:

$$2\mu_2'\beta_{11}-2\mu_2'\alpha_{10}'+2\alpha_{30}'+2\mu_2'\alpha_{10}+\alpha_{30}-\frac{3a_1\alpha_{10}^2}{4}\beta_{11}-3a_1h_1^2\beta_{11}=0.$$

$$2\alpha_{30}'+\alpha_{30}=h_2(\tau). \tag{3.96}$$

where

$$h_2(\tau)=2\mu_2'(\alpha_{10}'-\alpha_{10}-\beta_{11})+3a_1\beta_{11}\left(\frac{\alpha_{10}^2}{4}+h_1^2\right). \tag{3.97}$$

$$\alpha_{30}(\tau)=e^{-\frac{\tau}{2}}\left(\int_0^{\tau}h_2(s)e^{\frac{s}{2}}ds+\alpha_{30}(0)\right). \tag{3.98}$$

Hence

$$\frac{\partial^2 v^{31}}{\partial\hat{t}^2}+\Omega^2v^{31}=\left(\frac{4l_2'}{3}+\frac{2l_2}{3}+h_1\alpha_{10}\beta_{11}\right)\sin 2\Omega\hat{t}+\left(\frac{3l_3'}{4}+\frac{3l_3}{8}+\frac{\alpha_{10}^2}{4}\beta_{11}\right)\sin 3\Omega\hat{t}. \tag{3.99}$$

We set

$$l_4(\tau)=\frac{4l_2'}{3}+\frac{2}{3}l_2+h_1\alpha_{10}\beta_{11}. \tag{3.100a}$$

$$l_5(\tau)=\frac{3}{4}l_3'+\frac{3}{8}l_3+\frac{1}{4}\alpha_{10}^2\beta_{11}. \tag{3.100b}$$

Observe that

$$l_2'(\tau)=\frac{3}{2}\alpha_{10}^2h_1'a_1. \tag{3.101a}$$

$$l_3'(\tau)=\frac{3}{8}\alpha_{10}^3a_1. \tag{3.101b}$$

Therefore, $(3.100a)$ and $(3.100b)$can be reduced to

$$\begin{aligned}l_4(0)&=\left(h_1(0)\right)^2h_1'(0)(1-2a_1)-\frac{5}{3}\left(h_1(0)\right)^3a_1\\&=h_1^2(0)\left[h_1'(0)(1-2a_1)-\frac{5}{3}h_1(0)a_1\right].\end{aligned} \tag{3.102a}$$

$$l_5(0)=\frac{17}{32}h_1^3(0)a_1+\frac{1}{4}h_1^2(0)h_1'(0). \tag{3.102b}$$

Hence,

$$\frac{\partial^2 v^{31}}{\partial \hat{t}^2}+\Omega^2 v^{31}=l_4\sin 2\Omega\hat{t}+l_5\sin 3\Omega\hat{t}. \tag{3.103}$$

The solution to (3.103) is

$$v^{31}(\hat{t},\tau)=\alpha_{31}\cos\Omega\hat{t}+\beta_{31}\sin\Omega\hat{t}-\frac{l_4}{3}\sin 2\Omega\hat{t}-\frac{l_5}{8}\sin 3\Omega\hat{t}. \tag{3.104}$$

using (3.28) on (3.104), we get

$$\alpha_{31}(0)=0. \tag{3.105}$$

Using also (3.36) on (3.104) we get

$$\beta_{31}(0)=\frac{2}{3}l_4(0)+\frac{3}{8}l_5(0)-\mu_2'(0)\beta_{11}(0)-\alpha_{30}'(0)-l_1'(0)+\frac{1}{3}l_2'(0)-\frac{1}{8}l_3'(0). \tag{3.106}$$

Hence

$$u^{31}(\hat{t},\tau)=\beta_{31}(0)\sin\Omega\hat{t}-\frac{l_4}{3}\sin 2\Omega\hat{t}-\frac{l_5}{8}\sin 3\Omega\hat{t}. \tag{3.107}$$

Furthermore, (3.27) can be reduced to

$$\begin{aligned}\frac{\partial^2 v^{32}}{\partial \hat{t}^2}+\Omega^2 v^{32}=&-\frac{\partial^2 v^{30}}{\partial\tau^2}-2\mu_2'\frac{\partial^2 v^{12}}{\partial\hat{t}^2}-2\mu_2'\frac{\partial^2 v^{11}}{\partial\hat{t}\,\partial\tau}-2\frac{\partial^2 v^{31}}{\partial\hat{t}\,\partial\tau}-\frac{\partial v^{31}}{\partial\hat{t}}-2\mu_2'\frac{\partial v^{11}}{\partial\hat{t}}-2\frac{\partial v^{30}}{\partial\hat{t}}\\&-a_1\left[3\left(v^{10}\right)^2 v^{12}+\left(v^{11}\right)^2 v^{10}\right].\end{aligned}$$

Further simplification of coupled terms

$$\begin{aligned}\left(v^{10}\right)^2 v^{12}&=\left(\alpha_{10}\cos\Omega\hat{t}+h_1\right)^2\left(h_1''(0)\cos\Omega\hat{t}-h_1''\right)\\&=\left(\alpha_{10}^2\cos^2\Omega\hat{t}+2h_1\alpha_{10}\cos\Omega\hat{t}+h_1^2\right)\left(h_1''(0)\cos\Omega\hat{t}-h_1''\right)\\&=h_1''(0)\alpha_{10}^2\cos^3\Omega\hat{t}+2h_1h_1''(0)\alpha_{10}\cos^2\Omega\hat{t}\\&\quad+h_1^2h_1''(0)\alpha_{10}\cos\Omega\hat{t}-h_1''\alpha_{10}^2\cos^2\Omega\hat{t}-h_1''\alpha_{10}\cos\Omega\hat{t}-h_1^2h_1''.\end{aligned}$$

$$\left(v^{11}\right)^2 v^{10} = \left(\alpha_{10}\cos\Omega\hat{t} + h_1\right)\left(\beta_{11}\sin\Omega\hat{t}\right)^2 = \alpha_{10}\beta_{11}^2\cos\Omega\hat{t}\sin^2\Omega\hat{t} + h_1\sin^2\Omega\hat{t}.$$

$$\begin{aligned}\left(v^{10}\right)^2 v^{12} + \left(v^{11}\right)^2 v^{10} &= \frac{1}{4}\alpha_{10}\beta_{11}\left(\cos\Omega\hat{t} - \cos 3\Omega\hat{t}\right) + \frac{1}{2}h_1\beta_{11}\left(1-\cos 2\Omega\hat{t}\right)\\ &+\frac{1}{4}\alpha_{10}^2 h_1''\left(3\cos\Omega\hat{t} + \cos 3\Omega t\right) + 2\alpha_{10}h_1h_1''\left(1+\cos 2\Omega\hat{t}\right)\\ &+h_1^2 h_1''\cos\Omega\hat{t} + \frac{1}{2}\alpha_{10}^2 h_1''\left(1+\cos 2\Omega\hat{t}\right) - 2\alpha_{10}h_1''\cos\Omega\hat{t} - h_1^2 h_1''.\end{aligned}$$

$$\begin{aligned}\left(v^{10}\right)^2 v^{12} + \left(v^{11}\right)^2 v^{10} &= \frac{1}{2}h_1\beta_{11} + 2\alpha_{10}h_1h_1'' - \frac{1}{2}\alpha_{10}^2 h_1'' - h_1^2 h_1''\\ &+\left(\frac{1}{4}\alpha_{10}\beta_{11} + \frac{3}{4}\alpha_{10}^2 h_1'' + h_1^2 h_1'' - 2\alpha_{10}h_1''\right)\cos\Omega\hat{t}\\ &+\left(\alpha_{10}h_1h_1'' - \frac{1}{2}h_1\beta_{11} - \frac{1}{2}\alpha_{10}^2 h_1''\right)\cos 2\Omega\hat{t}\\ &+\left(\frac{1}{4}\alpha_{10}^2 h_1'' - \frac{1}{4}\alpha_{10}\beta_{11}\right)\cos 3\Omega\hat{t}.\end{aligned} \tag{3.109}$$

Substituting (3.109) and appropriate derivatives into (3.108) we get

$$\begin{aligned}\frac{\partial^2 v^{32}}{\partial\hat{t}^2} + \Omega^2 v^{32} &= -\alpha_{30}''\cos\Omega\hat{t} - \beta_{30}''\mu_2'\Omega^2\sin\Omega\hat{t} - l_1'' - \frac{l_2''}{3}\cos 2\Omega\hat{t} - \frac{l_3''}{8}\cos 3\Omega\hat{t}\\ &+2\mu_2'\Omega^2\alpha_{12}\cos\Omega\hat{t} + 2\mu_2'\Omega^2\beta_{12}\sin\Omega\hat{t} - 2\mu_2'\Omega\beta_{11}\cos\Omega\hat{t}\\ &+2\alpha_{31}'\Omega\sin\Omega\hat{t} - 2\beta_{31}'\Omega\cos\Omega\hat{t} + \frac{4\Omega l_4'}{3}\cos 2\Omega\hat{t} + \frac{3\Omega l_5'}{4}\cos 3\Omega\hat{t}\\ &+\alpha_{31}\Omega\sin\Omega\hat{t} - \beta_{31}\Omega\cos\Omega\hat{t} + \frac{4\Omega l_4}{3}\cos 2\Omega\hat{t} + \frac{3\Omega l_5}{4}\cos 3\Omega\hat{t}\\ &-2\mu_2'\Omega\beta_{11}\cos\Omega\hat{t} + 2\alpha_{30}\Omega\sin\Omega\hat{t} - 2\beta_{30}\Omega\cos\Omega\hat{t}\\ &-\frac{4\Omega l_2}{3}\sin 2\Omega\hat{t} - \frac{3\Omega l_3}{4}\sin 3\Omega\hat{t} + \frac{1}{2}h_1\beta_{11} + 2\alpha_{10}h_1h_1''\\ &-\frac{1}{2}\alpha_{10}^2 h_1'' - h_1^2 h_1'' + \left(\frac{1}{4}\alpha_{10}\beta_{11} + \frac{3}{4}\alpha_{10}^2 h_1'' + h_1^2 h_1'' - 2\alpha_{10}h_1''\right)\cos\Omega\hat{t}\\ &+\left(\alpha_{10}h_1h_1'' - \frac{1}{2}h_1\beta_{11} - \frac{1}{2}\alpha_{10}^2 h_1''\right)\cos 2\Omega\hat{t}\\ &+\left(\frac{1}{4}\alpha_{10}^2 h_1'' - \frac{1}{4}\alpha_{10}\beta_{11}\right)\cos 3\Omega\hat{t}.\end{aligned} \tag{3.110}$$

To ensure uniformly valid asymptotic solution in $\hat{t}$, we equate to zero the coefficients of $\cos\Omega\hat{t}$ and $\sin\Omega\hat{t}$ in (3.110)

Coefficients of $\cos\Omega\hat{t}$:

$$-\alpha_{30}' + 2\mu_2'\Omega^2\alpha_{12} - 2\mu_2'\Omega\beta_{11} - 2\Omega\beta_{31}' - \Omega\beta_{31} - 2\mu_2'\Omega\beta_{11} - 2\Omega\beta_{30} + \frac{1}{4}\alpha_{10}\beta_{11} + \frac{3}{4}\alpha_{10}^2 h_1'' + h_1^2 h_1'' - 2\alpha_{10}h_1'' = 0. \tag{3.111}$$

$$2\beta_{31}' + \beta_{31} = h_3(\tau). \tag{3.112}$$

where

$$h_3(\tau) = 2\mu_2'\left(\Omega^2\beta_{12} - \Omega\beta_{11}\right) + \alpha_{30}' + 2\Omega\beta_{30} - \frac{1}{4}\alpha_{10}\beta_{11} - \frac{3}{4}\alpha_{10}^2 h_1'' - h_1^2 h_1'' + 2\alpha_{10}h_1''. \tag{3.113}$$

$$\therefore\ \beta_{31}(\tau) = e^{-\frac{\tau}{2}}\left(\int_0^\tau h_3(s)e^{\frac{s}{2}}ds + \beta_{31}(0)\right). \tag{3.114}$$

Coefficients of $\sin\Omega\hat{t}$:

$$-\Omega^2\beta_{30}''\mu_2' + \mu_2'\Omega\beta_{12} + 2\Omega\alpha_{31}' + \Omega\alpha_{31} + 2\Omega\alpha_{30} = 0. \tag{3.115}$$

$$2\alpha_{31}' + \alpha_{31} = h_4(\tau). \tag{3.116}$$

where

$$h_4(\tau) = \Omega\beta_{30}''\mu_2' - \mu_2'\beta_{12} - 2\alpha_{30}. \tag{3.117}$$

$$\therefore\ \alpha_{31}(\tau) = e^{-\frac{\tau}{2}}\left(\int_0^\tau h_4(s)e^{\frac{s}{2}}ds + \alpha_{31}(0)\right). \tag{3.118}$$

Using (3.105) on (3.118), we get

$$\alpha_{31}(\tau) = e^{-\frac{\tau}{2}}\left(\int_0^\tau h_4(s)e^{\frac{s}{2}}ds\right). \tag{3.119}$$

The remaining equation (3.110) is

$$\frac{\partial^2 v^{32}}{\partial\hat{t}^2} + \Omega^2 v^{32} = l_6 + l_7\cos 2\Omega\hat{t} + l_8\sin 2\Omega\hat{t} + l_9\cos 3\Omega\hat{t} + l_{10}\sin 3\Omega\hat{t}, \tag{3.120}$$

where

$$l_6 = \left(\frac{1}{2}h_1\beta_{11} + 2\alpha_{10}h_1h_1'' + \frac{1}{2}\alpha_{10}^2h_1'' - h_1^2h_1''\right)a_1, \tag{3.121a}$$

$$l_7 = \alpha_{10} h_1 h_1'' - \frac{1}{2} h_1 \beta_{11} - \frac{1}{2} \alpha_{10}^2 h_1'' - \frac{l_2''}{3} + \frac{4l_4'}{3} + \frac{4l_4}{3}, \tag{3.121b}$$

$$l_8 = -\frac{4l_2}{3}, \tag{3.121c}$$

$$l_9 = \frac{\alpha_{10}^2 h_1''}{4} - \frac{\alpha_{10}\beta_{11}}{4} - \frac{l_3''}{8} + \frac{3l_5'}{4} + \frac{3l_5}{4}, \tag{3.121d}$$

$$l_{10} = -\frac{3l_3}{4}. \tag{3.121e}$$

The solution to (3.120) is

$$v^{32}\left(\hat{t},\tau\right) = \alpha_{32}\cos\Omega\hat{t} + \beta_{32}\sin\Omega\hat{t} + l_6 - \frac{l_7}{3}\cos 2\Omega\hat{t} - \frac{l_8}{3}\sin 2\Omega\hat{t} - \frac{l_9}{8}\cos 3\Omega\hat{t} - \frac{l_{10}}{8}\sin 3\Omega\hat{t}. \tag{3.122}$$

Using the initial condition in (3.30) on (3.122), we get

$$\alpha_{32}(0) + l_6(0) - \frac{l_7(0)}{3} - \frac{l_9(0)}{8} = 0.$$

$$\alpha_{32}(0) = \frac{l_7(0)}{3} + \frac{l_9(0)}{8} - l_6(0). \tag{3.123}$$

Using the initial condition in (3.38), we get

$$\beta_{32}(0) - \frac{2l_8(0)}{3} - \frac{3l_{10}(0)}{8} + \alpha_{31}'(0) = 0.$$

$$\beta_{32}(0) = \frac{2l_8(0)}{3} + \frac{3l_{10}(0)}{8} - \alpha_{31}'(0). \tag{3.124}$$

Hence

$$v^{32}\left(\hat{t},\tau\right) = \alpha_{32}(0)\cos\Omega\hat{t} + \beta_{32}(0)\sin\Omega\hat{t} + l_6 - \frac{l_7}{3}\cos 2\Omega\hat{t} - \frac{l_8}{3}\sin 2\Omega\hat{t} - \frac{l_9}{8}\cos 3\Omega\hat{t} - \frac{l_{10}}{8}\sin 3\Omega\hat{t}. \tag{3.125}$$

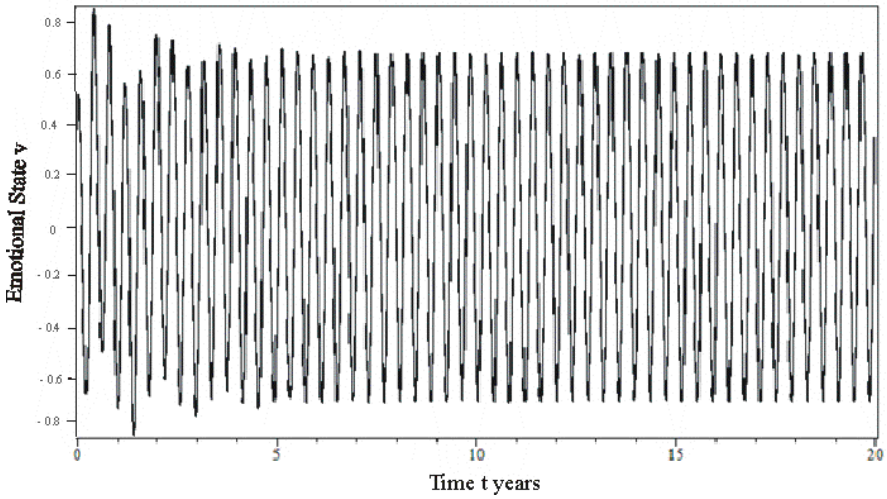
Therefore

$$
\begin{aligned}
v\left(\hat{t},\tau,\varepsilon,\delta\right) = \varepsilon\Bigg[& h_1(0)e^{-\frac{\tau}{2}}\cos\Omega\hat{t} + h_1(\tau) + \delta\left(h_1'(0)e^{-\frac{\tau}{2}}\sin\Omega\hat{t}\right) \\
& + \delta^2\left(h_1''(0)\cos\Omega\hat{t} - h''(\tau)\right) + \cdots\Bigg] + \varepsilon^3\Big\{\alpha_{30}(0)\cos\Omega\hat{t} + l_1 \\
& + \frac{l_2}{3}\cos 2\Omega\hat{t} - \frac{l_3}{8}\cos 3\Omega\hat{t} + \delta\left(\beta_{31}(0)\sin\Omega\hat{t} - \frac{l_4}{3}\sin 2\Omega\hat{t}\right) \\
& + \delta^2\Bigg(\alpha_{32}(0)\cos\Omega\hat{t} + \beta_{32}(0)\sin\Omega\hat{t} + l_6 - \frac{l_7}{3}\cos 2\Omega\hat{t} \\
& - \frac{l_8}{3}\sin 2\Omega\hat{t} - \frac{l_9}{8}\cos 3\Omega\hat{t} - \frac{l_{10}}{8}\sin 3\Omega\hat{t}\Bigg) + \cdots\Big\}.
\end{aligned}
\tag{3.126}
$$

$v\left(\hat{t},\tau,\varepsilon,\delta\right)$ represents the emotional state of a patient for any given time when the patient has started taking the prescription and subjected to psychotherapy: psychosocial approach; basically FFT. The proposed model captures the behavioral dynamics of both treated and untreated bipolar II disorder individuals; by changing the parameters we can understand the mood variations.

The graphing of (3.3) confirms the analytical result. Graphing (3.126) for the initial condition around the equilibrium point $(0,0)$ we obtain the following graphs

a



b

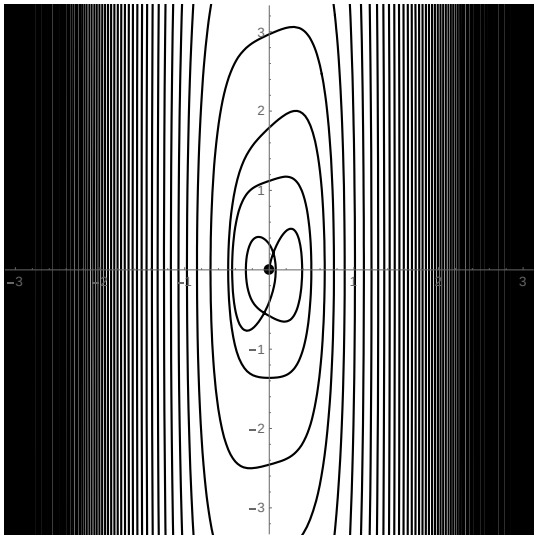
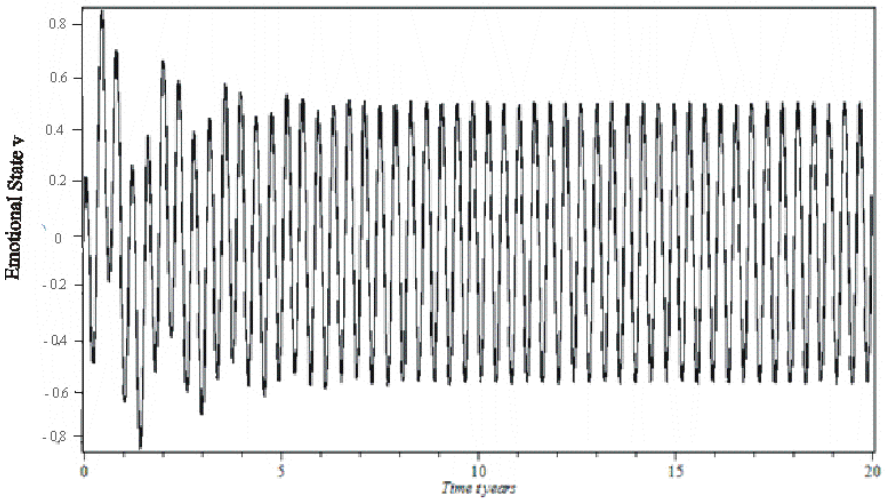


Fig. 3.1. Patient that is receiving treatment and placed on psychosocial therapy with parameter $\delta = 0.5, F = 0.9,\ w = 1.0, a_0 = 1, a_1 = 20, a_2 = 10, a_3 = 50$: (a) transition between an unstable larger limit cycle to a stable smaller limit cycle and (b) the phase plane corresponding to (a).

a



b

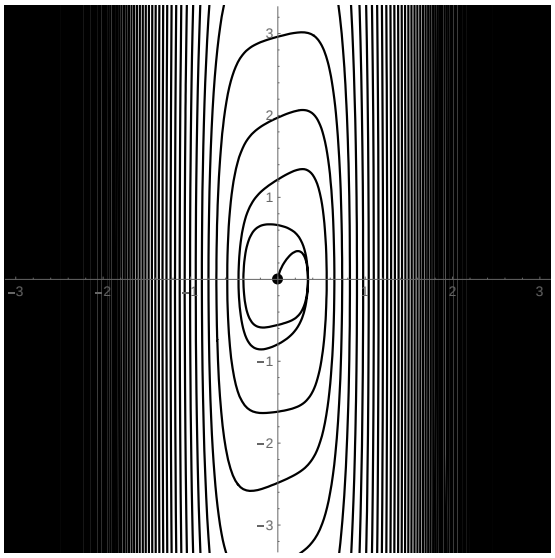


Fig. 3.2: Patient that is receiving treatment and placed on psychosocial therapy with parameter $\delta = 0.5, F = 0.9,\ \ w = 1.0, a_0 = 1, a_1 = 20, a_2 = 100, a_3 = 50$: (a) transition between an unstable larger limit cycle to a stable smaller limit cycle and (b) the phase plane corresponding to (a).

3.4 AMPLIFICATION OF THE LIMIT CYCLES

Supposing the particular solution of (3.3) is given as

$$u_p(t) = P\cos wt + Q\sin wt. \tag{3.127}$$

$$u_p'(t) = -Pw\sin wt + Qw\cos wt. \tag{3.128}$$

$$u_p''(t) = -Pw^2\cos wt - Qw^2\sin wt. \tag{3.129}$$

Hence (3.3) becomes

$$
\begin{aligned}
&-Pw^2\cos wt - Qw^2\sin wt - \delta\left(-Pw\sin wt + Qw\cos wt\right)\\
&+a_0\left(P\cos wt + Q\sin wt\right) + a_1\left(P\cos wt + Q\sin wt\right)^3\\
&+a_2\left(P\cos wt + Q\sin wt\right)^5 + a_3\left(P\cos wt + Q\sin wt\right)^7 = K\sin wt.
\end{aligned}
\tag{3.130}
$$

Neglecting the terms of higher order; because individuals with BD regardless of their chaotic mood variation still have a check in the swings. Appling the solvability condition, we have

$$\left(a_0 - w^2\right)P - \delta wQ = 0, \tag{3.131}$$

$$\delta wP + \left(a_0 - w^2\right)Q = K. \tag{3.132}$$

Using Cramer's rule, we have

$$P = \frac{K\delta w}{\left(a_0 - w^2\right)^2 + \delta^2 w^2}, \qquad Q = \frac{K\left(a_0 - w^2\right)}{\left(a_0 - w^2\right)^2 + \delta^2 w^2}. \tag{3.133}$$

Appling $(3.19a)$ to (3.133) , we have

$$P = \frac{K\delta w}{\left(\Omega^2 - w^2\right)^2 + \delta^2 w^2},\ Q = \frac{K\left(a_0 - w^2\right)}{\left(\Omega^2 - w^2\right)^2 + \delta^2 w^2}\ . \tag{3.134}$$

To study the amplitude as a function of w, we write the particular solution as

$$u_p(t) = A\sin(wt - \beta) \tag{3.135}$$

where A is the amplitude and β is the phase lag given by

$$
\begin{aligned}
A = \sqrt{P^2 + Q^2} &= \sqrt{\left(\frac{K\delta w}{\left(\Omega^2 - w^2\right)^2 + \delta^2 w^2}\right)^2 + \left(\frac{K\left(a_0 - w^2\right)}{\left(\Omega^2 - w^2\right)^2 + \delta^2 w^2}\right)^2}\\
&= \frac{K}{\sqrt{\left(\Omega^2 - w^2\right)^2 + \delta^2 w^2}}.
\end{aligned}
\tag{3.136}
$$

To obtain the maximum amplitude

$$A'(w) = \frac{Kw\left(\delta^2 - 2\left(\Omega^2 - w^2\right)\right)}{\left(\sqrt{\left(\Omega^2 - w^2\right)^2 + \left(\delta w\right)^2}\right)^3}. \tag{3.137}$$

For the critical Amplitude, $A'(w)=0,$ hence

$$A'(w)=Kw\left(\delta^2-2\left(\Omega^2-w^2\right)\right)=0,$$

$$\delta^2=2\left(\Omega^2-w^2\right), \tag{3.138}$$

$$w_{\max}^2=\Omega^2-\frac{\delta^2}{2}. \tag{3.139}$$

Substituting (3.139) into (3.136), we have

$$A(w_{\max})=\frac{K}{\sqrt{\left(\Omega^2-\left(\Omega^2-\frac{\delta^2}{2}\right)\right)^2+\delta^2\left(\Omega^2-\frac{\delta^2}{2}\right)}},$$

$$A(w_{\max})=\frac{2K}{\delta\sqrt{4\Omega^2-\delta^2}}. \tag{3.140}$$

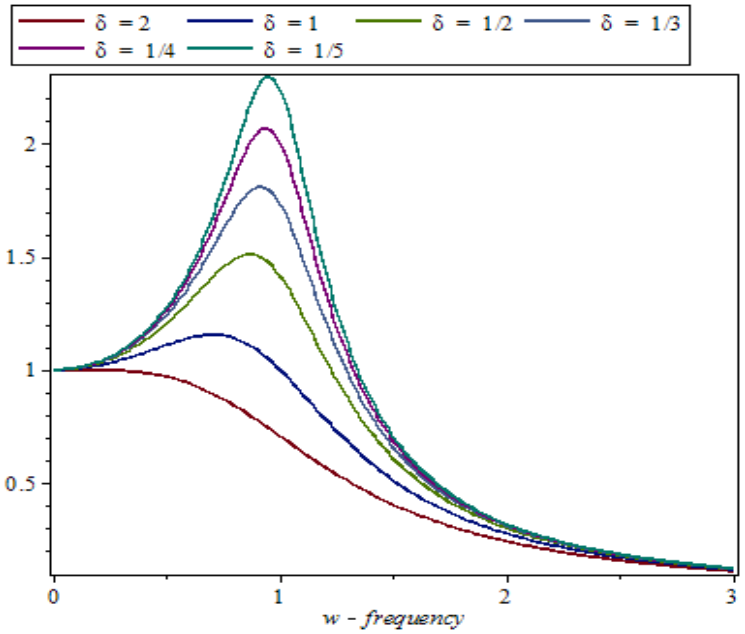


Figure 3.3: Amplification of the mood variation A/K and various values of the damping coefficient.

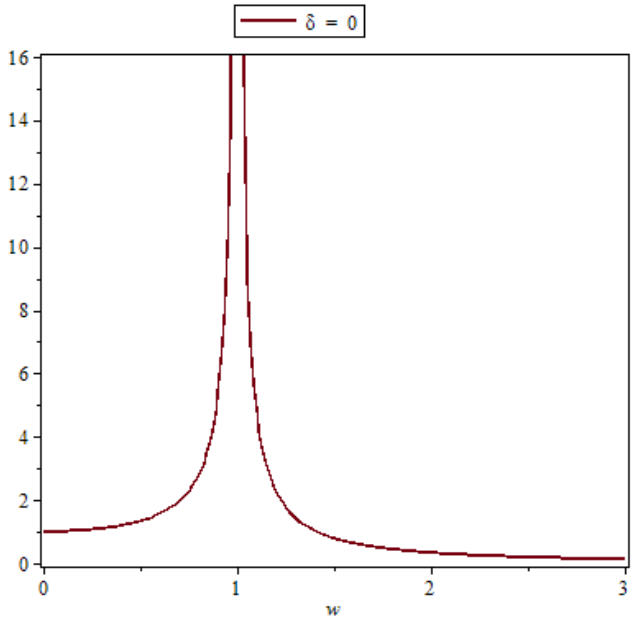


Figure 3.4 – Amplification of the mood variation A/K when the damping coefficient is zero.

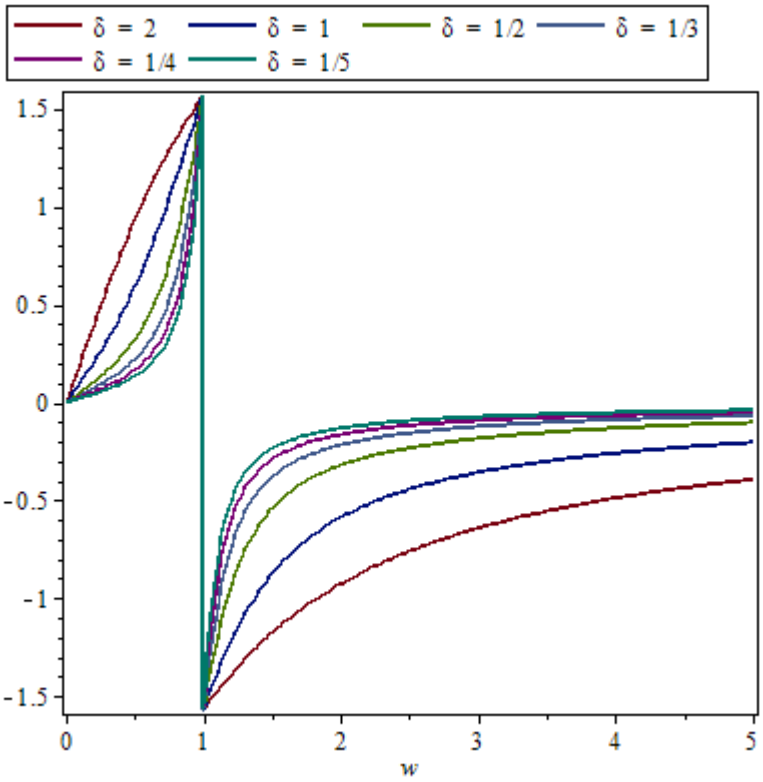


Figure 3.5 – Phase lag as a function of w and different damping coefficients.

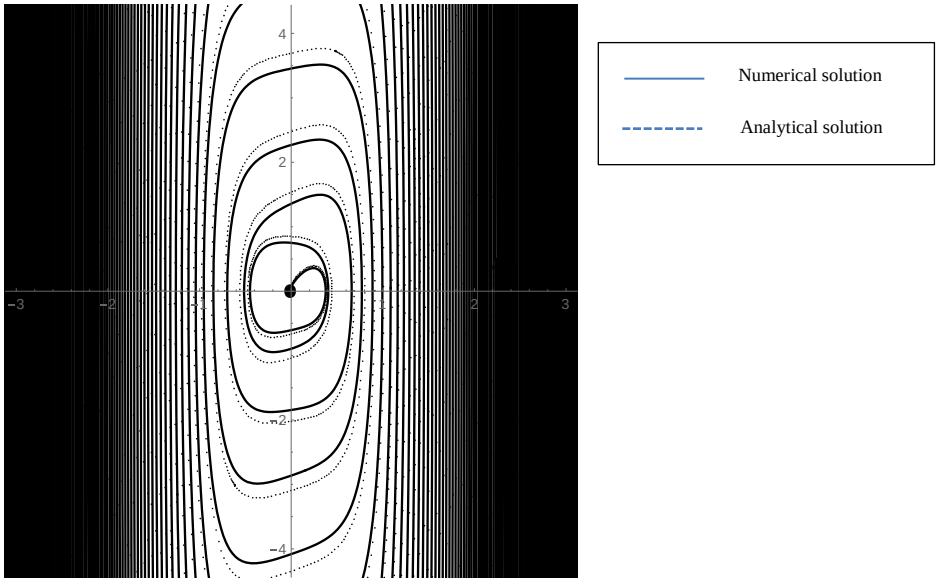


Fig. 3.6 Phase plane diagram: The numerical solution and approximate solution are represented by the tick line and dotted line respectively.

3.5 DISCUSSION

(3.140) yields the condition that must be met in order that the limit cycles will exist. These conditions are based on the values of a_0, δ and F. When the quantity $4\Omega^2 - \delta^2$ is large enough for the positive root, and small enough for negative roots, when there are no parametric excitation; the resultant limit cycle is always unstable. The limit cycle is stable if and only if $4\Omega^2 > \delta^2$ and the larger the difference the larger the limit cycle. When $\Omega = 0$ the limit cycle is unstable and the amplitude of the mood variation blows up when $\delta = 0$ which is considered as the worst case of a bipolar patients.

The numerical calculations suggest that the amplification of *K* has impact on the amplitude of these limit cycles but not on the stability of these limit cycles. Our results show that the amplitude of the parametric excitation is directly proportional to the amplitude of the stable limit cycles. Fig. 3.1 and Fig. 3.2 are in support of the above assertion.

The method of multiple scale perturbation that we used gave us an approximate solution of the non – linear oscillator, to validate and verify the correctness of the solution, we represent

it graphically and simulate the model using the following set of parameters $w = 1.0, a_0 = 1,$

$\delta = 0.5, F = 0.9, \quad a_1 = 20, a_2 = 100, a_3 = 50$.

The main goal of this work is the mathematical modeling of a mental illness which is characterized by mood swings of bipolar II disorder individuals. This minimalist model is essential because there is insufficient data at this time of the quantitative construction. The patient should be on medications which permit stability of the oscillations. The medication function we choose comprises of the drugs, psychosocial therapy and other forms of therapies that help in the stability of the mood. Assuming there is a great adherence to the prescribed drugs, we are particular on the effect of psychosocial therapy to the stability. The results presented by Figs. 3.1 and 3.2 illustrate two different situations. Fig. 3.1 illustrates the case of an individual on whom the drugs are administered with great adherence and psychosocial therapy (FFT) is neglected and Fig. 3.2 illustrates the total adherence to medication and full implementation of FFT. The results show that stability of the mood swings of a bipolar II disorder patient is reached faster when the psychosocial therapy is fully implemented. This kind of study of mental illness could improve the comprehension of the dynamical characteristics of psychosocial disorders and the medication approach. When the allostatic processes of a body system is healthy, medication is adhered to strickly and the psychosocial therapy is atticulated duely, then the amplification of the mood of a bipolar II disorder will reduced drastically and eventually standardized shown fully in Fig. 3.3. Fig. 3.4 shows that on the onset of Bipolar II disorder, if the homeostatic process is distorted such that total internal regulation can not be restored naturally, the amplification of the mood swing will be unbounded. Consequently, the patient may harm himself/herself when the damping coefficient is zero by suicide or other related acts that may hamper the flow of the quality of life. Regardless that the increase in the damping parameters both positively and negatively affects the amplification of the mood oscillation, a prescribed medication and other

psychosocial therapy should be adhered to avoid complicate health suituations as is shown in Fig. 3.5.

We proposed limit cycle oscillator model that make an effort to explicate qualitatively the moods swings of bipolar II individuals. At present there is insufficient data at this time to construct a quantitatively elaborate model describing bipolar II disorder. Standardized phenomenological models have produced significant insight into the dynamics of several oscillatory biological and physical phenomena (Daugherty et.al, 2009, Nana, 2009, Wirkus and Rand, 2002). Regardless that time-series data that describe the moods of bipolar II disorder patients are scarce, the model we have developed could help in the increase of the understanding of the effect of treatment (medication and psychosocial therapy) on the cyclic behavior of bipolar II individuals. Our model captures qualitatively the prevalent behaviour of treated and untreated bipolar II disorder patient. Our model will be refined using time-series data from clinical trials such that the quantitative analysis of the dynamics will represent that of a bipolar II disorder patient. We considered treatment: prescribed medication and family and friend therapy; FFT as a forcing function that led to a stable limit cycle with smaller amplitude, which we interpreted as a decrease in the severity of the mood swings of the bipolar patient. This model proposes that patients that are not diagnosed at a sufficiently tender age might need drastic intervention to bring their mood swings to a reasonable level. Given that patients are usually diagnosed in the depressive state and that bipolar disorder is frequently misdiagnosed initially, this aspect of model is especially noteworthy (Lewis, Vornik, 2003). A particular basic purpose of this work is to motivate the collection of such data so that detailed models of bipolar II disorder can ultimately be developed. Data describing the mood variations of ‘‘normal” persons should also be collected to provide a basis for comparison with time-series data describing the behaviour of bipolar II disorder patients.

CHAPTER 4

HPA AXIS EFFECT ON MOOD VARIATION OF BD PATIENT

4.1 INTRODUCTION

The hypothalamic – pituitary – adrenal (HPA) axis helps to maintain basal and stress related homeostasis of central nervous system (CNS), cardiovascular, metabolic and immune functions (Chrousos, 1998). Detailed dynamics of the HPA axis is complex, depending on the individual metabolic load of an organism, its current status and environmental impacts (Vladimir et al., 2011). Cortisol, the HPA axis arch – hormone in humans, exhibits complex dynamic behavior with two notable frequencies: ultradian oscillations, with a period of 20 – 120 min (Miller and Chrousos, 2001; Tsigos and Chrousos, 2002) superimposed on circadian oscillations, with a period of about 24 hours. There are many literatures that establish the importance of circadian rhythms in the functionality of HPA axis; recent experimental (Stavreva et al., 2009; Russel et al., 2010; Jeferry et al. 2011) and theoretical (Jelic et al., 2008, Walker et al., 2010; Markovic et al., 2010) results offer notable evidence to support the inherent roles of ultradian oscillatory dynamics of HPA hormones levels for normal physiology. Since the ultradian and circadian oscillations have disparity in their time scale, it will culminate that their effects result to disparate biological realms.

In the absence of an inherent oscillatory mode, it is difficult to attribute a role to HPA axis endogenous dynamics in the creation or amplification of circadian or ultradian cycles (Hosseinichimch et al., 2015). Regardless, circadian rhythms of hormones are synchronized by environmental factors such as light, they are generated by an endogenous system called circadian clock. The widely accepted understanding of the system is that the suprachiasmatic nucleus (SCN) of the hypothalamus controls the circadian system, but it is not limited to SCN (Dickmics et al., 2013). SCN coordinates the regulation of cellular clocks because circadian

rhythm exists even in the organ level by sending hormonal and electrical signals (Albrecht, 2012). Originally, it was believed that the pulsatile release of CRH from the hypothalamus creates ultradian oscillations. But blocking the effect of CRH on the pituitary did not eliminate the pulsatile release of ACTH (Bornstein, 2008). Hence it is agreed that multiple and redundant mechanisms regulate the ultradian oscillations (Hosseinichimch et al., 2015; Bornstein, 2008).

Changes in the detailed dynamics of the HPA axis emerge routinely while the axis copes with a myriad of external stimuli (Markovic et al., 2010). Stress and some ailments are associated with short or long – term perturbation of the HPA dynamics. These factors change the amplitude and /or frequency of the basal HPA hormones discharge that results to many health condition, which includes bipolar disorder, Cushing's syndrome, hypertension, visceral obesity, diabetes, osteoporosis (Miller and Chrousos, 2001).

Cortisol the arch – hormone of HPA axis, when elevated is associated with depression which also inhibits the production of thyroid stimulating hormone (TSH): [Thyroxin (T_4) and triiodothyronine (T_3)]. Elevated cortisol levels are potentially related to reduced feedback inhibition of the HPA axis while low levels of cortisol are associated with increased feedback inhibition of the HPA system (Belmaker and Agam, 2008). Besides the changes in the level of cortisol, alterations in the frequency of the ultradian oscillation have noticed in some patient with depression (Rand and Armbruser, 1985). The contextual model of the axis dynamics is significant as to curb this lag in frequency alteration.

Purpose of this study is to underpin the effect of circadian oscillations of cortisol as it relates to its effect to mood variation which is evidential in bipolar disorder patient. In addition, we will consider the change of emotional state of bipolar II disorder patient with respect to the quantity of cortisol in the bloodstream.

4.2 FORMULATION OF THE MODEL

For the purpose of formulating a mathematical model of bipolar II disorder, some assumptions are pertinent. There is a periodicity that governs the utradian and circadian oscillation which induces same for hypomanic and depressive episodes; that have rapid cycling when the patient is treated with only antidepressant (Chrousos, 1998),. The amount of cortisol in the system of a patient has great effect to the emotional state of the patient; either hypomanic or depressive episodes, hence endocrine dysfunctionality corresponds to bipolar II disorder. Additionally, the bipolar II patient has mood swings that oscillate; hence the formation of limit cycle is inevitable. We can model the mood variations of a bipolar patient with a negatively damped harmonic oscillator and show the effect of psychosocial therapy on the patient. Our model is a special form of Duffing – Van der Pol oscillator

$$\frac{d^2u}{dt^2} + \delta\frac{du}{dt} + w^2u = f\left(u', u, x, t\right) \tag{4.1}$$

where u is the emotional state of the patient, u' is the rate of mood changes between hypomania and severe depression, δ is the damping coefficient, w is the natural frequency of the oscillator. The solution of (4.1) often gives unbounded oscillations which is a major drawback of such a model. $f\left(u, u', x, t\right)$ in (4.1) represents the medication given to the patient, which we define as

$$f\left(u', u, x, t\right) = \alpha u^2 + \beta u^3 - \varepsilon F\frac{d^2\bar{u}}{dx^2} \tag{4.2}$$

where α, β are parameters that stabilize the emotional state of the patient, F is the resultant external and internal force that induces mood swing by changing the level of cortisol in the system or otherwise, ε is taken to be a bookkeeping device and $\bar{u}$ is the initial emotional state of patient at the point of observation initialization, x is the level of cortisol in the blood stream. Combining (4.1) and (4.2) we get

$$\frac{d^2u}{dt^2}+\delta\frac{du}{dt}+w^2u-\alpha u^2-\beta u^3=-\varepsilon F\frac{d^2\bar{u}}{dx}. \tag{4.3}$$

Considering the emotional state of the patient with respect to the amount of cortisol in the blood; we use the Van der Pol oscillator to represent an untreated bipolar patient

$$\frac{d^2u}{dx^2}+\delta\frac{du}{dx}+2\lambda u=0, \tag{4.4}$$

where 2λ is the natural frequency on which the arch – hormone of HPA axis is released into the bloodstream. The central neuroendocrine system; HPA axis has a feedback mechanism that mediate on the functionality of the hypothalamus, pituitary gland and adrenal gland, hence we assume $\delta=0$, therefore

$$\frac{d^2u}{dx^2}+2\lambda u=0. \tag{4.5}$$

Differentiating (4.5) twice and applying the treatment as an autonomous forcing function $f(u,x,t)$ we obtain

$$\frac{d^4u}{dx^4}+2\lambda\frac{d^2u}{dx^2}=f(u,x,t). \tag{4.6}$$

On coupling (4.3) and (4.6) we obtain that

$$\frac{\partial^2u}{\partial t^2}+\delta\frac{\partial u}{\partial t}+\frac{\partial^4u}{\partial x^4}+2\lambda\frac{\partial^2u}{\partial x^2}+w^2u-\alpha u^2-\beta u^3=-2\varepsilon F\frac{\partial^2\bar{u}}{\partial x^2} \tag{4.7}$$

where $\bar{u}=a_m\sin mx$; a_m is the initial amplitude of the emotional state and m is the frequency.

4.3 Analytical Solution

By using perturbation method (Rand and Armbruser, 1985) we can obtain information regarding the limit cycles of (4.7). Let

$$0\le x\le\pi,\ 0<\delta\ll 1. \tag{4.8}$$

Let

$$u(x,t)=U\left(x,\hat{t},\tau,\varepsilon\delta\right).$$

We assume the following homogenous initial conditions

$$u(x,0)=u'(x,0)=0 \tag{4.9}$$

and the boundary condition

$$u(0,t)=\frac{d^2u(0,t)}{dx^2}\ \text{at}\ x=0,\pi. \tag{4.10}$$

We introduce slow time scales τ and $\hat{t}$, given by

$$\tau=\delta t \tag{4.11}$$

and

$$\hat{t}=t+\frac{1}{\delta}\left(\varepsilon\mu_1+\varepsilon^2\mu_2+\varepsilon^3\mu_3+\cdots\right) \tag{4.12}$$

where $\mu_i=\mu_i(\tau),\ \mu_i(0)=0,\ i\in\mathbb{N}.$

Thus we get

$$\frac{du}{dt}=U'=\frac{\partial U}{\partial\hat{t}}+\left(\varepsilon\mu_1'(\tau)+\varepsilon^2\mu_2'(\tau)+\varepsilon^3\mu_3'(\tau)+\cdots\right)\frac{\partial U}{\partial\hat{t}}+\delta\frac{\partial U}{\partial\tau}. \tag{4.13}$$

$$\left.\begin{aligned}\frac{d^2U}{d\hat{t}^2}=&\frac{\partial^2U}{\partial\hat{t}^2}+2\left(\varepsilon\mu_1'(\tau)+\varepsilon^2\mu_2'(\tau)+\varepsilon^3\mu_3'(\tau)+\cdots\right)\frac{\partial^2U}{\partial\hat{t}^2}\\&+\left(\varepsilon\mu_1'(\tau)+\varepsilon^2\mu_2'(\tau)+\cdots\right)^2\frac{\partial^2U}{\partial\hat{t}^2}+2\left(\varepsilon\mu_1'(\tau)+\varepsilon^2\mu_2'(\tau)+\cdots\right)\delta\frac{\partial^2U}{\partial\hat{t}\,\partial\tau}\\&+2\delta\frac{\partial^2U}{\partial\hat{t}\,\partial\tau}+\delta\frac{\partial U}{\partial\hat{t}}\left(\varepsilon\mu_1''(\tau)+\varepsilon^2\mu_2''(\tau)+\varepsilon^3\mu_3''(\tau)+\cdots\right)+\delta^2\frac{\partial^2U}{\partial\tau^2}.\end{aligned}\right\} \tag{4.14}$$

We have let

$$U\left(x,\hat{t},\tau;\varepsilon\delta\right)=\sum_{i=1}^{\infty}\sum_{j=0}^{\infty}v^{ij}\left(x,\hat{t},\tau;\varepsilon\delta\right)\varepsilon^i\delta^j. \tag{4.15}$$

Substituting (4.13), (4.14) and (4.15) into (4.7), and equating coefficients of $\varepsilon^i\delta^j$ we get

$$O(\varepsilon):\frac{\partial^2v^{10}}{\partial\hat{t}^2}+\frac{\partial^4v^{10}}{\partial x^4}+2\lambda\frac{\partial^2v^{10}}{\partial x^2}+v^{10}=-2F\frac{d^2\bar{U}}{dx^2}. \tag{4.16}$$

$$O(\varepsilon\,\delta):\frac{\partial^2 v^{11}}{\partial \hat{t}^2}+\frac{\partial^4 v^{11}}{\partial x^4}+2\lambda\frac{\partial^2 v^{11}}{\partial x^2}+v^{11}=-2\frac{\partial^2 v^{10}}{\partial \hat{t}\,\partial\tau}+\frac{\partial v^{10}}{\partial \hat{t}}. \tag{4.17}$$

$$O(\varepsilon\,\delta^2):\frac{\partial^2 v^{12}}{\partial \hat{t}^2}+\frac{\partial^4 v^{12}}{\partial x^4}+2\lambda\frac{\partial^2 v^{12}}{\partial x^2}+v^{12}=-2\frac{\partial^2 v^{11}}{\partial \hat{t}\,\partial\tau}+\frac{\partial v^{11}}{\partial \hat{t}}-\frac{\partial^2 v^{10}}{\partial\tau^2}. \tag{4.18}$$

$$O(\varepsilon^2):\frac{\partial^2 v^{20}}{\partial \hat{t}^2}+\frac{\partial^4 v^{20}}{\partial x^4}+2\lambda\frac{\partial^2 v^{20}}{\partial x^2}+v^{20}=-2\mu_1'\frac{\partial^2 v^{10}}{\partial \hat{t}^2}+\alpha\left(v^{10}\right)^2 \tag{4.19}$$

$$\begin{aligned}O(\varepsilon^2\,\delta):\frac{\partial^2 v^{21}}{\partial \hat{t}^2}+\frac{\partial^4 v^{21}}{\partial x^4}+2\lambda\frac{\partial^2 v^{21}}{\partial x^2}+v^{21}&=-2\mu_1'\frac{\partial^2 v^{11}}{\partial \hat{t}^2}-2\mu_1'\frac{\partial^2 v^{10}}{\partial \hat{t}\,\partial\tau}-2\frac{\partial^2 v^{20}}{\partial \hat{t}\,\partial\tau}\\&\quad-\mu_1''\frac{\partial v^{10}}{\partial \hat{t}}+\frac{\partial v^{20}}{\partial \hat{t}}+\mu_1'\frac{\partial v^{10}}{\partial \hat{t}}+2v^{10}v^{11}.\end{aligned} \tag{4.20}$$

$$\begin{aligned}O(\varepsilon^2\,\delta^2):\frac{\partial^2 v^{22}}{\partial \hat{t}^2}+\frac{\partial^4 v^{22}}{\partial x^4}+2\lambda\frac{\partial^2 v^{22}}{\partial x^2}+v^{22}&=-2\mu_1'\frac{\partial^2 v^{12}}{\partial \hat{t}^2}-2\mu_1'\frac{\partial^2 v^{11}}{\partial \hat{t}\,\partial\tau}-2\frac{\partial^2 v^{21}}{\partial \hat{t}\,\partial\tau}\\&\quad-\mu_1''\frac{\partial v^{11}}{\partial \hat{t}}+\frac{\partial v^{21}}{\partial \hat{t}}+\mu_1'\frac{\partial v^{11}}{\partial \hat{t}}+\frac{\partial v^{20}}{\partial\tau}\\&\quad+\alpha\left(\left(v^{11}\right)^2+2v^{10}v^{12}\right).\end{aligned} \tag{4.21}$$

$$\begin{aligned}O(\varepsilon^3):\frac{\partial^2 v^{30}}{\partial \hat{t}^2}+\frac{\partial^4 v^{30}}{\partial x^4}+2\lambda\frac{\partial^2 v^{30}}{\partial x^2}+v^{30}&=-\left(\mu_1'\right)^2\frac{\partial^2 v^{10}}{\partial \hat{t}^2}-2\left(\mu_1'\frac{\partial^2 v^{20}}{\partial \hat{t}^2}+\mu_2'\frac{\partial^2 v^{10}}{\partial \hat{t}^2}\right)\\&\quad+\alpha v^{10}v^{20}+\beta\left(v^{10}\right)^3\end{aligned} \tag{4.22}$$

$$\left.\begin{aligned}O(\varepsilon^3\,\delta):\frac{\partial^2 v^{31}}{\partial \hat{t}^2}+\frac{\partial^4 v^{31}}{\partial x^4}+2\lambda\frac{\partial^2 v^{31}}{\partial x^2}+v^{31}&=-2\left(\mu_1'\frac{\partial^2 v^{21}}{\partial \hat{t}^2}+\mu_2'\frac{\partial^2 v^{11}}{\partial \hat{t}^2}\right)\\&\quad-\left(\mu_1'\right)^2\frac{\partial^2 v^{11}}{\partial \hat{t}^2}-2\frac{\partial^2 v^{30}}{\partial \hat{t}\,\partial\tau}-2\left(\mu_1'\frac{\partial^2 v^{20}}{\partial \hat{t}\,\partial\tau}+\mu_2'\frac{\partial^2 v^{10}}{\partial \hat{t}\,\partial\tau}\right)\\&\quad+\left(\frac{\partial v^{30}}{\partial \hat{t}}+\mu_1'\frac{\partial v^{20}}{\partial \hat{t}}+\mu_2'\frac{\partial v^{10}}{\partial \hat{t}}\right)+\alpha\left(v^{10}v^{21}+v^{20}v^{11}\right)+3\beta\left(v^{10}\right)^2v^{11},\end{aligned}\right\} \tag{4.23}$$

$$\left.\begin{aligned}O(\varepsilon^3\,\delta^2):\frac{\partial^2 v^{32}}{\partial \hat{t}^2}+\frac{\partial^4 v^{32}}{\partial x^4}+2\lambda\frac{\partial^2 v^{32}}{\partial x^2}+v^{32}&=-\left(\mu_1'\right)^2\frac{\partial^2 v^{12}}{\partial \hat{t}^2}-\frac{\partial^2 v^{30}}{\partial\tau^2}\\&\quad-2\left(\mu_1'\frac{\partial^2 v^{22}}{\partial \hat{t}^2}+\mu_2'\frac{\partial^2 v^{12}}{\partial \hat{t}^2}\right)-2\left(\mu_1'\frac{\partial^2 v^{21}}{\partial \hat{t}\,\partial\tau}+\mu_2'\frac{\partial^2 v^{11}}{\partial \hat{t}\,\partial\tau}\right)-2\frac{\partial^2 v^{31}}{\partial \hat{t}\,\partial\tau}\\&\quad-\left(\mu_1''\frac{\partial v^{21}}{\partial \hat{t}}+\mu_2''\frac{\partial v^{11}}{\partial \hat{t}}\right)+\left(\frac{\partial v^{31}}{\partial \hat{t}}+\mu_1'\frac{\partial v^{21}}{\partial \hat{t}}+\mu_2'\frac{\partial v^{11}}{\partial \hat{t}}+\frac{\partial v^{30}}{\partial \hat{t}}\right)\\&\quad+\alpha\left(v^{10}v^{22}+v^{11}v^{21}+v^{12}v^{20}\right)+\beta\left(3\left(v^{10}\right)^2v^{12}+v^{10}\left(v^{11}\right)^2\right).\end{aligned}\right\} \tag{4.24}$$

With the following initial conditions

$$O(\varepsilon): \frac{\partial v^{10}(0,0)}{\partial \hat{t}} = 0, \tag{4.25}$$

$$O(\varepsilon\,\delta): \frac{\partial v^{11}(0,0)}{\partial \hat{t}} + \frac{\partial v^{10}(0,0)}{\partial \tau} = 0, \tag{4.26}$$

$$O(\varepsilon\,\delta^2): \frac{\partial v^{12}(0,0)}{\partial \hat{t}} + \frac{\partial v^{11}(0,0)}{\partial \tau} = 0, \tag{4.27}$$

$$O(\varepsilon^2): \frac{\partial v^{20}(0,0)}{\partial \hat{t}} + \mu_1'(0)\frac{\partial v^{10}(0,0)}{\partial \hat{t}} = 0, \tag{4.28}$$

$$O(\varepsilon^2\,\delta): \frac{\partial v^{21}(0,0)}{\partial \hat{t}} + \mu_1'(0)\frac{\partial v^{11}(0,0)}{\partial \hat{t}} + \frac{\partial v^{20}(0,0)}{\partial \tau} = 0, \tag{4.29}$$

$$O(\varepsilon^2\,\delta^2): \frac{\partial v^{22}(0,0)}{\partial \hat{t}} + \mu_1'(0)\frac{\partial v^{12}(0,0)}{\partial \hat{t}} + \frac{\partial v^{21}(0,0)}{\partial \tau} = 0, \tag{4.30}$$

$$O(\varepsilon^3): \frac{\partial v^{30}(0,0)}{\partial \hat{t}} + \mu_1'(0)\frac{\partial v^{20}(0,0)}{\partial \hat{t}} + \mu_2'(0)\frac{\partial v^{10}(0,0)}{\partial \hat{t}} = 0, \tag{4.31}$$

$$O(\varepsilon^3\,\delta): \frac{\partial v^{31}(0,0)}{\partial \hat{t}} + \mu_1'(0)\frac{\partial v^{21}(0,0)}{\partial \hat{t}} + \mu_2'(0)\frac{\partial v^{11}(0,0)}{\partial \hat{t}} + \frac{\partial v^{30}(0,0)}{\partial \tau} = 0, \tag{4.32}$$

$$O(\varepsilon^3\,\delta^2): \frac{\partial v^{32}(0,0)}{\partial \hat{t}} + \mu_1'(0)\frac{\partial v^{22}(0,0)}{\partial \hat{t}} + \mu_2'(0)\frac{\partial v^{12}(0,0)}{\partial \hat{t}} + \frac{\partial v^{31}(0,0)}{\partial \tau} = 0. \tag{4.33}$$

For solution, we assume

$$v^{i\,j}\left(x,\hat{t},\tau\right) = \sum_{n=1}^{\infty} v_n^{i\,j} \sin nx, \tag{4.34}$$

where

$$\bar{U} = a_m \sin mx,\ m \text{ is fixed},\ \|a_m\| \ll 1. \tag{4.35}$$

We then solve the sequence of differential equations; on substituting (4.34) and (4.35) into (4.16), we have

$$\sum_{n=1}^{\infty}\left[\frac{\partial^2 v_n^{10}}{\partial \hat{t}^2} + \left(n^4 - 2\lambda n^2 + 1\right)v_n^{10}\right]\sin nx = 2Fm^2 a_m \sin mx. \tag{4.36}$$

Multiplying (4.36) by $\sin mx$ and integrating from $x = 0$ to $x = \pi$, for $n = m$, we get

$$\frac{\partial^2 v_m^{10}}{\partial \hat{t}^2} + w_m^2 v_m^{10} = 2F\, m^2 a_m \tag{4.37}$$

where

$$w_m^2 = n^4 - 2\lambda n^2 + 1. \tag{4.38}$$

The solution of (4.37) is

$$v_m^{10}\left(\hat{t},\tau\right) = \alpha_m^{10}\left(\tau\right)\cos w_m \hat{t} + \beta_m^{10}\left(\tau\right)\sin w_m \hat{t} + B_m, \tag{4.39}$$

where

$$B_m = \frac{2F\, m^2 a_m}{w_m^2}. \tag{4.40}$$

Applying (4.25) on (4.39) we obtain

$$v_m^{10}\left(0,0\right) = \alpha_m^{10}\left(0\right) + B_m = 0$$

$$\alpha_m^{10}\left(0\right) = -B_m, \tag{4.41}$$

and

$$\beta_m^{10}\left(0\right) = 0. \tag{4.42}$$

When $i = 1$ and $j = 1$, (4.34) becomes

$$v^{11}\left(x,\hat{t},\tau\right) = \sum_{n=1}^{\infty} v_n^{11}\left(\hat{t},\tau\right)\sin nx. \tag{4.43}$$

Substituting (4.43) into (4.24), we get

$$\sum_{n=1}^{\infty}\left[\frac{\partial^2 v_n^{11}}{\partial \hat{t}^2} + w_n^2 v_n^{11}\right]\sin nx = \left(-2\frac{\partial^2 v_m^{10}}{\partial \hat{t}^2} + \frac{\partial v_m^{10}}{\partial \hat{t}}\right)\sin mx. \tag{4.44}$$

Multiplying (4.44) by $\sin mx$, integrating from $x = 0$ to $x = \pi$ and dividing through by $\frac{\pi}{2}$, we obtain

$$\frac{\partial^2 v_n^{11}}{\partial \hat{t}^2} + w_n^2 v_n^{11} = -2\frac{\partial^2 v_m^{10}}{\partial \hat{t}^2} + \frac{\partial v_m^{10}}{\partial \hat{t}}$$
$$= -2\left(-\alpha_m^{10'} \sin w_m \hat{t} + \beta_m^{10'} \cos w_m \hat{t}\right) \tag{4.45}$$
$$+\left(-\alpha_m^{10} \sin w_m \hat{t} + \beta_m^{10} \cos w_m \hat{t}\right).$$

Applying the solvability condition, we have

$$2\beta_m^{10'} - \beta_m^{10} = 0, \tag{4.46}$$

and

$$2\alpha_m^{10'} - \alpha_m^{10} = 0. \tag{4.47}$$

The solution of (4.46) and (4.47) are given respectively

$$\beta_m^{10}(\tau) = \beta_m^{10}(0)e^{\frac{\tau}{2}} = 0 \tag{4.48}$$

and

$$\alpha_m^{10}(\tau) = \alpha_m^{10}(0)e^{\frac{\tau}{2}} = -B_m e^{\frac{\tau}{2}}. \tag{4.49}$$

Therefore

$$v_m^{10}(\hat{t}, \tau) = \alpha_m^{10}(0)\cos w_m \hat{t} + B_m \tag{4.50}$$

and

$$v^{10}(x, \hat{t}, \tau) = v_m^{10}(\hat{t}, \tau)\sin mx. \tag{4.51}$$

The solution of the remaining equation in (4.45) is

$$v_m^{11}(\hat{t}, \tau) = \alpha_m^{11}(\tau)\cos w_m \hat{t} + \beta_m^{11}(\tau)\sin w_m \hat{t}. \tag{4.52}$$

Using the appropriate initial conditions we obtain

$$\alpha_m^{11}(0) = 0 \tag{4.53}$$

and

$$\beta_{\mathrm{m}}^{11}(0) = -\frac{\alpha_m^{10'}(0)}{w_m} = \frac{B_m}{w_m}. \tag{4.54}$$

When $i = 1$ and $j = 2$, (4.34) become

$$v^{12}\left(x,\hat{t},\tau\right) = \sum_{n=1}^{\infty} v_n^{12}\left(\hat{t},\tau\right)\sin nx. \tag{4.55}$$

Substituting (4.55) into (4.18), we get

$$\sum_{n=1}^{\infty}\left[\frac{\partial^2 v_n^{12}}{\partial \hat{t}^2} + w_n^2 v_n^{12}\right]\sin nx = \left(-2\frac{\partial^2 v_m^{11}}{\partial \hat{t}\,\partial\tau} + \frac{\partial v_m^{11}}{\partial \hat{t}} - \frac{\partial^2 v_m^{10}}{\partial \hat{t}\,\partial\tau}\right)\sin mx. \tag{4.56}$$

Multiplying by $\sin mx$, integrating from $x = 0$ to $x = \pi$ and dividing through by $\frac{\pi}{2}$, we obtain

$$\begin{aligned}\frac{\partial^2 v_n^{12}}{\partial \hat{t}^2} + w_n^2 v_n^{12} &= -2\frac{\partial^2 v_m^{11}}{\partial \hat{t}\,\partial\tau} + \frac{\partial v_m^{11}}{\partial \hat{t}} - \frac{\partial^2 v_m^{10}}{\partial \hat{t}\,\partial\tau} \\ &= -2w_m\left(-\alpha_m^{11\prime}\sin w_m\hat{t} + \beta_m^{11\prime}\cos w_m\hat{t}\right) \\ &\quad + w_m\left(-\alpha_m^{11}\sin w_m\hat{t} + \beta_m^{11}\cos w_m\hat{t}\right) - \alpha_m^{10\prime\prime}\cos w_m\hat{t}.\end{aligned} \tag{4.57}$$

Using the secularity condition in (4.57), we get

$$-2\beta_m^{11\prime} + \beta_m^{11} = \frac{\alpha_m^{10\prime\prime}}{w_m}, \tag{4.58}$$

$$-2\alpha_m^{11\prime} + \alpha_m^{11} = 0. \tag{4.59}$$

The solution to (4.58) is

$$\beta_m^{11}\left(\tau\right) = -e^{\frac{\tau}{2}}\left(\int_0^{\tau}\left(\frac{\alpha_m^{10\prime\prime}}{w_m}\right)e^s ds + k_1\right), \tag{4.60}$$

$$\beta_m^{11}\left(\tau\right) = -e^{\frac{\tau}{2}}\left(\int_0^{\tau}\left(\frac{\alpha_m^{10\prime\prime}}{w_m}\right)e^s ds - \frac{B_m}{w_m}\right) = -\frac{B_m}{w_m}e^{\frac{\tau}{2}}\left(\int_0^{\tau} e^s ds - 1\right). \tag{4.61}$$

Solution to (4.59) is

$$\alpha_m^{11}\left(\tau\right) = \alpha_m^{11}\left(0\right)e^{\frac{\tau}{2}} = 0. \tag{4.62}$$

Therefore

$$v^{11}\left(x,\hat{t},\tau\right)=v_m^{11}\left(\hat{t},\tau\right)\sin mx. \tag{4.63}$$

The solution of the remaining equation in (4.57) is

$$v_m^{12}\left(\hat{t},\tau\right)=\alpha_m^{12}\left(\tau\right)\cos w_m\hat{t}+\beta_m^{12}\left(\tau\right)\sin w_m\hat{t}. \tag{4.64}$$

Applying the proper initial condition we have

$$\alpha_m^{12}\left(0\right)=0, \tag{4.65}$$

$$\beta_m^{12}\left(0\right)=-\frac{\beta_m^{11'}\left(0\right)}{w_m}=\frac{-2B_m}{w_m^2}. \tag{4.66}$$

Therefore

$$v^{12}\left(x,\hat{t},\tau\right)=v_m^{12}\left(\hat{t},\tau\right)\sin mx. \tag{4.67}$$

Furthermore, substituting $\left(4.34\right)$ into (4.19) when $i=2$ and $j=0,$ we get

$$\begin{aligned}\sum_{n=1}^{\infty}\left[\frac{\partial^2 v_n^{20}}{\partial\hat{t}^2}+w_n^2v_n^{20}\right]\sin nx&=-2\mu_1'\frac{\partial^2 v_m^{10}}{\partial\hat{t}^2}\sin mx+\alpha\left(v_m^{10}\right)^2\sin^2 mx\\&=-2\mu_1'\frac{\partial^2 v_m^{10}}{\partial\hat{t}^2}\sin mx+\frac{\alpha}{2}\left(v_m^{10}\right)^2\left(1-\cos 2mx\right).\end{aligned} \tag{4.68}$$

Multiplying (4.68) by $\sin mx$, integrating from $x=0$ to $x=\pi$, we obtain

$$\frac{\pi}{2}\left[\frac{\partial^2 v_n^{20}}{\partial\hat{t}^2}+w_n^2v_n^{20}\right]=-\pi\mu_1'\frac{\partial^2 v_m^{10}}{\partial\hat{t}^2}+\frac{\alpha}{2}\left(v_m^{10}\right)^2\int_0^{\pi}\left(1-\cos 2mx\right)\sin mx\,dx. \tag{4.69}$$

On appropriate substitution of the value of v_m^{10} in (4.69) and simplification, we have

$$\begin{aligned}\frac{\partial^2 v_n^{20}}{\partial\hat{t}^2}+w_n^2v_n^{20}&=-2\mu_1'\left(w_m^2\alpha_m^{10}\cos w_m\hat{t}\right)\\&\quad+\frac{16\alpha}{3\pi m}\left[\left(\frac{\left(\alpha_m^{10}\right)^2}{2}+B_m\right)+\frac{\left(\alpha_m^{10}\right)^2}{2}\cos 2w_m\hat{t}+2B_m\alpha_m^{10}\cos w_m\hat{t}\right].\end{aligned} \tag{4.70}$$

To ensure uniformly valid asymptotic solution in $\hat{t}$, we equate to zero in (4.70) the coefficients of $\cos w_m \hat{t}$, we obtain

$$\mu_1'(\tau) = \frac{16\alpha B_m}{3m\pi w_m^2}. \tag{4.71}$$

The remaining equation in (4.70) is

$$\frac{\partial^2 v_n^{20}}{\partial \hat{t}^2} + w_n^2 v_n^{20} = r_0 + r_1 \cos 2w_m \hat{t}, \tag{4.72}$$

where

$$r_0(\tau) = \frac{16\alpha}{3m\pi}\left(\frac{\left(\alpha_m^{10}(\tau)\right)^2}{2} + B_m^2\right), \tag{4.73}$$

$$r_1(\tau) = \frac{8\alpha}{3m\pi}\left(\alpha_m^{10}(\tau)\right)^2. \tag{4.74}$$

The solution of (4.72) is

$$v_m^{20}(\hat{t},\tau) = \alpha_m^{20}(\tau)\cos w_m \hat{t} + \beta_m^{20}(\tau)\sin w_m \hat{t} + \frac{r_0}{w_m^2} - \frac{r_1 \cos 2w_m \hat{t}}{3w_m^2}. \tag{4.75}$$

We substitute (4.34) into (4.20) when $i = 2$ and $j = 1$,we get

$$\begin{aligned}\sum_{n=1}^{\infty}\left[\frac{\partial^2 v_n^{21}}{\partial \hat{t}^2} + w_n^2 v_n^{21}\right]\sin nx = \Bigg(& -2\mu_1'\frac{\partial^2 v_m^{11}}{\partial \hat{t}^2} - 2\mu_1'\frac{\partial^2 v_m^{10}}{\partial \hat{t}\,\partial \tau} - \mu_1''\frac{\partial v_m^{10}}{\partial \hat{t}} \\ & -\mu_1'\frac{\partial^2 v_m^{20}}{\partial \hat{t}\,\partial \tau} + \frac{\partial v_m^{20}}{\partial \hat{t}} + 2\mu'\frac{\partial v_m^{10}}{\partial \hat{t}}\Bigg)\sin mx \\ & +2\alpha v_m^{10} v_m^{11}\sin^2 mx.\end{aligned} \tag{4.76}$$

Multiplying (4.76) $\sin mx$ and integrating from 0 to π, we get

$$\frac{\pi}{2}\left(\frac{\partial^2 v_n^{21}}{\partial \hat{t}^2}+w_n^2 v_n^{21}\right)=-\frac{\pi}{2}\left(2\mu_1'\frac{\partial^2 v_m^{11}}{\partial \hat{t}^2}+2\mu_1'\frac{\partial^2 v_m^{10}}{\partial \hat{t}\,\partial \tau}+\mu_1''\frac{\partial v_m^{10}}{\partial \hat{t}}\right.$$
$$\left.+\mu_1'\frac{\partial^2 v_m^{20}}{\partial \hat{t}\,\partial \tau}-\frac{\partial v_m^{20}}{\partial \hat{t}}-2\mu'\frac{\partial v_m^{10}}{\partial \hat{t}}\right) \tag{4.77}$$
$$+2\alpha\int_0^{\pi} v_m^{10}v_m^{11}\sin^3 mx\,dx.$$

On appropriate substitution, we have

$$\frac{\partial^2 v_n^{21}}{\partial \hat{t}^2}+w_n^2 v_n^{21}=-\left(-2\mu_1'\beta_m^{11}w_m^{11}\sin w_m\hat{t}-2w_m\alpha_m^{10\prime}\sin w_m\hat{t}\right.$$
$$+2\left(-w_m\alpha_m^{20\prime}\sin w_m\hat{t}+w_m\beta_m^{10\prime}\cos w_m\hat{t}+\frac{2w_m r_1'\sin 2w_m\hat{t}}{3w_m^2}\right)$$
$$-w_m\alpha_m^{20}\sin w_m\hat{t}+w_m\beta_m^{20}\cos w_m\hat{t}+\frac{2w_m r_1\sin 2w_m\hat{t}}{3w_m^2}$$
$$\left.-2w_m\mu_1'\alpha_m^{10}\sin w_m\hat{t}\right)$$
$$+\frac{16\alpha\beta_m^{11}}{3m\pi}\left(\frac{\alpha_m^{10}}{2}\sin 2w_m\hat{t}+B_m\sin w_m\hat{t}\right). \tag{4.78}$$

Using the secularity condition, we obtain that

$$\beta_m^{20}(\tau)\equiv 0, \tag{4.79}$$

$$\alpha_m^{20}(\tau)=e^{\frac{\tau}{2}}\left(\int_0^{\tau}h_1(s)e^s ds+k_2\right), \tag{4.80}$$

where

$$h_1(\tau)=-2\left(\mu_1'\beta_m^{11}w_m+\alpha_m^{10\prime}+\mu_1'\alpha_m^{10}+\frac{8\alpha\beta_m^{11}B_m}{3m\pi}\right). \tag{4.81}$$

The solution to the remaining equation in (4.78) is

$$v_m^{21}(\hat{t},\tau)=\alpha_m^{21}(\tau)\cos w_m\hat{t}+\beta_m^{21}(\tau)\sin w_m\hat{t}-\frac{r_2\sin 2w_m\hat{t}}{3w_m^2}. \tag{4.82}$$

We substitute (4.34) into (4.21) when $i=2$ and $j=2$, and we get

$$\sum_{n=1}^{\infty}\left(\frac{\partial^2 v_n^{22}}{\partial \hat{t}^2}+w_n^2 v_n^{22}\right)\sin nx=\left(2\mu_1'\frac{\partial^2 v_m^{12}}{\partial \hat{t}^2}-2\mu_1'\frac{\partial^2 v_m^{11}}{\partial \hat{t}\,\partial\tau}-\frac{\partial^2 v_m^{21}}{\partial \hat{t}\,\partial\tau}-\mu_1''\frac{\partial v_m^{11}}{\partial \hat{t}}\right.$$
$$\left.+\frac{\partial v_m^{21}}{\partial \hat{t}}+\mu_1'\frac{\partial v_m^{11}}{\partial \hat{t}}+\frac{\partial v_m^{20}}{\partial\tau}\right)\sin mx \qquad (4.83)$$
$$+\alpha\left(v_m^{11}\right)^2\sin^2 mx+2\alpha v_m^{10}v_m^{12}\sin^2 mx.$$

Multiplying (4.83) by $\sin mx$, integrating from 0 to π, and making appropriate substitution we get

$$\frac{\partial^2 v_m^{22}}{\partial \hat{t}^2}+w_m^2 v_m^{22}=-2\mu_1'\beta_m^{12}w_m^2\cos w_m\hat{t}-2\mu_1'\beta_m^{11\prime}w_m\cos w_m\hat{t}+\alpha_m^{21\prime}w_m\sin w_m\hat{t}$$
$$-\beta_m^{21\prime}w_m\cos w_m\hat{t}+\frac{2w_m r_2'}{3w_m^2}\cos 2w_m\hat{t}-\alpha_m^{21}w_m\sin w_m\hat{t}$$
$$+\beta_m^{21}w_m\cos w_m\hat{t}-\frac{2w_m r_2}{3w_m^2}\cos 2w_m\hat{t}+\mu_1'\beta_m^{11}\cos w_m\hat{t} \qquad (4.84)$$
$$+\alpha_m^{20\prime}\cos w_m\hat{t}+\beta_m^{20\prime}\sin w_m\hat{t}+\frac{r_0'}{w_m^2}-\frac{r_1'}{3w_m^2}\cos 2w_m\hat{t}$$
$$+\frac{8\alpha}{3m\pi}\left[\frac{\left(\beta_m^{11}\right)^2}{2}\left(1-\cos 2w_m\hat{t}\right)+\frac{\beta_m^{12}}{2}\left(\alpha_m^{10}\cos 2w_m\hat{t}+1\right)\right].$$

Using the solvability condition on (4.84), we get

$$\beta_m^{21}(\tau)=e^{-\tau}\left(\int_0^{\pi}h_2(s)e^s ds+k_3\right), \qquad (4.85)$$

and

$$\alpha_m^{21}(\tau)\equiv 0. \qquad (4.86)$$

The solution to the remaining equation in (4.84) is

$$v_m^{22}(\tau)=\alpha_m^{22}\cos w_m\hat{t}+\beta_m^{22}\sin w_m\hat{t}+\frac{r_3}{w_m^2}-\frac{r_4}{3w_m^2}\cos 2w_m\hat{t}, \qquad (4.87)$$

and

$$v^{22}\left(x,\hat{t},\tau\right)=v_m^{22}\left(\hat{t},\tau\right)\sin mx. \tag{4.88}$$

We substitute (4.34) into (4.22) when $i=3$ and $j=0$,we get

$$\begin{aligned}\sum_{n=1}^{\infty}\left(\frac{\partial^2 v_n^{30}}{\partial\hat{t}^2}+w_n^2v_n^{30}\right)\sin nx=&\left(-\left(\mu_1'\right)^2\frac{\partial^2 v_m^{10}}{\partial\hat{t}^2}-2\mu_1'\frac{\partial^2 v_m^{20}}{\partial\hat{t}^2}-2\mu_2'\frac{\partial^2 v_m^{10}}{\partial\hat{t}^2}\right)\sin mx\\&+\frac{\alpha}{2}v_m^{10}v_m^{20}\left(1-\cos 2mx\right)+\frac{\beta}{4}\left(v_m^{10}\right)^3\left(3\sin mx-\sin 3mx\right).\end{aligned} \tag{4.89}$$

Multiplying through by $\sin mx$ at $n=m$, simplifying the coupling terms and integrating form 0 to π we obtain

$$\begin{aligned}\frac{\partial^2 v_m^{30}}{\partial\hat{t}^2}+w_m^2v_m^{30}=&\left(\mu_1'\right)^2w_m^2\alpha_m^{10}\cos w_m\hat{t}-2\mu_1'\left(-\alpha_m^{20}w_m^2\cos w_m\hat{t}+w_m^2\beta_m^{20}\sin w_m\hat{t}\right.\\&\left.-\frac{4r_1}{3}\cos 2w_m\hat{t}\right)+2\mu_2'w_m^2\alpha_m^{10}\cos w_m\hat{t}\\&+\frac{3\beta}{4}\left(\frac{\left(\alpha_m^{10}\right)^3}{4}\left(\cos 3w_m\hat{t}+3\cos w_m\hat{t}\right)+\frac{3\left(\alpha_m^{10}\right)^2B_m}{2}\left(\cos 2w_m\hat{t}+1\right)\right)\\&+\frac{8\alpha}{3m\pi}\left\{\frac{\alpha_m^{10}\alpha_m^{20}}{2}\cos 2w_m\hat{t}+\frac{\alpha_m^{10}\beta_m^{20}}{2}+\frac{\alpha_m^{10}r_0}{w_m^2}\cos w_m\hat{t}\right.\\&-\frac{\alpha_m^{10}r_1}{6w_m^2}\left(\cos 3w_m\hat{t}+\cos w_m\hat{t}\right)+B_m\alpha_m^{10}\cos w_m\hat{t}+B_m\beta_m^{20}\sin w_m\hat{t}\\&\left.+\frac{B_mr_0}{w_m^2}-\frac{B_mr_1}{3w_m^2}\cos 2w_m\hat{t}\right\}.\end{aligned} \tag{4.90}$$

To ensure uniformly valid asymptotic solution in $\hat{t}$, we equate to zero in (4.90) the coefficients of $\cos w_m\hat{t}$ and $\sin w_m\hat{t}$

$$\therefore\ \mu_2'\left(0\right)=\frac{\beta B_m^2}{\left(m\pi w_m^2\right)^2}s_{30} \tag{4.91}$$

where

$$s_{30}=\frac{\alpha^2}{\beta}\left\{\frac{32}{9w_m}-\left(\frac{16}{27}+\frac{9}{4}\left(m\pi w_m\right)^2\right)\right\}. \tag{4.92}$$

The solution of the remaining equation in (4.90) is

$$v_m^{30}\left(\hat{t},\tau\right)=\alpha_m^{30}\cos w_m\hat{t}+\beta_m^{30}\sin w_m\hat{t}+\frac{r_5}{w_m^2}-\frac{r_6\cos 2w_m\hat{t}}{3w_m^2}-\frac{r_7\cos 3w_m\hat{t}}{8w_m^2}. \tag{4.93}$$

Thus the emotional state $u\left(x,\hat{t},\tau\right)$ becomes

$$\begin{aligned}u\left(x,\hat{t},\tau\right)=&\varepsilon\left(v_m^{10}\sin mx+\delta v_m^{11}\sin mx+\delta^2 v_m^{12}\sin mx+\cdots\right)\\&+\varepsilon^2\left(v_m^{20}\sin mx+\delta v_m^{21}\sin mx+\delta^2 v_m^{12}\sin mx+\cdots\right)\\&+\varepsilon^3\left(v_m^{30}\sin mx+v_{3m}^{30}\sin mx+\delta\left(v_m^{31}\sin mx++v_{3m}^{31}\sin mx\right)+\cdots\right)+\cdots\end{aligned} \tag{4.94}$$

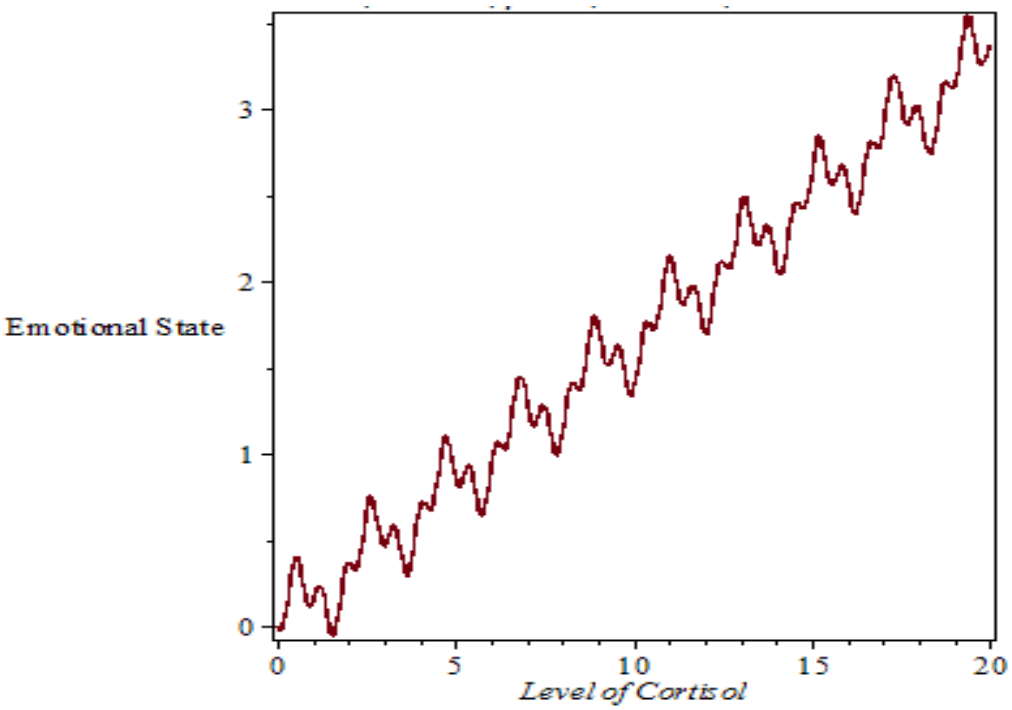


Fig. 4.1: Mood variation and level of cortisol in the blood ($\mu gm/100ml$), when $\delta = 0.01, \alpha = -30, \beta = 40$, $F = 0.50, \lambda = 0.43$.

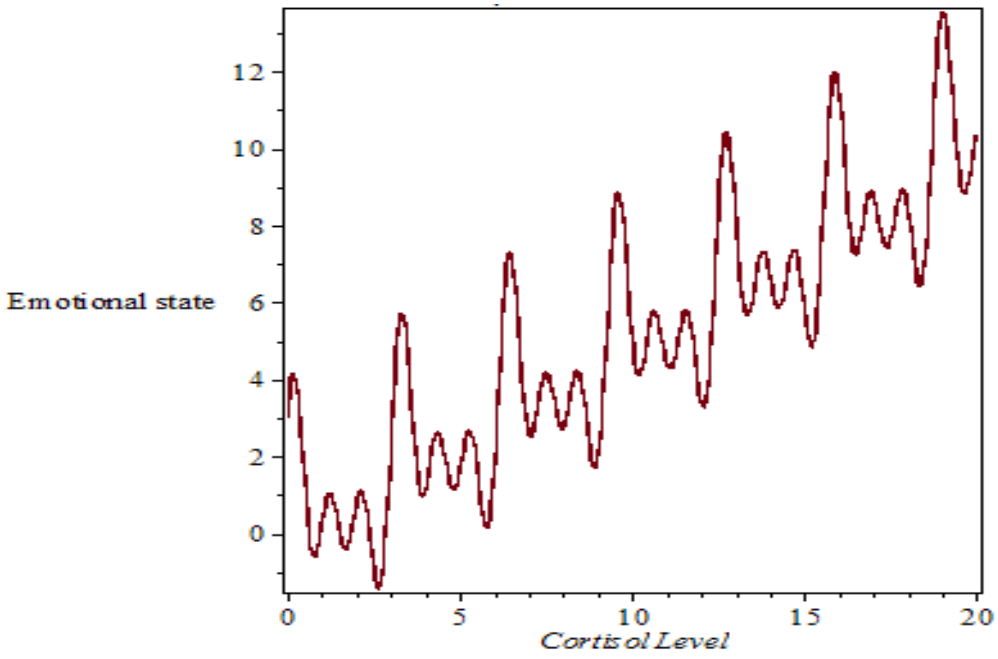


Fig. 4.2: Mood variation and level of cortisol in the blood ($\mu gm/100ml$), when $\delta = 0.05, \alpha = 30, \beta = -40$, $F = 0.50, \lambda = 0.5$.

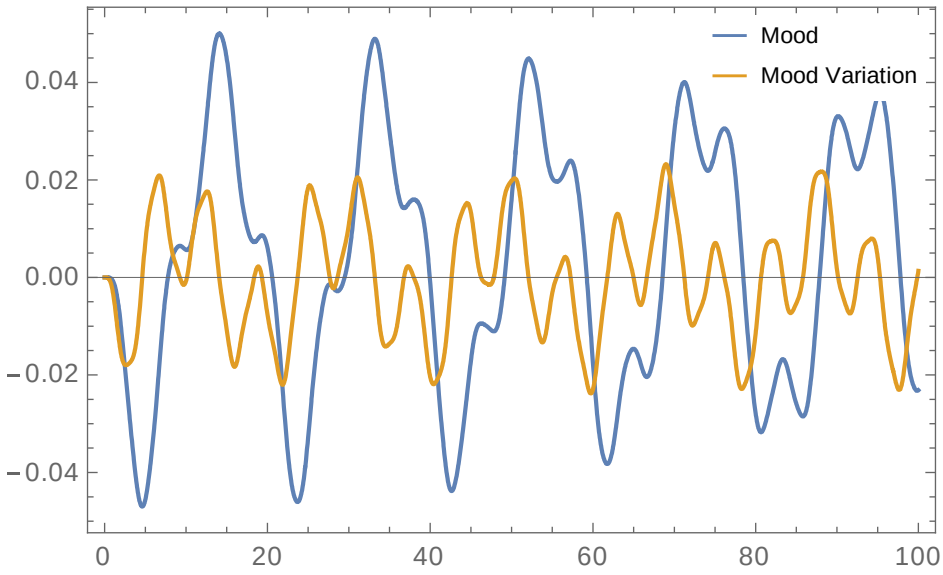


Fig. 4.3: Mood variation versus mood and level of cortisol in the blood ($\mu gm/100ml$), when $\delta = 0.05$, $\alpha = 30, \beta = -40, F = 0.50, \lambda = 0.5$.

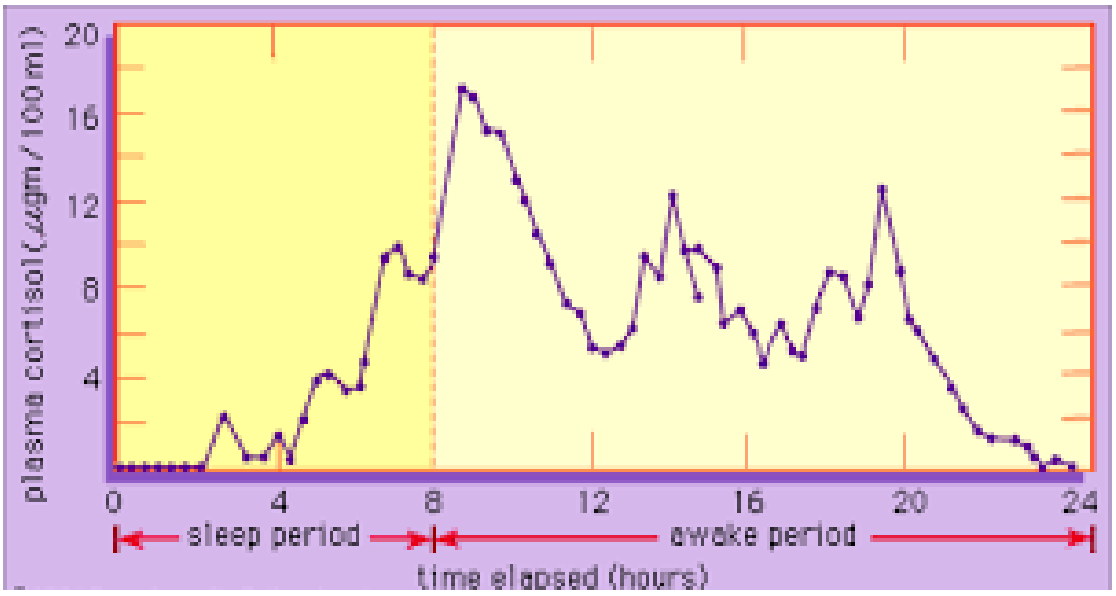


Fig. 4.4: Circadian rhythm of Plasma cortisol in the blood ($\mu gm/100ml$) for normal human adopted from Encyclopedia Britannica 2018.

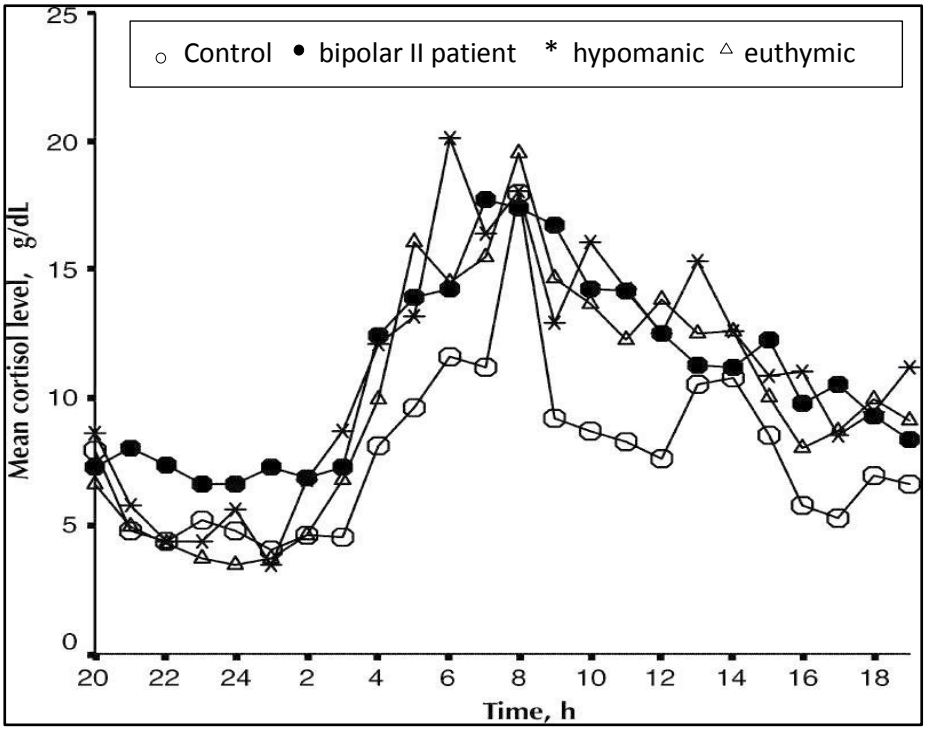


Fig. 4.5: Mean 24-h cortisol secretion of normal controls, patients with bipolar disorder in depressed, hypomanic and euthymic phases of their illness.

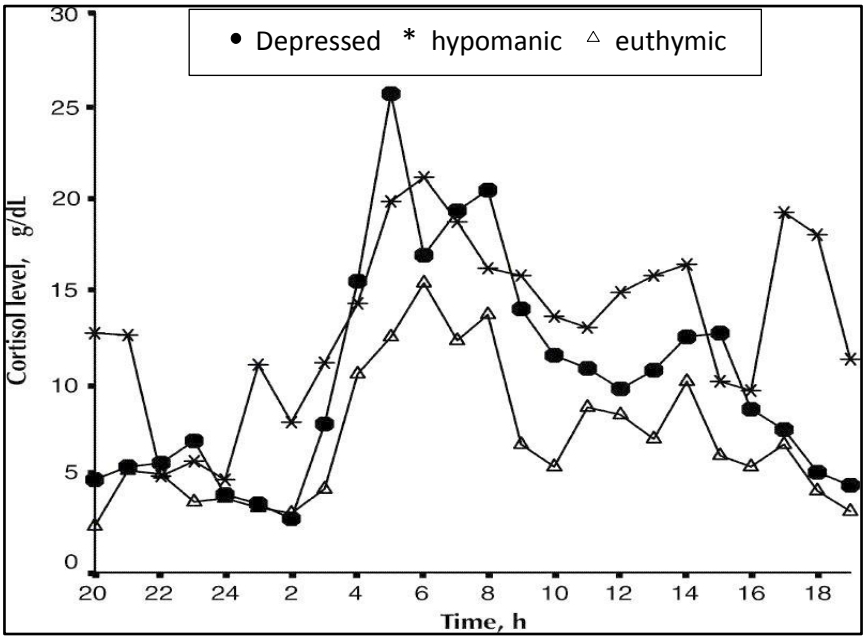


Fig. 4.6: The 24-h cortisol secretion profile of Mr. J.B. in 3 mood phases of bipolar disorder. Depressed phase; euthymic phase, hypomanic phase.

4.4 Discussion

Cortisol is the main byproduct of HPA axis activities. Stress situations trigger the HPA axis, which is essential in raising the concentration of cortisol that leads to release of energy to the organism. Stress, both acute and chronic, has been identified as an essential etiological factor of depression. Fig. 4.1 and Fig. 4.2 show that hypercortisolism and hypocortisolism have significant effect on the mood variation of bipolar II disorder patient. HPA axis hyperactivity or hypoactivity can be termed as HPA axis dysregulation that might partly mediate the increased risk of BD relapse following intense psychosocial stress (Weiss et al., 2015). HPA axis hyperactivity predicted clinical relapses (Havermans et al., 2011) and hypoactivity is associated with a higher number of mood episodes (Ellenbogen et al., 2013). Maripuu et al. (2017) explains that relative hypercortisolism were common among younger and more often females while hypocortisolism is common among older patients; must often inherent in patients that was not on Lithium. Since hypercortisolism is more peculiar among younger BD patients, we can suggest that hypocortisolism results from accumulated stress load from physiology, environmental and severe ailment episodes. This view is buttressed by (Maripuu et al. 2017, Gustafsson et al., 2012) with studies performed on stress – related disorder and general population samples that collectively point at increased chronic stress and increased accumulated stress load as central to the development of the phenomenon.

Fig. 4.3 relates the mood variation and mood as the circadian rhythm of the cortisol is regulated. The observation shows that there is no significant change but the mood and its variation responds to the physiological reactions and environmental pulls. Fig. 4.4 is a typical circadian rhythm of plasma cortisol regulations in the blood stream for a normal human; hence, the oscillation buttress the indication in Fig. 4.1, 4.2 and 4.3. Fig. 4.5 – 4.6 represent cortisol secretion profile for the different episode of bipolar II disorder patients. They show that there are no significant circadian phase shifts associated with that of ailment. The

increase and decrease in cortisol secretion in BD patients in both depressed and hypomanic phases suggest that cortisol level is not emblematic of bipolar II disorder but should not be relegated.

BD has a multifactorial etiology, depending on both genetic and environmental factors. Lately (Craddock and Sklar, 2013) estimated that monozygotic twin show concordance between 40 and 70%, and a heritabitity of around 90%. Enormous research has been conducted on the genetic risk factors of BD (Belvederi et al., 2016), genes related to HPA axis activity were not found to be significant risk factors for BD. Common polymorphisms of HPA – related genes are associated with different clinical features of BD. Variants of "clock" genes confer a vulnerability to circadian rhythms instability and to BD itself (Gonzalez, 2014). Environmental stressors such as parental neglect can lead to a vertical, intergenerational transmission of HPA axis abnormalities (Maripuu et al., 2017); suggested that it might occur as a result of childhood trauma and dysregulated parenting style (Ellenbogen et al., 2013). Recently (Perroud et al., 2014) showed that childhood traumatic experiences can determine epigenetic modifications of the glucocortisolic receptors (GR) gene in patients with BD, HPA axis dysfunction might act as a mediator, on the basis of gene – environmental interactions (Ostiguy et al., 2011). Summarily, HPA axis hyperactivity or hypoactivity can be considered as an endophenotype, i.e. an etiological factor of BD but rather as a pathogenetic mechanism that can contribute to shape the clinical presentation of the disorder, on the ground of genetic – environmental interplay.

4.5 Conclusion

Hyperactive hypothalamic – pituitary – adrenal (HPA) axis is eminent occurrence in bipolar disorder. Nevertheless, hypocortisolism has also been designed and concomitant with depression, low quality of life and cardiovascular risk factors in BD patients. Although the

pathophysiology related to hypocortisolism in BD is basically unknown, hypocortisolism is associated with lingering stress exposure and after prompting an initial rise in cortisol long – term stress may result in a transition to hypocortisolism. BD patients are throughout life often exposed to chronic stress. We therefore hypothesized that higher age would be associated with lower HPA – axis activity especially among patients without previous mood stabilizing treatment (Maripuu et al. 2017). In general, humans respond to stress through a complex system that affects nearly every part of the body, from the brain down to the stomach. But once cortisol suppresses the immune system, it slows down digestion and causes a blockage that could lead to sleeplessness, depression, and obesity. When a person is suffering from bipolar disorder or depression, they experience high level of cortisol in their system as a result of long-term stress. Over time, chronic stress causes the body to into crisis mode, which in turn drops cortisol levels low enough to trigger even more weight gain.

Bipolar II disorder and HPA axis activities are highly related. HPA axis hyperactivity in young folks and hypoactivity in older folks are associated with significant capacity to the hypomanic episode, likewise the depressive episode; as a result HPA abnormalities will partly affect BD patient. Numereous evidence suggests that HPA axis abnormalities should not be considered as an etiological or endophenotype factor of BD but as a pathogenetic and pathophysiological mechanism that contributes to shape BD clinical presentation (Belveder et al., 2016; Watson et al. 2012). Conclusively, HPA axis might be a great target pharmacologically to improvement of bipolar II disorder patients regardless that there are no significant circadian phase shifts in the various episodes.

CHAPTER 5

FRACTIONAL ORDERED DAMPING OF MOOD VARIATION

5.1 INTRODUCTION

Fractional calculus is an essential branch of Mathematics that has been in vogue since 17th century. Researchers have been focusing on its application enormously in the field of physics and engineering (Jingfei et al. 2017, Machado et al., 2011, Mainardi et al., 2010, Baleanu et al. 2012). Fractional – order derivative has significant phenomena in control engineering (Li et al., 2010), heat transfer (Losa et al., 2005), signal processing (Chen et al., 2012), fluid mechanics (Chen et al., 2011), vibrations and dynamics (Shen, 2016). Several real phenomena are better understood by science of complexity that provides new view to what seemed inexplicable and hidden properties of such complex systems can be explored (Nigmalulin et al., 2012). Recently there is a trend observed in research community where fractional calculus has been used in modeling complex phenomena. Many researches observed fractional – order derivative as an essential tool for solving problems in viscoelasticity, diffusion and electrochemistry (Li et al., 2011; Chen et al. 2011; Ortigueira and Machado, 2006; Hilfer et al., 2012; Agrawal, 2012) that have their application in many field of study. D. Paola discussed the relation between creep/relaxation and multiphase fractional hereditary material and their electrical analogue models (Ala et al., 2014). Such models are often expressed as impedence models, which is the form normally used to represent bioimpedence measurements in respiratory system. The dynamic processes that are inherent in biological tissues are complex because they are characterized by processes that occur at different timescale and length. Fractional – order derivative models are often necessary to account for the rich phenomena that take place within biological or dynamic processes at different scales (Nigmalulin et al., 2012; Shen et al., 2016; Ala et al., 2014, Vosika et al., 2014).

Biological processes have been modeled using fractional order derivative; it has recently been suggested that neuronal adaptation allows neuronal spiking to communicate a fractional derivative of the actual computed signal (Lundstrom et al., 2010), the kinetics of drug distribution throughout the human body is conventionally compartment models that is evolving rapidly into the fractional domain (Bao et al., 2013). Fractional derivative is useful in investigating the impulse time response of the human respiratory impendence of patients diagnosed of asthma and cystic fibrosis (Ionescu et al., 2011).

Bipolar disorder is a psychiatric condition associated with abnormalities in many cognitive and regulatory functions of which the etiology is not fully understood (Sachs and Thase, 2000). Several researchers linked the neurobiology to abnormalities in structure and/or function at many levels of the nervous system (Buckjohn et al., 2010, McEwen et al., 2000), neurotransmitter function with abnormalities in γ - aminobutyric acid (GABA) and glutamatergic pathways (Rothbaum and Astin, 2000, Leow et al., 2013), pathogenesis in the circadian system and abnormal patterns of corticocortical and subcortical connectivity (Baghdadi et al., 2015; Strakowski et al. 2012). The initial emotional trigger of bipolar disorder results in a type of crisis in the system, in which the destruction of basal emotion is accompanied with formation of two abnormal emotion/attractors (mania and depression) and chaotic transients between them (Tanaka et al., 2005). Models of chaotic systems such as Forced Duffing oscillator which demonstrate various kind of crisis by changing their parameters could be deployed to characterize the basic features of human emotional states, when they are presenting multistable and intermittent behaviors, as in the case of bipolar disorder. Chaotic intermittency has been observed in circuit oscillators, economic variables, non- periodic associative dynamics in chaotic neural networks as well as in psychiatric disorders like obsessive – compulsive disorder (Tanaka et al., 2005; Rabinovich and Varona,

2011). However, we believe that such concept also could be applied to mood variation pattern in bipolar disorder.

Integer order differential operators are local operators while the fractional order differential operators are non – local i.e. systems depend not only upon its current state but also upon all of its historical states. The latter is the reason behind the popularity of fractional order nonlinear oscillators. Fractional derivatives are non – local operators, and they provide a wonderful instrument for the modeling of memory and heredity properties of viscoelastic materials. In addition, such models have the ability of describing the viscoelastic behavior with small number of parameters (Jingfei et al., 2017).

In study of fractional – order derivatives, one should note that finding an analytical or approximate solution is a challenging problem, therefore, accurate methods for finding the solutions of fractional – order derivatives are still under investigation. The study of fractional – order derivative has been possible using various analytical and numerical techniques including averaging method (Chen et al., 2011), multiple – scale approach (Xu et al., 2013), the various homotopy analysis method (Mishra et al., 2016), the differential transform method (Arikoghi and Ozkol, 2007), variational iteration method (Cao et al., 2010), decomposition method (Odibat and Momani, 2008) and numerical methods (Jafari et al., 2013). Some numerical or analytical methods have been investigated for solving a system of fractional – order derivatives, such as an iterative Laplace transforms method (Jafari et al., 2013), and adaptive observer (Zhang and Gong, 2014).

In current literature, regardless of the existence of many priced researches in this field, only few researchers have delved into the application of fractional derivative to mood variation of a human. In this work we shall investigate this mood variation using a special form of Duffing Oscillator with an additional nonlinear term and fractional damping. We shall employ the Lindstedt – Poincare and multiple scales perturbation technique in solving the

suggested model of bipolar II disorder patient; in addition we validate our result from existing literature.

5.2 PROBLEM FORMULATION AND ANALYTICAL SOLUTION

The approach in this work is based on the representation of the fractional derivative as a fractional power of the ordinary time derivative operator d/dt, a representation typically given by the equality

$$\left(\frac{d}{dt}\right)^{\delta} u(t) = D_{+}^{\delta} u(t) \tag{5.1}$$

where

$$D_{+}^{\delta} u(t) = \frac{d}{dt}\int_{0}^{t} \frac{u(t-r)\,dr}{\Gamma(1-\delta)\,r^{\delta}} \tag{5.2}$$

is the Riemann – Liouville fractional time – derivative. Equation (5.1) allows us to use the Liouville representation of the fractional derivative applied to the exponential function:

$$D_{+}^{\delta} e^{i\omega t} = (i\omega)^{\delta} e^{i\omega t}. \tag{5.3}$$

We use another definition based on Riemann – Liouville fractional derivative

$$D_{0}^{\delta} e^{i\omega t} = \frac{d}{dt}\int_{0}^{t} \frac{e^{i\omega(t-r)}}{\Gamma(1-\delta)\,r^{\delta}}\,dr = (i\omega)^{\delta} e^{i\omega t} + \frac{\sin\delta\pi}{\pi}\int_{0}^{\infty} \frac{u^{\delta} e^{-ut}}{u+i\omega}\,du \tag{5.4}$$

which turns to (5.3) when $t \to +\infty$ and $\Gamma(.)$ is the gamma function. We consider the force – driven vibrations of the Duffing oscillator with fractional derivative as defined in (5.1).

$$u''(t) + \varepsilon^{k}\mu\left(\frac{d}{dt}\right)^{\delta} u(t) + w_0^2 u(t) + k_2\left[u(t)\right]^3 = \varepsilon^{k+1} f\cos(wt) \tag{5.5}$$

where $k = 1, 2$, μ is the damping parameter, w_0 is the natural frequency of the oscillator, u is the emotional state of the patient, k_2 is the medication parameter that involves the medication and its adherence and general psychotherapy, f is the resultant of the external and internal

forces, δ is the fractional order, $0 < \delta < 1$. The damping parameter, μ depends on the mood of patient when it was induced or applied, hence we can assume it to be

$$\mu = -\left(\alpha + \alpha_1 + \alpha_2\right). \tag{5.6}$$

The parameter α represent the factors that causes damping with no connection with the emotional state of the patient, α_1 is some parameters that will affect the mood of a patient during the hypomania episode and α_2 is the parameters that help to stabilizer the emotional state of the patient when in the depressive episode. The variations in these parameters determine if the damping will be positive or negative. We will assume that the linear natural frequency w_0 is approximately equal to the frequency of the external excitation w, hence

$$w_0 \approx w. \tag{5.7}$$

Let an approximate solution of (5.5) for small amplitude varying weakly with time be represented by

$$u(t) = v\left(\zeta\right) = \varepsilon v_1\left(\zeta\right) + \varepsilon^2 v_2\left(\zeta\right) + \varepsilon^3\left(\zeta\right) + \cdots \tag{5.8}$$

where $v_n\left(\zeta\right) = v_n\left(\zeta_0, \zeta_1, \zeta_2, \cdots\right)$ are new independent variables , among them: $\zeta_0 = t$ is a fast scale characterizing motions with w and w_0, also

$$\zeta_1 = \varepsilon t, \quad \zeta_2 = \varepsilon^2 t \tag{5.9}$$

are slow scales characterizing the modulations of the amplitude and phase lag. By definition of first and second fractional derivatives, we have that

$$\begin{aligned} \frac{d}{dt} &= D_0 + \varepsilon D_1 + \varepsilon^2 D_2 + \cdots \\ \frac{d^2}{dt^2} &= D_0^2 + 2\varepsilon D_0 D_1 + \varepsilon^2\left(D_1^2 + 2D_0 D_2\right) + \cdots, \end{aligned} \tag{5.10}$$

$$\left(\frac{d}{dt}\right)^{\delta} = \left(D_0 + \varepsilon D_1 + \varepsilon^2 D_2 + \cdots\right)^{\delta}$$
$$= D_+^{\delta} + \varepsilon\delta D_+^{\delta-1} + \frac{1}{2}\varepsilon^2\delta\left((\delta-1)D_+^{\delta-2}D_1^2 + 2D_+^{\delta-1}D_2\right) + \cdots, \quad (5.11)$$

where $D_n = \dfrac{\partial}{\partial \zeta_n}$ and $D_+^{\delta}, D_+^{\delta-1}, D_+^{\delta-2}$ are the Riemann – Liouville fractional time derivatives

$$D_+^{\delta-n}u(t) = \frac{d}{dt}\int_0^t \frac{u(t-r)\,dr}{\Gamma(n-\delta+1)r^{\delta-n}},\ (n = 0,1,2,\cdots). \quad (5.12)$$

$$v''(\zeta) = D_0^2\left(\varepsilon v_1(\zeta) + \varepsilon^2 v_2(\zeta) + \varepsilon^3(\zeta) + \cdots\right) + 2\varepsilon D_0 D_1\left(\varepsilon v_1(\zeta) + \varepsilon^2 v_2(\zeta) + \varepsilon^3(\zeta) + \cdots\right)$$
$$+ \varepsilon^2\left[D_1^2\left(\varepsilon v_1(\zeta) + \varepsilon^2 v_2(\zeta) + \cdots\right) + 2D_0 D_1\left(\varepsilon v_1(\zeta) + \varepsilon^2 v_2(\zeta) + \cdots\right)\right] + \cdots. \quad (5.13)$$

Substituting (5.8), (5.11) and (5.13) into (5.5), we obtain

$$\begin{aligned}
&D_0^2\left(\varepsilon v_1(\zeta) + \varepsilon^2 v_2(\zeta) + \varepsilon^3(\zeta) + \cdots\right) + 2\varepsilon D_0 D_1\left(\varepsilon v_1(\zeta) + \varepsilon^2 v_2(\zeta) + \cdots\right)\\
&+\varepsilon^2\left[D_1^2\left(\varepsilon v_1(\zeta) + \varepsilon^2 v_2(\zeta) + \cdots\right) + 2D_0 D_1\left(\varepsilon v_1(\zeta) + \varepsilon^2 v_2(\zeta) + \cdots\right)\right] + \cdots\\
&+\varepsilon^k\mu(D_+^y\left(\varepsilon v_1(\zeta) + \varepsilon^2 v_2(\zeta) + \cdots\right) + \varepsilon\delta D_+^{\delta-1}\left(\varepsilon v_1(\zeta) + \varepsilon^2 v_2(\zeta) + \cdots\right)\\
&+\frac{1}{2}\varepsilon^2\delta\left((\delta-1)D_+^{\delta-2}D_1^2\left(\varepsilon v_1(\zeta) + \cdots\right) + 2D_+^{\delta-1}D_2\left(\varepsilon v_1(\zeta) + \cdots\right)\right) + \cdots)\\
&+w_0^2\left(\varepsilon v_1(\zeta) + \varepsilon^2 v_2(\zeta) + \varepsilon^3(\zeta) + \cdots\right)\\
&+k_2\left(\varepsilon v_1(\zeta) + \varepsilon^2 v_2(\zeta) + \varepsilon^3(\zeta) + \cdots\right)^3\\
&= \varepsilon^{k+1} f\cos(w\zeta_0).
\end{aligned} \quad (5.14)$$

Equating coefficients of equal powers of ε, we obtain a set of recurrence equations:

Order of ε:

$$D_0^2 v_1 + w_0^2 v_1 = 0, \quad (5.15)$$

Order of ε^2:

$$D_0^2 v_2 + 2D_0 D_1 v_1 + \mu D_+^{\delta} v_1 + w_0^2 v_2 = f\cos(w\zeta_0),$$

$$D_0^2 v_2 + w_0^2 v_2 = -2D_0 D_1 v_1 - \mu(2-k)D_+^{\delta} v_1 + (2-k)f\cos(w\zeta_0), \quad (5.16)$$

Order of ε^3:

$$D_0^2 v_3 + w_0^2 v_3 = -2D_0 D_1 v_2 - \left(D_1^2 + 2D_0 D_2\right) v_1 - \mu D_+^{\delta} v_2 - \mu(k-1) D_+^{\delta} v_1 \\ -\mu\delta D_+^{\delta-1} D_1 v_1 - k_2 v_1^3 + (k-1) f \cos\left(w\zeta_0\right). \tag{5.17}$$

The general solution of (5.15) is of the form

$$v_1\left(\zeta_0, \zeta_1, \zeta_2\right) = A_1\left(\zeta_1, \zeta_2\right) e^{i w_0 \zeta_0} + \bar{A}_1\left(\zeta_1, \zeta_2\right) e^{-i w_0 \zeta_0}, \tag{5.18}$$

where A_1 and $\bar{A}_1$ are yet unknown complex conjugate functions. We now consider the damping and excitation when $k = 1$. Hence (5.5) transforms into

$$u''(t) + \varepsilon\mu\left(\frac{d}{dx}\right)^{\delta} u(t) + w_0^2 u(t) + k_2\left[u(t)\right]^3 = \varepsilon^2 f \cos(wt). \tag{5.19}$$

Substituting (5.18) into (5.16) with $k = 1$, having (5.4) in mind we have

$$\begin{aligned} D_0^2 v_2 + w_0^2 v_2 = & -2i w_0 \left(\frac{1}{2}\left(i w_0\right)^{\delta-1} \mu A_1 + D_1 A_1\right) e^{i w_0 \zeta_0} \\ & + 2i w_0 \left(\frac{1}{2}\left(-i w_0\right)^{\delta-1} \mu A_2 + D_1 \bar{A}_1\right) e^{-i w_0 \zeta_0} \\ & + \frac{1}{2} f\left(e^{i w_0 \zeta_0} + e^{-i w_0 \zeta_0}\right) - \mu A_1 \frac{\sin\delta\pi}{\pi} \int_0^{\infty} \frac{u^{\delta} e^{-i u \zeta_0}}{u + i w_0} du \\ & - \mu \bar{A}_1 \frac{\sin\delta\pi}{\pi} \int_0^{\infty} \frac{u^{\delta} e^{-i u \zeta_0}}{u + i w_0} du. \end{aligned} \tag{5.20}$$

To obtain a valid asymptotical solution, we apply the solvability criterion by equating to zero the coefficients of $e^{\pm i w_0 \zeta_0}$.

$$D_1 A_1 + \frac{1}{2}\left(i w_0\right)^{\delta-1} \mu A_1 - \frac{f}{4 i w_0} = 0$$

$$D_1 A_1 = -\frac{1}{2}\left(i w_0\right)^{\delta-1} \mu A_1 + \frac{f}{4 i w_0}, \tag{5.21}$$

whose solution is

$$A_1\left(\zeta_1, \zeta_2\right) = A_2\left(\zeta_2\right) e^{-\frac{\left(i w_0\right)^{\delta-1} \mu}{2} \zeta_1} + \frac{f}{2\mu\left(i w_0\right)^{\delta}}. \tag{5.22}$$

The remaining part of (5.20) is

$$D_0^2 v_2 + w_0^2 v_2 = -\mu \frac{\sin \delta \pi}{\pi} \int_0^\infty u^\delta e^{-i u \zeta_0} \left(A_1 \frac{u - i w_0}{u^2 + w_0^2} + \bar{A}_1 \frac{u + i w_0}{u^2 + w_0^2} \right) du \,. \tag{5.23}$$

Observe that A_1 and $\bar{A}_1$ are complex conjugates, hence we can write

$$A_1 = a + ib, \quad \bar{A}_1 = a - ib \tag{5.24}$$

and substituting (5.24) into (5.23) we obtain

$$\begin{aligned} D_0^2 v_2 + w_0^2 x_2 &= -\mu \frac{\sin \delta \pi}{\pi} \int_0^\infty u^\delta e^{-i u \zeta_0} \left(a + ib \left(\frac{u - i w_0}{u^2 + w_0^2} \right) + a - ib \left(\frac{u + i w_0}{u^2 + w_0^2} \right) \right) du \\ &= -\mu \frac{\sin \delta \pi}{\pi} \int_0^\infty u^\delta e^{-i u \zeta_0} \left(\frac{au - i a w_0 + i ub + w_0 b + au + i a w_0 - i ub + w_0 b}{u^2 + w_0^2} \right) du \end{aligned}$$

$$\begin{aligned} &= -\mu \frac{\sin \delta \pi}{\pi} \int_0^\infty u^\delta e^{-i u \zeta_0} \left(\frac{2au + 2w_0 b}{u^2 + w_0^2} \right) du \\ &= -2\mu \frac{\sin \delta \pi}{\pi} \int_0^\infty u^\delta e^{-i u \zeta_0} \left(\frac{au + w_0 b}{u^2 + w_0^2} \right) du. \end{aligned}$$

Therefore

$$D_0^2 v_2 + w_0^2 x_2 = -2\mu \frac{\sin \delta \pi}{\pi} F\left(\zeta_0, \zeta_1, \zeta_2\right) \tag{5.25}$$

where

$$F\left(\zeta_0, \zeta_1, \zeta_2\right) = \int_0^\infty u^\delta e^{-i u \zeta_0} \left(\frac{au + w_0 b}{u^2 + w_0^2} \right) du. \tag{5.26}$$

The solution to (5.25) is of the form

$$\begin{aligned} v_2 = M\left(\zeta_1, \zeta_2\right) e^{i w_0 \zeta_0} + \bar{M}\left(\zeta_1, \zeta_2\right) e^{-i w_0 \zeta_0} + C\left(\zeta_0, \zeta_1, \zeta_2\right) e^{i w_0 \zeta_0} \\ + \bar{C}\left(\zeta_0, \zeta_1, \zeta_2\right) e^{-i w_0 \zeta_0} \end{aligned} \tag{5.27}$$

where M, $\bar{M}$, C, and $\bar{C}$ are complex conjugate functions that represent the general solution and the particular solution of (5.25).

Substituting the particular solution of (5.27) into (5.25), we obtain

$$D_0^2\left(C\left(\zeta_0,\zeta_1,\zeta_2\right)e^{i w_0\zeta_0}+\bar{C}\left(\zeta_0,\zeta_1,\zeta_2\right)e^{-i w_0\zeta_0}\right)+w_0^2\left(C\left(\zeta_0,\zeta_1,\zeta_2\right)e^{i w_0\zeta_0}\right.$$
$$\left.+\bar{C}\left(\zeta_0,\zeta_1,\zeta_2\right)e^{-i w_0\zeta_0}\right)=-2\mu\frac{\sin\delta\pi}{\pi}F\left(\zeta_0,\zeta_1,\zeta_2\right),$$
$$\Rightarrow D_0\left(C\left(\zeta_0',\zeta_1,\zeta_2\right)e^{i w_0\zeta_0}+i w_0C\left(\zeta_0,\zeta_1,\zeta_2\right)e^{i w_0\zeta_0}+\bar{C}\left(\zeta_0',\zeta_1,\zeta_2\right)e^{-i w_0\zeta_0}\right.$$
$$\left.-i w_0\bar{C}\left(\zeta_0,\zeta_1,\zeta_2\right)e^{-i w_0\zeta_0}\right)+w_0^2\left(C\left(\zeta_0,\zeta_1,\zeta_2\right)e^{i w_0\zeta_0}+\bar{C}\left(\zeta_0,\zeta_1,\zeta_2\right)e^{-i w_0\zeta_0}\right)$$
$$=-2\mu\frac{\sin\delta\pi}{\pi}F\left(\zeta_0,\zeta_1,\zeta_2\right),$$

$$\Rightarrow\left(C\left(\zeta_0'',\zeta_1,\zeta_2\right)e^{i w_0\zeta_0}+2i w_0C\left(\zeta_0',\zeta_1,\zeta_2\right)e^{i w_0\zeta_0}-w_0^2C\left(\zeta_0,\zeta_1,\zeta_2\right)e^{i w_0\zeta_0}\right.$$
$$-\bar{C}\left(\zeta_0'',\zeta_1,\zeta_2\right)e^{-i w_0\zeta_0}-2w_0\bar{C}\left(\zeta_0',\zeta_1,\zeta_2\right)e^{-i w_0\zeta_0}-w_0^2\bar{C}\left(\zeta_0,\zeta_1,\zeta_2\right)e^{-i w_0\zeta_0}\Big)$$
$$+w_0^2\left(C\left(\zeta_0,\zeta_1,\zeta_2\right)e^{i w_0\zeta_0}+\bar{C}\left(\zeta_0,\zeta_1,\zeta_2\right)e^{-i w_0\zeta_0}\right)=-2\mu\frac{\sin\delta\pi}{\pi}F\left(\zeta_0,\zeta_1,\zeta_2\right),$$

$$\Rightarrow C\left(\zeta_0'',\zeta_1,\zeta_2\right)e^{i w_0\zeta_0}+\bar{C}\left(\zeta_0'',\zeta_1,\zeta_2\right)e^{-i w_0\zeta_0}+2i w_0C\left(\zeta_0',\zeta_1,\zeta_2\right)e^{i w_0\zeta_0}$$
$$-2i w_0\bar{C}\left(\zeta_0',\zeta_1,\zeta_2\right)e^{-i w_0\zeta_0}=-2\mu\frac{\sin\delta\pi}{\pi}F\left(\zeta_0,\zeta_1,\zeta_2\right).$$
$$\Rightarrow C\left(\zeta_0'',\zeta_1,\zeta_2\right)e^{i w_0\zeta_0}+\bar{C}\left(\zeta_0'',\zeta_1,\zeta_2\right)e^{-i w_0\zeta_0}-2i w_0\left(C\left(\zeta_0',\zeta_1,\zeta_2\right)e^{i w_0\zeta_0}+\bar{C}\left(\zeta_0',\zeta_1,\zeta_2\right)e^{-i w_0\zeta_0}\right)$$
$$=-2\mu\frac{\sin\delta\pi}{\pi}F\left(\zeta_0,\zeta_1,\zeta_2\right).$$

Integrating the above equation twice, we obtain

$$C\left(\zeta_0,\zeta_1,\zeta_2\right)=-2\mu\frac{\sin\delta\pi}{\pi}\int_0^{\zeta_0}e^{-2i w_0\zeta_0'}d\zeta_0'\int_0^{\zeta_0'}F\left(\zeta_0'',\zeta_1,\zeta_2\right)e^{i w_0\zeta_0''}d\zeta_0''.\qquad(5.28)$$

Substituting (5.18), (5.22), (5.27) and (5.28) into (5.17) for $k=1$, we obtain

$$D_0^2v_3+w_0^2v_3=$$
$$-2D_0D_1\left(M\left(\zeta_1,\zeta_2\right)e^{i w_0\zeta_0}+\left(-2\mu\frac{\sin\delta\pi}{\pi}\int_0^{\zeta_0}e^{-2i w_0\zeta_0}d\zeta_0\int_0^{\zeta_0'}F\left(\zeta_0'',\zeta_1,\zeta_2\right)e^{i w_0\zeta_0''}d\zeta''\right)e^{i w_0\zeta_0}\right)$$
$$-\left(D_1^2+2D_0D_2\right)\left(\left[A_2\left(\zeta_2\right)e^{-\frac{\left(i w_0\right)^{\delta-1}\mu\zeta_1}{2}}+\frac{f}{2\mu\left(i w_0\right)^{\delta}}\right]e^{i w_0\zeta_0}+\frac{f}{2\mu\left(i w_0\right)^{\delta}}e^{-i w_0\zeta_0}\right)$$
$$-\mu D_+^{\delta}\left(M\left(\zeta_1,\zeta_2\right)e^{i w_0\zeta_0}+\left(-2\mu\frac{\sin\delta\pi}{\pi}\int_0^{\zeta_0}e^{-2i w_0\zeta_0}d\zeta_0\int_0^{\zeta_0'}F\left(\zeta_0'',\zeta_1,\zeta_2\right)e^{i w_0\zeta_0''}d\zeta''\right)e^{i w_0\zeta_0}\right.$$

$$-\mu(k-1)D_+^{\delta}\left(\left[A_2(\zeta_2)e^{-\frac{(iw_0)^{\delta-1}\mu\zeta_1}{2}}+\frac{f}{2\mu(iw_0)^{\delta}}\right]e^{iw_0\zeta_0}\right)$$

$$-\mu\delta D_+^{\delta-1}D_1\left(\left[A_2(\zeta_2)e^{-\frac{(iw_0)^{\delta-1}\mu\zeta_1}{2}}+\frac{f}{2\mu(iw_0)^{\delta}}\right]e^{iw_0\zeta_0}\right) \tag{5.29}$$

$$-k_2\left(\left[A_2(\zeta_2)e^{-\frac{(iw_0)^{\delta-1}\mu\zeta_1}{2}}+\frac{f}{2\mu(iw_0)^{\delta}}\right]e^{iw_0\zeta_0}\right)^3+(k-1)f\cos(w\zeta_0)+cc.$$

where cc denotes the complex conjugate of the terms in the equation.

Applying the solvability condition, we obtain

$$D_2A_2(\zeta_2)+A_2\left(\frac{1}{8}\mu^2(1-2\delta)(iw_0)^{2\delta-3}-\lambda\frac{3k_2f^2}{4\mu^2w_0^{2\delta+1}}\right)=0, \tag{5.30}$$

whose solution is

$$A_2=A_3\exp\left(-\frac{1}{8}\mu^2(1-2\delta)(iw_0)^{2\delta-3}-\lambda\frac{3k_2f^2}{4\mu^2w_0^{2\delta+1}}\right)\zeta_2, \tag{5.31}$$

where A_3 is a constant and $\lambda=\mathrm{i}\cos 2\delta\pi+\sin 2\delta\pi$.

Having (5.31) in mind, we can express the a and b in (5.27) as (Rossikhin and Shitikova, 2009; Rossikhin et al., 2009)

$$\begin{aligned}a(\zeta_1,\zeta_2)=A_3\exp&\left(-\tfrac{1}{2}\mu\zeta_1w_0^{\delta-1}\sin\left(\tfrac{1}{2}\delta\pi\right)+\tfrac{1}{8}\mu^2\zeta_2(1-2\delta)w_0^{2\delta-3}\sin\pi\right)\\&\times\cos\left(\tfrac{1}{2}\mu\zeta_1w_0^{\delta-1}\sin\left(\tfrac{1}{2}\delta\pi\right)+\tfrac{1}{8}\mu^2\zeta_2(2\delta-1)w_0^{2\delta-3}\cos\delta\pi\right.\\&\left.+\frac{3k_2f^2}{4\mu^2w_0^{2\delta+1}}\zeta_2\cos 2\delta\pi\right)+\frac{f}{\mu w_0^{\delta}}\cos\frac{\delta\pi}{2},\end{aligned} \tag{5.32}$$

$$\begin{aligned}b(\zeta_1,\zeta_2)=A_3\exp&\left(-\tfrac{1}{2}\mu\zeta_1w_0^{\delta-1}\sin\left(\tfrac{1}{2}\delta\pi\right)+\tfrac{1}{8}\mu^2\zeta_2(1-2\delta)w_0^{2\delta-3}\sin\pi\right)\\&\times\sin\left(\tfrac{1}{2}\mu\zeta_1w_0^{\delta-1}\sin\left(\tfrac{1}{2}\delta\pi\right)+\tfrac{1}{8}\mu^2\zeta_2(2\delta-1)w_0^{2\delta-3}\cos\delta\pi\right.\\&\left.+\frac{3k_2f^2}{4\mu^2w_0^{2\delta+1}}\zeta_2\cos 2\delta\pi\right)-\frac{f}{\mu w_0^{\delta}}\sin\frac{\delta\pi}{2}.\end{aligned} \tag{5.33}$$

Fusing (5.22), (5.31) and (5.18) we have

$$v_1 = e^{i w_0 \zeta_0}\left(A_3 \exp\left(-\tfrac{1}{8}\mu^2 (1-2\delta)(iw_0)^{2\delta-3} + \lambda \frac{3k_2 f^2}{4\mu^2 w_0^{2\delta+1}} \right)\zeta_2 \exp\left(-\tfrac{1}{2}(iw_0)^{\delta-1}\mu\zeta_1 \right) + \frac{f}{2\mu(iw_0)^{\delta}} \right) \times \exp(iw_0\zeta_0) + c.c \tag{5.34}$$

The second term of (5.4) does not affect the solution within the limits of this approximation (Rossikhin and Shitikova, 2009), hence we limit ourselves to first term of (5.8). Hence the solution of (5.5) is in the form

$$u = \varepsilon\left(\sigma e^{-\rho t}\cos\phi t + \frac{f}{\mu w_0^{\delta}}\cos\left(w_0 t - \tfrac{1}{2}\delta\pi \right) \right), \tag{5.35}$$

where $\sigma = 2A_3$,

$$\rho = \frac{1}{2}\varepsilon\mu w_0^{\delta-1}\sin\tfrac{1}{2}\delta\pi\left(1 + \tfrac{1}{2}\varepsilon\mu(2\delta-1)w_0^{\delta-2}\cos\tfrac{1}{2}\delta\pi\right) - \varepsilon^2\frac{3k_2 f^2}{4\mu^2 w_0^{2\delta+1}}\sin 2\delta\pi, \tag{5.36}$$

and

$$\phi = w_0\left(1 + \tfrac{1}{2}\varepsilon\mu w_0^{\delta-2}\cos\left(\tfrac{1}{2}\delta\pi\right) + \tfrac{1}{8}\varepsilon^2\mu^2(1-2\delta)w_0^{2(\delta-2)}\cos\delta\pi + \varepsilon^2\frac{3k_2 f^2}{4\mu^2 w_0^{2\delta+1}}\cos 2\delta\pi \right). \tag{5.37}$$

Observe that the solution in (5.35) is fragmented into two: first part corresponds to the damping oscillations and its observed swing in mood, while the latter is non - damping in exhibitions and describes forced oscillations with the frequency of the restoring force and the phase difference depending on the fractional parameter.

5.3 DAMPING OF THE ORDER OF ε^2, $k = 2$.

For $k = 2$, (5.5) becomes

$$u''(t) + \varepsilon^2\mu\left(\frac{d}{dt}\right)^{\delta} u(t) + w_0^2 u(t) + k_2\left[u(t)\right]^3 = \varepsilon^3 f\cos(wt). \tag{5.38}$$

Substituting (5.18) into (5.16) with $k = 2$, we obtain

$$D_0^2 v_2 + w_0^2 v_2 = -2i w_0 D_1 A_1 e^{iw_0\zeta_0} + c.c. \tag{5.39}$$

To ensure uniformly asymptotically valid solution, we apply the secularity principle, and we obtain that

$$D_1 A_1\left(\zeta_1,\zeta_2\right)=0\,, \tag{5.40}$$

hence A_1 does not depend on ζ_1. The general solution of the remaining equation in (5.39) is of the form

$$v_2 = A_2\left(\zeta_1,\zeta_2\right)e^{iw_0\zeta_0} + \bar{A}_2\left(\zeta_1,\zeta_2\right)e^{-iw_0\zeta_0}\,. \tag{5.41}$$

Substituting (5.18) and (5.41) into (5.17) with $k=2$, having (5.4) in mind we obtain

$$\begin{aligned} D_0^2 v_3 + w_0^2 v_3 = &-2i\,w_0 D_1 A_2\, e^{iw_0\zeta_0} - k_2 A_1^3 e^{3iw_0\zeta_0} - \Big(2iw_0 D_2 A_1 + \mu\left(i\,w_0\right)^{\delta} A_1 \\ &+ 3k_2 A_1^3\bar{A}_1 - \tfrac{1}{2}\,f\Big)e^{iw_0\zeta_0} - \mu A_1\,\frac{\sin\delta\pi}{\pi}\int_0^{\infty}\frac{u^{\delta}e^{-u\zeta_0}}{u+i\,w_0}\,du + c.c. \end{aligned} \tag{5.42}$$

Applying the solvability conditions

$$D_1 A_2\left(\zeta_1,\zeta_2\right)=0\,, \tag{5.43}$$

$$2iw_0 D_2 A_1 + \mu\left(iw_0\right)^{\delta} A_1 + 3k_2 A_1^2\bar{A}_1 - \tfrac{1}{2}\,f = 0\,. \tag{5.44}$$

Observe that A_2 is independent of τ_1. Multiplying (5.44) by $\bar{A}_1$, we obtain

$$2i\,w_0\bar{A}_1 D_2 A_1 + \mu\left(i\,w_0\right)^{\delta} A_1\bar{A}_1 + 3k_2 A_1^2\bar{A}_1^2 - \tfrac{1}{2}\,f\bar{A}_1 = 0\,. \tag{5.45}$$

Equation (5.45) can be rewritten as

$$\begin{aligned} &i\,\bar{A}_1 D_2 A_1 + \frac{\mu}{2}\left(\,w_0\right)^{\delta-1} i^{\delta} A_1\bar{A}_1 + \frac{3}{2}k_2 w_0^{-1}A_1^2\bar{A}_1^2 - \frac{1}{4w_0}\,f\,\bar{A}_1 \\ &= i\,\bar{A}_1 D_2 A_1 + \frac{\mu}{2}\left(\,w_0\right)^{\delta-1} A_1\bar{A}_1\left(\cos\frac{\pi}{2}\delta + i\sin\frac{\pi}{2}\delta\right) \\ &+ \frac{3}{2}k_2 w_0^{-1}A_1^2\bar{A}_1^2 - \frac{1}{4w_0}\,f\,\bar{A}_1 = 0. \end{aligned} \tag{5.46}$$

The conjugate of (5.46) is

$$-i\,A_1 D_2\bar{A}_1 + \frac{\mu}{2}\left(\,w_0\right)^{\delta-1} A_1\bar{A}_1\left(\cos\frac{\pi}{2}\delta - i\sin\frac{\pi}{2}\delta\right) + \frac{3}{2}k_2 w_0^{-1}A_1^2\bar{A}_1^2 - \frac{1}{4w_0}\,f\,A_1 = 0. \tag{5.47}$$

Adding (5.46) and (5.47), we obtain

$$3k_2 w_0^{-1} A_1^2 \bar{A}_1^2 + i\left(\bar{A}_1 D_2 A_1 - A_1 D_2 \bar{A}_1\right) + \mu w_0^{y-1} A_1 \bar{A}_1 \cos\tfrac{\pi}{2}\delta - \frac{f}{4w_0}\left(A_1 + \bar{A}_1\right) = 0, \quad (5.48)$$

and subtracting them produces

$$i\left(\bar{A}_1 D_2 A_1 + A_1 D_2 \bar{A}_1\right) + \mu w_0^{y-1} A_1 \bar{A}_1 \sin\tfrac{\pi}{2}\delta + \frac{f}{4w_0}\left(A_1 - \bar{A}_1\right) = 0. \quad (5.49)$$

We define $A(\zeta_2)$ in polar form

$$A_1 = a_1 e^{i\theta}. \quad (5.50)$$

Therefore (5.48) is reduced to

$$\frac{3k_2}{w_0} a_1^2 e^{2i\theta} e^{-2i\theta} + i\left(i2a_1^2\dot{\theta}\right) + 2\mu w_0^{\delta-1} a_1^2 \cos\tfrac{\pi}{2}\delta - \frac{f}{4w_0} a_1\left(e^{i\theta} + e^{-i\theta}\right) = 0$$

$$\Rightarrow \frac{3k_2}{w_0} a_1^2 - 2a_1^2\dot{\theta} + 2\mu w_0^{\delta-1} a_1^2 \cos\tfrac{\pi}{2}\delta - \frac{f}{2w_0} a_1 \cos\theta = 0. \quad (5.51)$$

Dividing (5.51) by $-2a_1^2$ and reducing (5.48) we obtain

$$\dot{\theta} - \frac{1}{2}\tau - \frac{3k_2}{2w_0} a_1^2 + \frac{1}{4w_0} f\, a_1^{-1} \cos\theta = 0, \quad (5.52)$$

$$\left(a_1^2\right)^{\cdot} + r a_1^2 + \frac{1}{2w_0} f a_1 \sin\theta = 0 \quad (5.53)$$

where $\tau = \mu w_0^{\delta-1} \cos\tfrac{\pi}{2}\delta$, $r = \mu w_0^{\delta-1} \sin\tfrac{\pi}{2}\delta$ and the dots denote the τ_2 – derivatives. Equation (5.53) when divided by a_1 can be written as

$$\dot{a}_1 + \frac{1}{2} r a_1 = -\frac{f}{4w_0} \sin\theta, \quad (5.54)$$

whose solution is

$$a_1 = \left(a_0 - \frac{f}{4w_0}\int_0^{\zeta_2} e^{\frac{r}{2}\zeta_2} \sin\left[\theta\left(\zeta_2\right)\right] d\zeta_2\right) e^{-\frac{r}{2}\zeta_2}. \quad (5.55)$$

We transform (5.53) as

$$\left(\ln a_1^2\right)^{\cdot} = -r - \frac{f}{2w_0} a_1^{-1} \sin\theta\,,$$

multiplying the result by $\cos\theta$, we obtain

$$\cos\theta\left(\ln a_1^2\right)^{\cdot} = \left(-r - \frac{f}{2w_0} a_1^{-1} \sin\theta\right)\cos\theta\,. \tag{5.56}$$

Multiplying (5.52) by $-\sin\theta$, we obtain

$$\left(-\sin\theta\right)\dot{\theta} + \frac{1}{2}\tau\sin\theta + \frac{3k_2}{2w_0} a_1^2 \sin\theta - \frac{1}{4w_0}\, f\, a_1^{-1}\cos\theta\sin\theta = 0\,. \tag{5.57}$$

Simplifying further we obtain

$$\left(\cos\theta\right)^{\cdot} + \frac{1}{2}\tau\sin\theta + \frac{3k_2}{2w_0} a_1^2 \sin\theta - \frac{f}{4w_0} a_1^{-1}\sin\theta\cos\theta = 0$$

$$\begin{aligned}\left(\cos\theta\right)^{\cdot} &- \left(a_0 - \frac{f}{4w_0}\int_0^{\zeta_2} e^{\frac{r}{2}\zeta_2}\sqrt{1-\cos^2\theta}\,d\zeta_2\right)^{-1} \frac{f}{4w_0} e^{\frac{r}{2}\zeta_2}\cos\theta\sqrt{1-\cos^2\theta} \\ &+ \left(a_0 - \frac{f}{4w_0}\int_0^{\zeta_2} e^{\frac{r}{2}\zeta_2}\sqrt{1-\cos^2\theta}\,d\zeta_2\right)^{2} \frac{3k_2}{2w_0} e^{\frac{r}{2}\zeta_2}\sqrt{1-\cos^2\theta} \\ &+ \frac{1}{2}\tau\sqrt{1-\cos^2\theta} = 0.\end{aligned} \tag{5.58}$$

Equations (5.55) and (5.58) can be used to obtain the amplitude and the phase lag of the oscillations respectively.

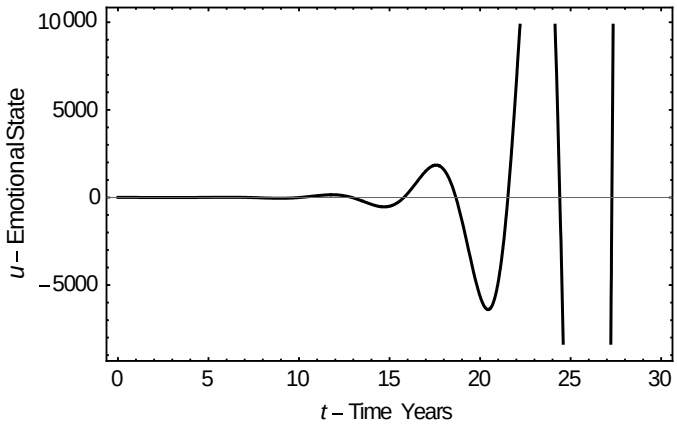


Fig. 5.1: Emotional variation of patient with $\varepsilon = 0.1, \sigma = 0.25, k_2 = 10, f = 5nN, w = 1\mathrm{p}Hz,$, $h = 0, \mu = 2, \delta = 0.25$.

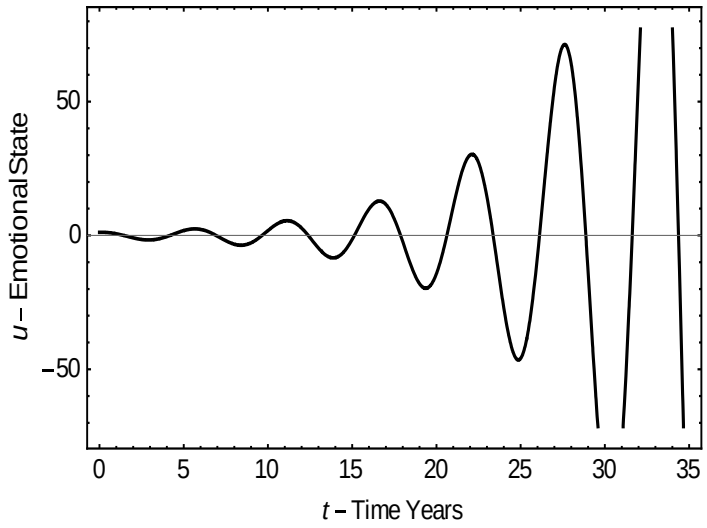


Fig. 5.2: Emotional variation of patient with $\varepsilon = 0.1, \sigma = 0.25, k_2 = 10, f = 5nN, w = 1\text{p}Hz, h = 0, \mu = 3, \delta = 0.25$.

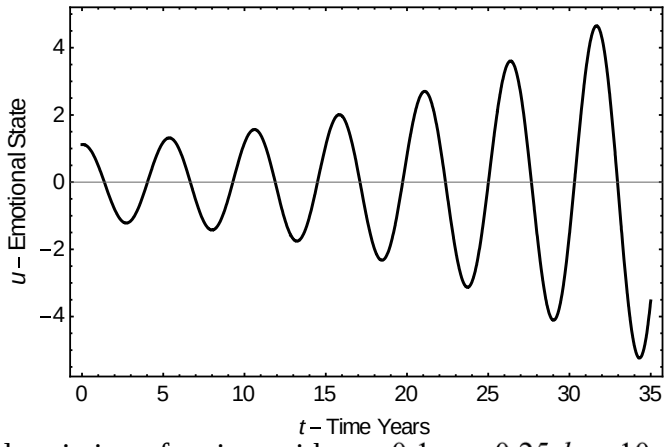


Fig. 5.3: Emotional variation of patient with $\varepsilon = 0.1, \sigma = 0.25, k_2 = 10, f = 5nN, w = 1\text{p}Hz, h = 0, \mu = 5, \delta = 0.25$.

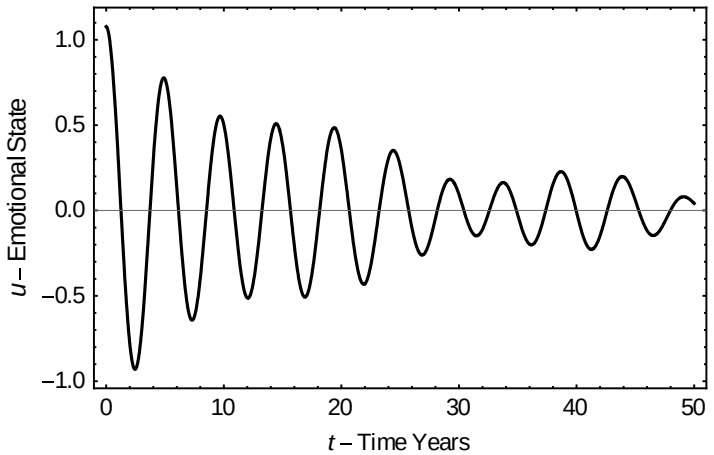


Fig. 5.4: Emotional variation of patient with $\varepsilon = 0.1, \sigma = 0.25, k_2 = 10, f = 5nN, w = 1\text{p}Hz, h = 0, \mu = 10, \delta = 0.25$.

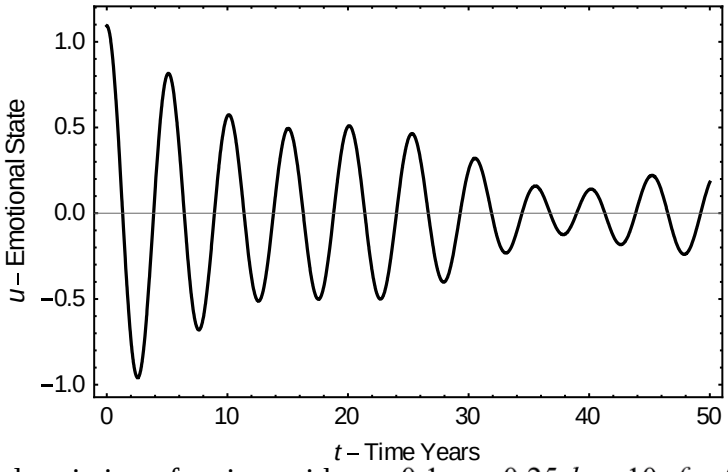


Fig. 5.5: Emotional variation of patient with $\varepsilon = 0.1, \sigma = 0.25, k_2 = 10, f = 5nN,$ $w = 1\text{p}Hz, h = 0, \mu = 16, \delta = 0.25$.

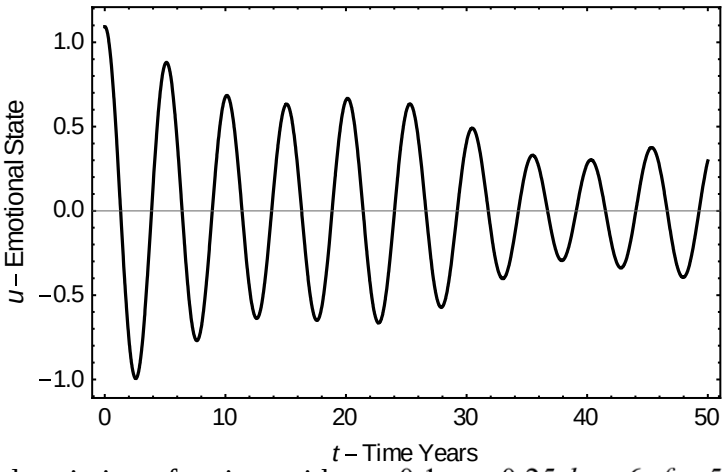


Fig. 5.6: Emotional variation of patient with $\varepsilon = 0.1, \sigma = 0.25, k_2 = 6, f = 5nN, w = 1\text{p}Hz,$ $h = 0, \mu = 5, \delta = 0.75$.

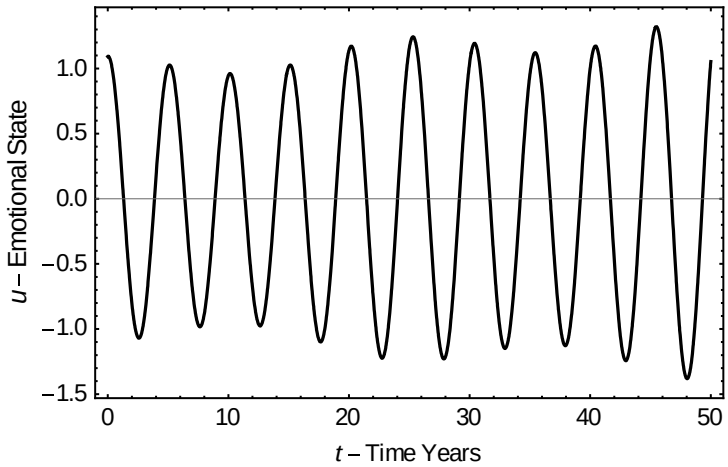


Fig. 5.7: Emotional variation of patient with $\varepsilon = 0.1, \sigma = 0.25, k_2 = 15, f = 5nN, w = 1\text{p}Hz,$ $h = 0, \mu = 5, \delta = 0.75$.

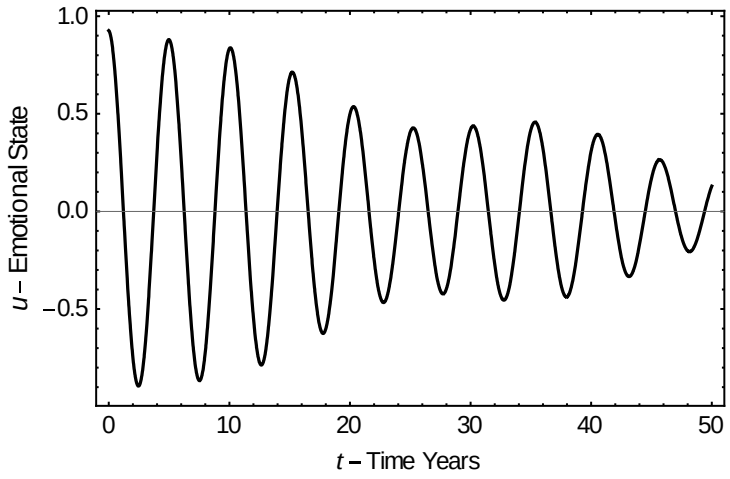


Fig. 5.8: Emotional variation of patient with $\varepsilon = 0.1, \sigma = 0.25, k_2 = 15, f = -5nN,$ $w = 1\text{p}Hz, h = 0, \mu = 5, \delta = 0.75$.

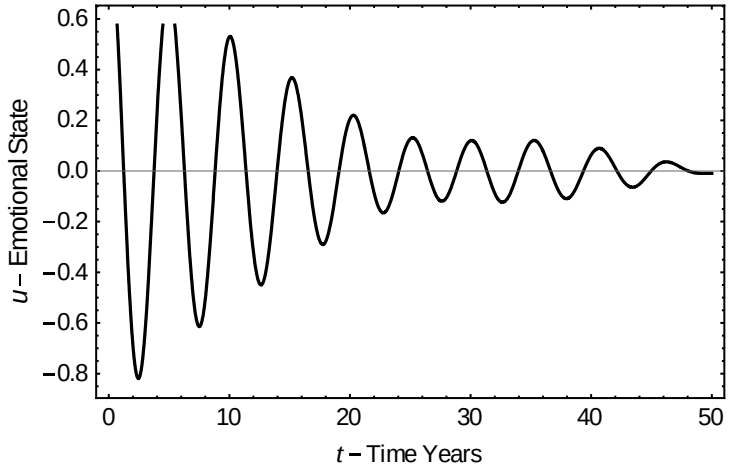


Fig. 5.9: Emotional variation of patient with $\varepsilon = 0.1, \sigma = 0.25, k_2 = 15, f = -2nN,$ $w = 1\text{p}Hz, h = 0, \mu = 5, \delta = 0.75$.

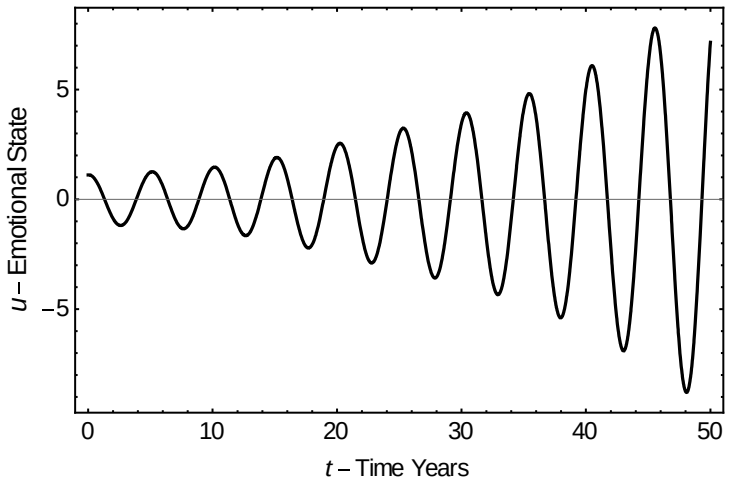


Fig. 5.10: Emotional variation of patient with $\varepsilon = 0.1, \sigma = 0.25, k_2 = 15, f = 6nN,$ $w = 1\text{p}Hz, h = 0, \mu = 5, \delta = 0.75$.

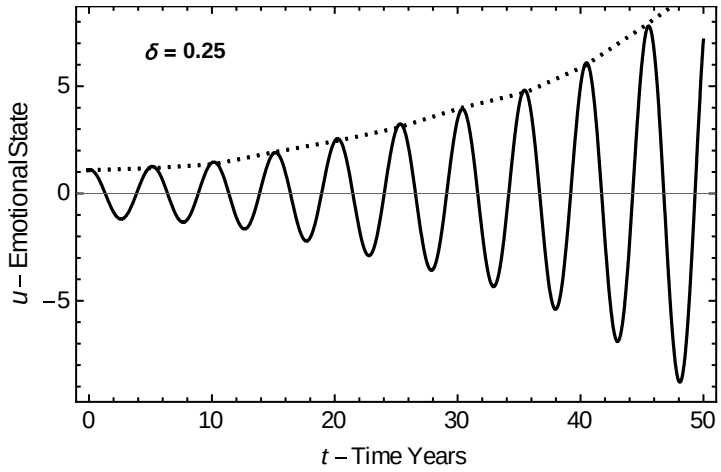


Fig. 5.11: Emotional variation of patient with $\varepsilon = 0.1, \sigma = 5, k_2 = 12, f = 6nN, w = 1\text{p}Hz,$ $h = 0, \mu = 5, \delta = 0.25$.

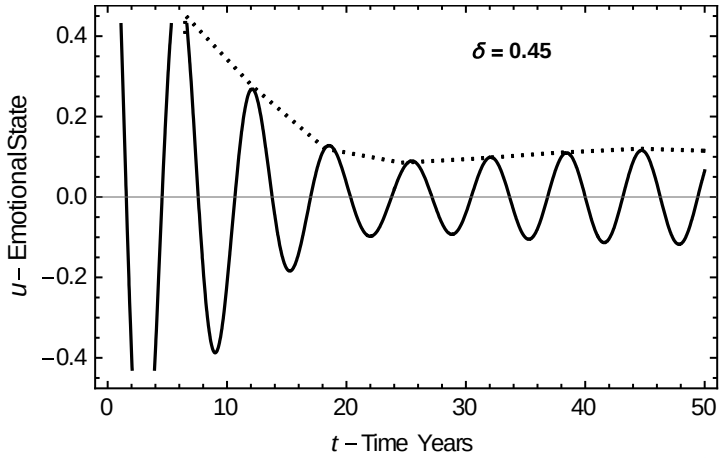


Fig. 5.12: Emotional variation of patient with $\varepsilon = 0.1, \sigma = 5, k_2 = 12, f = 6nN, w = 1\text{p}Hz,$ $h = 0, \mu = 5, \delta = 0.45$.

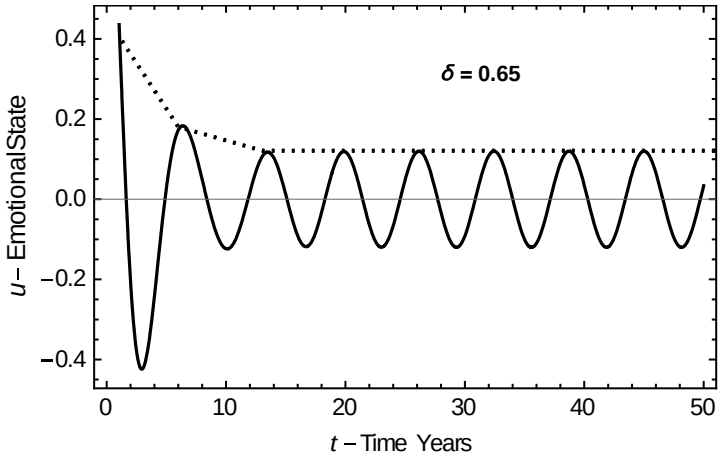


Fig. 5.13: Emotional variation of patient with $\varepsilon = 0.1, \sigma = 5, k_2 = 12, f = 6nN, w = 1\text{p}Hz,$ $h = 0, \mu = 5, \delta = 0.65$.

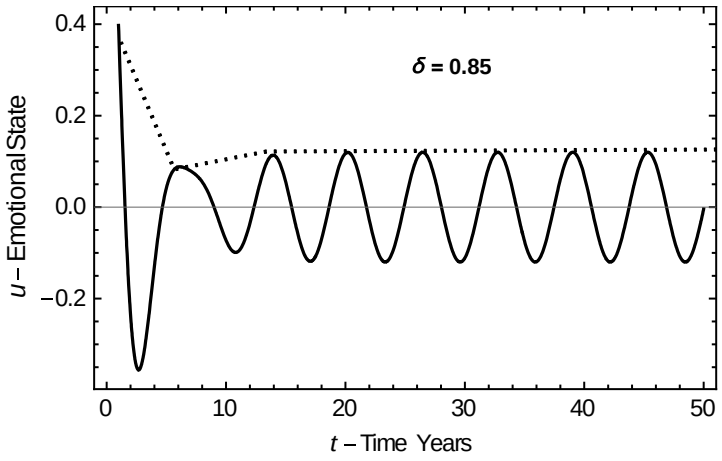


Fig. 5.14: Emotional variation of patient with $\varepsilon = 0.1, \sigma = 5, k_2 = 12, f = 6nN, w = 1\text{p}Hz,$ $h = 0, \mu = 5, \delta = 0.65$.

5.4 DISCUSSION

In this section, we graphed the asymptotic result in (5.35) to observe its consistency; in addition, finding new behavior of our system. The parameters are chosen as $\varepsilon = 0.1, \sigma = 0.25, k_2 = 10,\ f = 5nN, w = 1\text{p}Hz, h = 0$.

In Fig. 5.1 we choose $\mu = 2$ and $\delta = 0.25$. It shows that the mood of the patient is stable at the onset but if left untreated it will lead to a large limit cycles that signify unbounded mood variation. The forcing function is needful for the standardization of the mood, for the patient goes too long without being diagnosed. In Fig. 5.2 we choose to increase the damping parameter, $\mu = 3$ and $\delta = 0.25$. It shows an obvious reduction in the unbounded mood variation that represents the large limit cycles. It suggests that when the patient is yet to be diagnosed but lives a healthy life pattern; the body system is designed to activate the controller of the mood variation to their optimum functionality.

In Fig. 5.3 we choose to increase the damping parameter to $\mu = 5$ and $\delta = 0.25$. This situation suggests that the patient has been diagnosed and has started the medication (external medication and psychotherapy) but there is irregularity in the medication adherence. Family and friends therapy might create such a ripple effect but the hustling and bustling in the contemporary world may led to negligence of the efficacy of the therapy and hence, the mood

variation may start growing unboundly. In Fig. 5.4 we choose $\mu = 10$ and $\delta = 0.25$. It shows that if the treatment which we consider as the forcing function is judiciously administered, it leads to stable limit cycle with smaller amplitude, which we interpreted as a decrease in the intensity of the mood variation of the bipolar patient. Successful treatment is characterized by limiting the mood variations (Sachs and Thase, 2000). Fig. 5.5 is in support of the assertion because the damping parameter in increased to $\mu = 16$.

In Fig. 5.6 and Fig. 5.7 the medication parameter is increased to $k_2 = 6$ and $k_2 = 10$ respectively. It is observed that limit cycles are more stable when pharmacotherapy is greatly administered. Bipolar mood disorders have great rates of relapse on discontinuation of drug therapy (Buckjohn et al., 2010), hence the pharmacotherapy should be conceptualized as long – term phenomenon.

In Fig. 5.8, Fig. 5.9 and Fig. 5.10, we try to vary the intensity of the external and internal forcing term. We choose $f = -5nN$, $f = -2nN$, and $f = 6nN$. It is observed that stressors aggravate the amplification of the limit cycles. It is a known fact that stress is pervasive in human nature, and it plays a paramount role in modulating both the onset and severity of many psychiatric syndromes of which bipolar II disorder is inclusive. The stressor may emanate as a result of environmental events and psychological undetected physiological challenges representing threats to the potent natural fight against such misnomer. Examples of such stressors are patient encounter with pathogen such as virus and bacteria, presence of hyperthermia, and hypoglycemia etc.

In Figs. 5.11 – 5.14, we vary the fractional part of the derivative. The figures suggest that fractional order model has a great effect on the limit cycles. We used the following parameters $\varepsilon = 0.1, \mu = 5, w = 1\text{p}Hz, k = 12, f = 6nN, h = 0$. In Fig. 5.11 we choose $\delta = 0.25$. We observe that the limit cycle is increasing uncontrollably, hence immediate attentions to

pharmacotherapy is needed. In Fig. 5.12 $\delta = 0.45$, the fractional order model shows a great sensitivity because in this graph the unbounded mood swings are maintaining a steady amplitude. In Fig. 5.13 when $\delta = 0.65$, we can observe that steady mood oscillation is realized earlier, which is also supported by Fig. 5.14 when $\delta = 0.85$. The increase in the value δ also leads to increase in the amplitude. In general, we observe that the graphs generated from the fractional order system enables us to have a better result in exploring the mood variation of bipolar II disorder patients.

5.5 THE RESPONSE OF MOOD VARIATION AMPLITUDE TO FRACTIONAL DAMPING.

In this section we restructure (5.5) as

$$u''(t) + \varepsilon^2 \mu D^{\alpha} u(t) + w_0^2 u(t) + \varepsilon k_2 \left[u(t)\right]^3 = \varepsilon^2 f \cos(\Omega t + h) \tag{5.59}$$

where all the parameters remain the same with h the intensity of noise emanating from other endocrine secretion and the environment**,** $D^{\alpha} u(t)$ is a fractional – order operator as the damping term that is defined using Caputo's definition. It is defined as

$$D^{\alpha}\left[u(t)\right] = \frac{1}{\Gamma(1-\alpha)} \int_0^t \frac{u'(s)}{(t-s)^{\alpha}} ds. \tag{5.60}$$

We then transform (5.59) by introducing (Rossikhin and Shitikova, 2009)

$$\tau = wt. \tag{5.61}$$

Substituting (5.61) into (5.59), we obtain

$$w^2 u''(t) + \varepsilon^2 \mu w^{\alpha} D^{\alpha} u(t) + w_0^2 u(t) + \varepsilon k_2 \left[u(t)\right]^3 = \varepsilon^2 f \cos\left(\tfrac{\Omega}{w}\tau + h\right). \tag{5.62}$$

We make use of the scales in (5.9), where

$$\zeta_0 = \tau, D_0 = \partial / \partial \zeta_0, D_1 = \partial / \partial \zeta_1, D_2 = \partial / \partial \zeta_2 \tag{5.63}$$

that stands for partial derivative that we can write as the transformation of the ordinary derivatives as (Rossikhin and Shitikova, 2009) in (5.10). We make use of the expansion

$$w_0^2 = w^2 - \varepsilon w_1 - \varepsilon^2 w_2 \tag{5.64}$$

and assume an approximate solution of (5.62) as

$$u(t) = v_1(\zeta) + \varepsilon v_2(\zeta) + \varepsilon^2(\zeta) + \cdots. \tag{5.65}$$

On substituting (5.8), (5.64) and (5.65) into (5.62) , we have

$$\begin{aligned} & w^2\Big(D_0^2\left(v_0(\zeta)+\varepsilon v_1(\zeta)+\varepsilon^2 v_2(\zeta)+\cdots\right) \\ & \quad +2\varepsilon D_0\left(v_0(\zeta)+\varepsilon v_1(\zeta)+\cdots\right)D_1\left(v_0(\zeta)+\varepsilon v_1(\zeta)+\cdots\right)+\cdots\Big) \\ & \quad +\varepsilon^2\mu w^\delta\left(D_0^\delta\left(v_0(\zeta)+\varepsilon v_1(\zeta)+\cdots\right)+\varepsilon D_1^\delta\left(v_0(\zeta)+\varepsilon v_1(\zeta)+\cdots\right)+\cdots\right) \\ & \quad +\left(w^2-\varepsilon w_1-\varepsilon^2 w_2\right)\left(v_0(\zeta)+\varepsilon v_1(\zeta)+\varepsilon^2 v_2(\zeta)+\cdots\right) \\ & \quad +\varepsilon k_2\left(v_0(\zeta)+\varepsilon v_1(\zeta)+\varepsilon^2 v_2(\zeta)+\cdots\right)^3 = \varepsilon^2 f\cos\left(\tfrac{\Omega}{w}\tau+h\right). \end{aligned} \tag{5.66}$$

Separating terms of different power of ε , we obtain the following differential equations

$$O\left(\varepsilon^0\right): w^2 D_0^2 v_0 + w^2 v_0 = 0\,, \tag{5.67}$$

$$O\left(\varepsilon^1\right): w^2 D_0^2 v_1 + w^2 v_1 = -2w^2 D_0 D_1 v_0 + w_1 v_0 - k_2 v_0^3\,, \tag{5.68}$$

$$\begin{aligned} O\left(\varepsilon^2\right): w^2 D_0^2 v_2 + w^2 v_2 = & -2w^2 D_0 D_1 v_1 - w^2\left(D_1^2 + 2D_0 D_2\right)v_0 + w_1 v_1 + w_2 v_0 \\ & - \mu w^\delta D_0^\delta v_0 - 3k_2 v_0^2 v_1 + f\cos\left(\tfrac{\Omega}{w}\tau + h\right). \end{aligned} \tag{5.69}$$

The solution of (5.67) can be written as

$$v_0 = A(\zeta_1, \zeta_2)e^{i\zeta_0} + c.c. \tag{5.70}$$

Substituting (5.70) into (5.68) we have

$$\begin{aligned} w^2 D_0^2 v_1 + w^2 v_1 = & -2w^2 D_0 D_1\left(A(\zeta_1,\zeta_2)e^{i\zeta_0} + c.c\right) + w_1\left(A(\zeta_1,\zeta_2)e^{i\zeta_0} + c.c\right) \\ & - k_2\left(A(\zeta_1,\zeta_2)e^{i\zeta_0} + c.c\right)^3 \\ = & -2iw^2 D_1 A e^{i\zeta_0} + c.c. + w_1 A e^{i\zeta_0} + c.c. \\ & - k_2\left(A^3 e^{3i\zeta_0} + 3A^2\bar{A}e^{2i\zeta_0}e^{-i\zeta_0} + 3A\bar{A}^2 e^{i\zeta_0}e^{-2i\zeta_0} + \bar{A}^3 e^{-3i\zeta_0}\right). \end{aligned} \tag{5.71}$$

Applying the secularity rule, we obtain

$$-2iw^2 D_1 A + w_1 A - 3k_2 A^2 \bar{A} = 0. \tag{5.72}$$

To solve (5.72) we either set $D_1 A = 0$ or $w_1 = 0$ but if we are choosing the former, the value of w_1 has to be a real number not complex for it to be meaningful (Wedig, 1990). If we choose $D_1 A = 0$, then $A = A(\zeta_2)$ and

$$w_1 = 3k_2 A\bar{A}. \tag{5.73}$$

Equation (5.71) reduces to

$$w^2 D_0^2 v_1 + w^2 v_1 = -k_2 A^3 e^{3i\zeta_0} + c.c.$$

$$D_0^2 v_1 + v_1 = -\frac{k_2 A^3}{w^2} e^{3i\zeta_0} + c.c. \tag{5.74}$$

Hence the solution of (5.74) can be written as

$$v_1 = \frac{k_2 A^3}{8w^2} e^{3i\zeta_0} + c.c. \tag{5.75}$$

To examine the resonance, we express the harmonic excitation frequency Ω near w as

$$\Omega = w\left(1 + \varepsilon^2 \sigma\right), \tag{5.76}$$

then

$$\frac{\Omega}{w}\zeta_0 = \left(1 + \varepsilon^2 \sigma\right)\zeta_0 = \zeta_0 + \sigma\zeta_2. \tag{5.77}$$

We then substitute (5.70) and (5.75) into (5.69) to obtain

$$\begin{aligned} w^2 D_0^2 v_2 + w^2 v_2 = {} & -2w^2 D_0 D_1 \left(\frac{k_2 A^3}{8w^2} e^{3i\zeta_0} + c.c \right) - w^2 \left(D_1^2 + 2D_0 D_2 \right)\left(A(\zeta_1, \zeta_2) e^{i\zeta_0} + c.c \right) \\ & + w_1 \left(\frac{k_2 A^3}{8w^2} e^{3i\zeta_0} + c.c \right) + w_2 \left(A(\zeta_1, \zeta_2) e^{i\zeta_0} + c.c \right) - \mu w^\delta D_0^\delta \left(A(\zeta_1, \zeta_2) e^{i\zeta_0} + c.c \right) \\ & - 3k_2 \left(A(\zeta_1, \zeta_2) e^{i\zeta_0} + c.c \right)^2 \left(\frac{k_2 A^3}{8w^2} e^{3i\zeta_0} + c.c \right) + f \cos\left(\zeta_0 + \sigma\zeta_2 + h\right). \end{aligned} \tag{5.78}$$

For asymptotically valid solution, we equate the coefficient of $e^{i\zeta_0}$ to zero to obtain

$$-2iw^2 D_2 A + w_2 A - \mu w^{\delta} A i^{\delta} - \frac{3k_2}{8w^2} A^3 \bar{A}^2 + \frac{1}{2} f\, e^{i(\zeta_0 + \sigma\zeta_2 + h)} = 0\,. \tag{5.79}$$

If

$$\phi = \sigma\zeta_2 - \psi + h, \qquad A = \frac{1}{2} a e^{i\psi}\,. \tag{5.80}$$

Substituting (5.80) into (5.79), we obtain

$$-w^2\left(D_2 a + i\, a\, D_2\psi\right) - \frac{1}{2} a\,\mu w^{\delta}\left(\cos\frac{\delta\pi}{2} + i\sin\frac{\delta\pi}{2}\right) - \frac{3k_2^2}{256w^2} a^5 + \frac{1}{2} f\, e^{i\phi} = 0\,. \tag{5.81}$$

Using the secularity condition on (5.79) we choose $w_2 = 0$ and then solve the remaining equation since the choice of $D_2 A = 0$ will give w_2 as a complex number. Having (5.64), (5.73), (5.80) and the above assertion in mind , we obtain

$$w^2 = w_0^2 + \varepsilon w_1 = w_0^2 + 3\mu\varepsilon A\bar{A}\,,$$

$$w = \sqrt{w_0^2 + \tfrac{3}{4}\mu\varepsilon a^2}\,. \tag{5.82}$$

Separating the real and imaginary parts of (5.81) we obtain

$$D_2 a = -\tfrac{1}{2}\mu w^{\delta-2}\sin\tfrac{\delta\pi}{2} a + \tfrac{f}{2w^2}\sin\phi\,, \tag{5.83}$$

$$aD_2\phi = a\left(\sigma + h\right) - \tfrac{1}{2}\mu w^{\delta-2}\cos\tfrac{\delta\pi}{2} a - \frac{3k_2^2}{256w^4} a^5 + \frac{f}{2w^2}\cos\phi\,. \tag{5.84}$$

Hence coupling (5.70) and (5.75) we can represent the approximate mood variation of a bipolar II disorder patient as

$$\begin{aligned} u &= Ae^{i\zeta_0} + c.c + \varepsilon\left(\frac{\mu}{8w^2} A^3 e^{3i\zeta_0} + c.c\right) + \cdots \\ &= \frac{1}{2} a e^{i\psi} e^{i\zeta_0} + c.c + \varepsilon\left(\frac{\mu}{8w^2}\left(\frac{1}{2} a e^{i\psi}\right)^3 e^{3i\zeta_0} + c.c\right) + \cdots \\ &= \frac{1}{2} a e^{i(\zeta_0+\psi)} + c.c + \varepsilon\left(\frac{\mu}{64w^2} a^3 e^{3i(\zeta_0+\psi)} + c.c\right) + \cdots \end{aligned}$$

$$u(t) = a\cos\left(\zeta_0 + \psi\right) + \varepsilon\frac{k_2}{32w^2} a^3 \cos 3\left(\zeta_0 + \psi\right) + O\left(\varepsilon^2\right). \tag{5.85}$$

5.6 THE AMPLITUDE – FREQUENCY RESPONSE

The steady – state solution of (5.83) and (5.84) shall be considered, where the phase lag $h = 0$. For the steady – state solution, $D_2 a = 0$ and $D_2 \phi = 0$, hence (5.70) and (5.75) is transformed to

$$-\tfrac{1}{2}\mu w^{\delta-2}\sin\tfrac{\delta\pi}{2}a + \tfrac{f}{2w^2}\sin\phi = 0, \tag{5.86}$$

$$a_0(\sigma) - \tfrac{1}{2}\mu w^{\delta-2}\cos\tfrac{\delta\pi}{2}a_0 - \frac{3k_2^2}{256w^4}a_0^5 + \frac{f}{2w^2}\cos\phi = 0. \tag{5.87}$$

From the above equations we obtain that

$$\frac{f}{2a_0 w^2}\sin\phi = -\frac{1}{2}\mu w^{\delta-2}\sin\tfrac{\delta\pi}{2}, \tag{5.88}$$

$$\sigma = \tfrac{1}{2}\mu w^{\delta-2}\cos\tfrac{\delta\pi}{2} + \frac{3k_2^2}{256w^4}a_0^4 + \frac{f}{2w^2 a_0}\cos\phi. \tag{5.89}$$

To obtain the frequency – amplitude response of the emotional variation, we do the following simplifications

$$\left(\frac{f}{2a_0 w^2}\sin\phi\right)^2 + \left(\frac{f}{2a_0 w^2}\cos\phi\right)^2 = \left(\frac{f}{2a_0 w^2}\right)^2$$

$$\left(\frac{f}{2a_0 w^2}\cos\phi\right)^2 = \frac{f^2}{4a_0^2 w^4} - \left(\frac{f}{2a_0 w^2}\sin\phi\right)^2$$

$$= \frac{f^2}{4a_0^2 w^4} - \left(-\frac{1}{2}\mu w^{\delta-2}\sin\tfrac{\delta\pi}{2}\right)^2$$

$$= \frac{f^2}{4a_0^2 w^4} - \frac{1}{4}\mu^2 w^{2\delta-4}\sin^2\tfrac{\delta\pi}{2},$$

$$\therefore\ \frac{f}{2a_0 w^2}\cos\phi = \pm\frac{1}{2}\sqrt{\left(\frac{f^2}{a_0^2 w^4} - \mu^2 w^{2\delta-4}\sin^2\tfrac{\delta\pi}{2}\right)}. \tag{5.90}$$

Coupling(5.88), (5.89) and (5.90) into (5.76), we obtain

$$\sigma = w\left(1+\varepsilon^2\left(\tfrac{1}{2}\mu w^{\delta-2}\cos\tfrac{\delta\pi}{2}+\frac{3k_2^2}{256w^4}a_0^4 \pm \frac{1}{2}\sqrt{\frac{f^2}{a_0^2w^4}-\mu^2w^{2\delta-4}\sin^2\tfrac{\delta\pi}{2}}\right)\right). \qquad (5.91)$$

Graphing (5.91) using MATHEMATICA, we obtain the following graphs

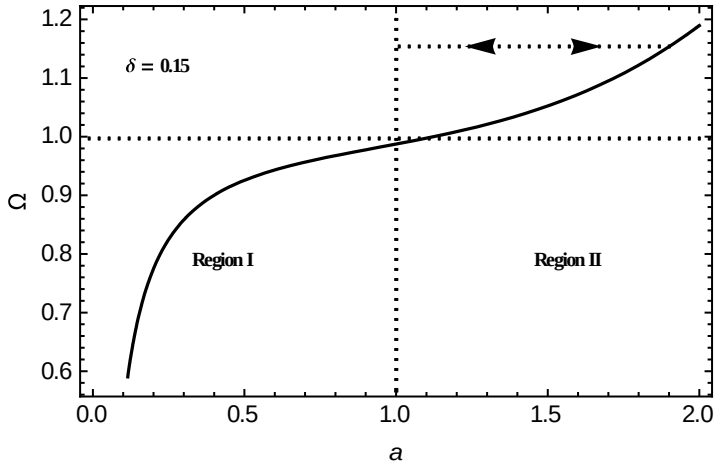


Fig. 5.15: Frequency – amplitude curve, $\varepsilon = 0.1, f = 10nN, w = 1pHz, h = 0, \mu = 5, k = 10$.

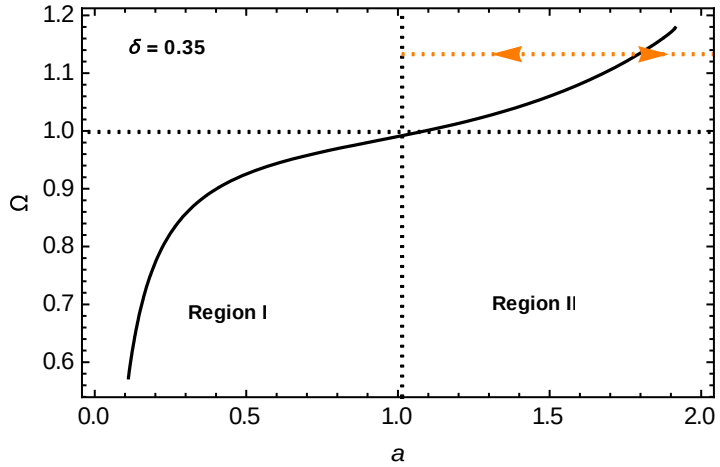


Fig. 5.16: Frequency – amplitude curve, $\varepsilon = 0.1, f = 10nN, w = 1pHz, h = 0, \mu = 5, k = 10$.

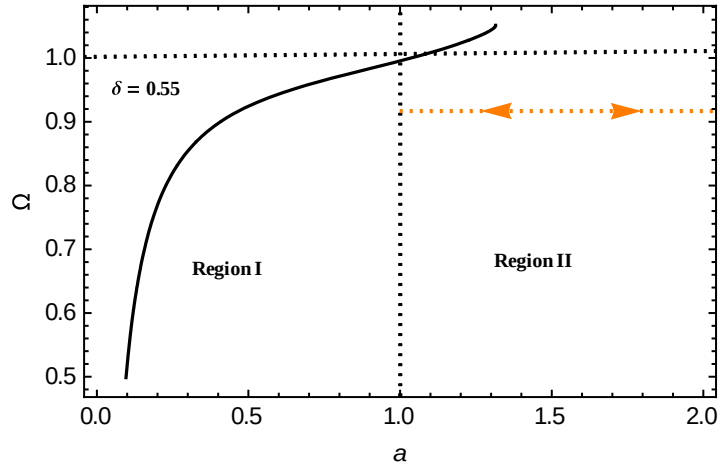


Fig. 5.17: Frequency – amplitude curve, $\varepsilon = 0.1, f = 10nN, w = 1pHz, h = 0, \mu = 5, k = 10$.

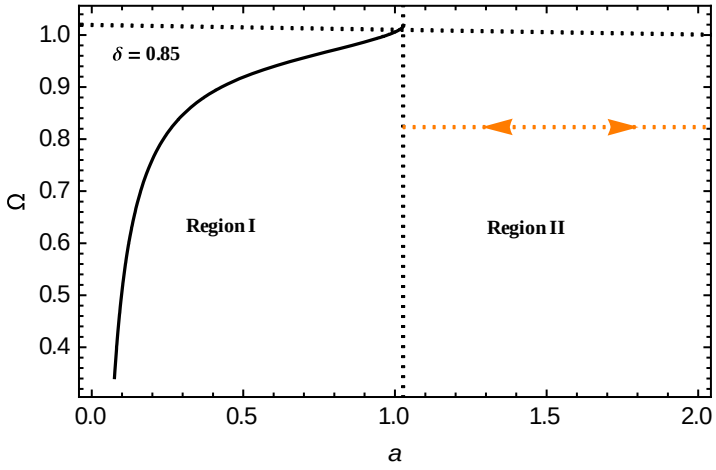


Fig. 5.18: Frequency – amplitude curve, $\varepsilon = 0.1, f = 10nN, w = 1pHz, h = 0, \mu = 5, k = 10$.

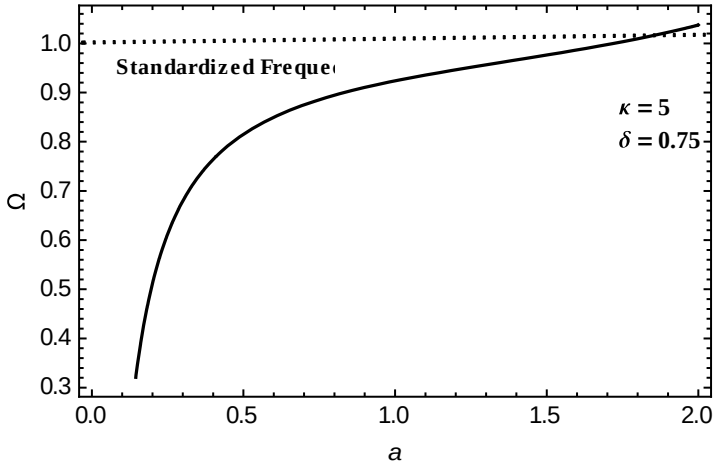


Fig. 5.19: Frequency – amplitude curve, $\varepsilon = 0.1, f = 10nN, w = 1pHz, h = 0, \mu = 5$.

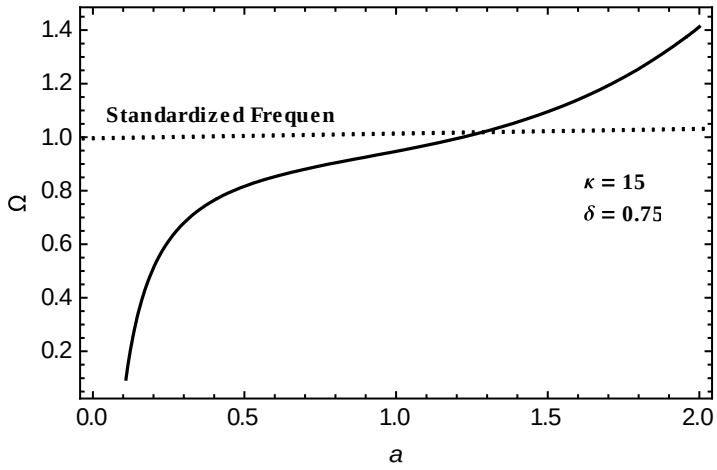


Fig. 5. 20: Frequency – amplitude curve, $\varepsilon = 0.1, f = 10nN, w = 1pHz, h = 0, \mu = 5$.

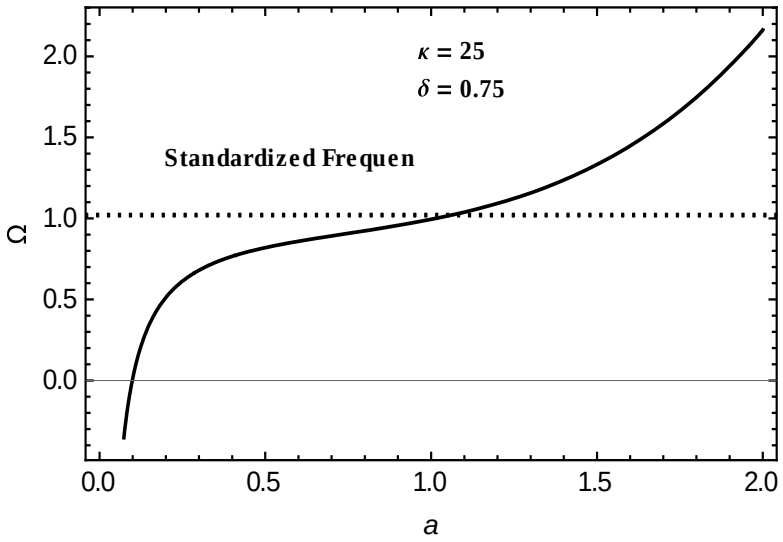


Fig. 5.21: Frequency – amplitude curve, $\varepsilon = 0.1, f = 10nN, w = 1pHz, h = 0, \mu = 5$.

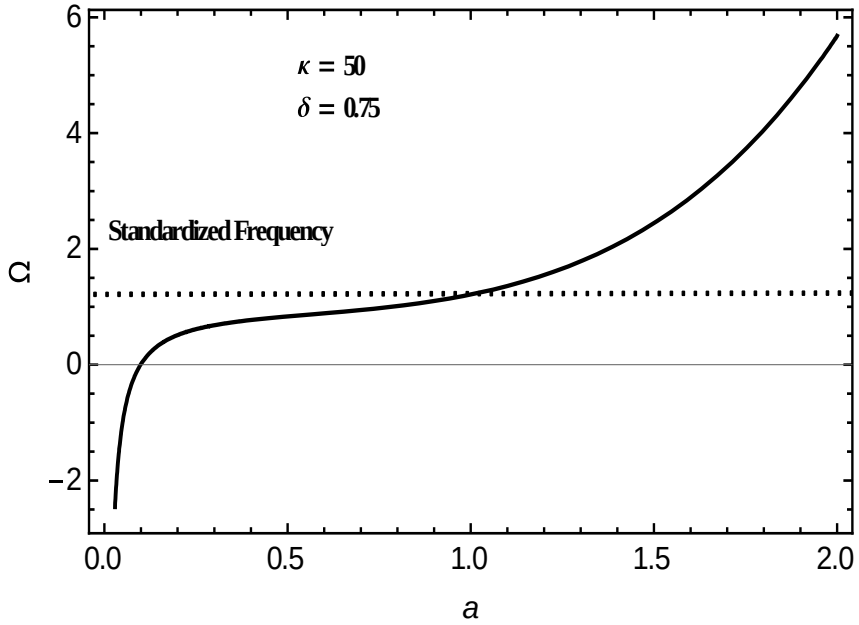


Fig. 5.22: Frequency – amplitude curve, $\varepsilon = 0.1, f = 10nN, w = 1pHz, h = 0, \mu = 5$.

5.7 Further Discussion

In this section we want to study the effect of fractional order system to the frequency – amplitude curves. In Fig. (5.15 – 5.18) we study this effects by varying the value of fractional order parameter, δ. The frequency – amplitude curve is divided into two Region I and Region II. Region I represents a steady limit cycle that depicts stability in the mood variation of bipolar II disorder patients while Region II represents unbounded oscillation. It is observed

from the figures that as the fractional parameter increases, the curve shifts to the assumed amplitude which in this work we considered as unity. Frequency – amplitude curve is sensitive to variation in the fractional coefficient. In Fig. (5.19 – 5.22), we fixed the fractional coefficient and vary the nonlinear coefficient i.e. the medication parameter, k_2.

5.8 Conclusion

We believe the model proposed here has qualities not present in the existing mathematical models of bipolar disorder; modeling with fractional derivative is new in the models for bipolar disorder in current literature. All control parameters embedded in the proposed plan have a substantial role in replicating the diverse aspects of the illness. Moreover, the prospective manicogenic significance of antidepressants can be mathematically represented in the control parameter corresponding to preconceived notion and so is the psychosocial therapy. We have investigated the importance of psychosocial therapy to bipolar II disorder patients using Modified Duffing – Van der Pol oscillators. We modeled the medication parameter as a quitic – cubic function. The nonlinearity of this function made it impossible for us to use the convention method of obtaining the solution of ordinary differential equations. We used Lindstedt – Poincare – Multiple scale perturbation technique that enabled us to get a valid asymptotical solution for the model. From the analysis of the solution obtained, we observed that when the medication parameter is increased considerably, the limit cycle or the stable mood variation of the patient is achieved faster. In addition, the amplification of the mood can be curtailed when the damping coefficient is increased because the body system naturally develops a shock – absorber to contain the under secretion of cortisol and other endocrine secretions responsible for the mood swing. When the damping coefficient is zero we have the two extrema.

Furthermore, we introduced one of the suprachiasmatic nuclei secretions into the system to study its relevancy to the aggravation of bipolar II disorder mood variation. We solve the model generated using multi – scale perturbation. The graph of the asymptotic analytic solution suggests that bipolar II disorder patient should be monitored to avoid involving in activities that will either cause the over secretion or under secretion of the HPA axis hormones i.e. coticotropin – releasing – hormone (CRH), adrenocorticortropic hormone (ACTH) and cortisol. The hormonal concentration has been correlated to depression when it is in the state of hypercortsolism.

On the other hand, we obtained a fractional – order damping oscillator that we use to study the effect of fractional damping to the limit cycle or mood variation of bipolar II disorder patients. The asymptotic solution of the model is obtained using modified Lindstedt – Poincare multiple scale perturbation method. The asymptotic solution obtained is graphed using MATHEMATICA. Our results indicate that the fractional – order damping oscillator allows for the better and quicker trend observation. It was also observed that any slight change in the damping function affects the mood variation of bipolar II disorder patient; also the mood variation is sensitive to the fractional order change. The stressors represented as the forcing function has adverse effects on the mood variation, succinctly leads to unbounded amplitude increase; which is checkmated by increasing the damping coefficient and the nonlinearity parameter or medication parameter. The analysis also revealed that the value of the fractional order has vivid effect on the frequency – amplitude curve of the mood swings.

There is a protracted term void in the time series data on emotional state or real biological signals, the proposed theoretical model will enhance the understanding of the evolution of emotional states in bipolar disorder and also to inspect the effects of pharmacological and psychological therapies in control over the state. Future testing of our model will be an improvement of the ‘big data’ revolution in human sciences, which offers for the first time

high resolution time-series data on complex system function in the human case (Indic et al., 2011). Not only do non- intrusive monitoring devices make available meaningful data for testing competing mathematical models of bipolar disorder, but they also have immediate translation potential for early intervention and prevention if our models prove correct (McIntyre et al., 2013).

CHAPTER 6

GENERAL DISCUSSION

6. 1 Mood Variation

In this work, we propose three oscillator models that attempt to explain qualitatively the moods variations of a bipolar II disorder patient. There is inadequate data at the time of this research to construct a quantitatively detailed model describing bipolar II disorder, consequently this step to employ minimalist models is a right move. Undeniably, similar phenomenological models have yielded momentous insight into the dynamics of several oscillatory biological and physical phenomena (Camacho et al. 2004). Even without time – series data to describe the moods of bipolar II disorder patient, the models we have developed could prove important in snowballing the understanding of the effect of treatment that includes medication and psychotherapy – psychosocial therapy on the cyclic behaviour of bipolar II disorder patient. The three – dimensional dynamical systems we employed provide simple distortions of the behaviour of bipolar II disorder patient; it is concurrently easy to analyze these models. Furthermore, despite their simplicity, they successfully capture qualitatively the known behavioural trend of treated and untreated bipolar II individuals. A quantitative analysis of the dynamics will require refining our models using time-series data from clinical trials. It is our hope that this work will stimulate auxiliary mathematical analyses that will incorporate such data as well as the data collection that will permit these modeling efforts.

In Model 1, we considered treatment as a forcing polynomial function that led to a stable limit cycle with smaller amplitude, which we interpreted as a decrease in the severity of the mood swings of the bipolar patient. This model suggests that individuals that are not

diagnosed at a sufficiently young age might need drastic intervention to bring their mood swings to a reasonable level. Given that individuals are usually diagnosed in the depressive state and that bipolar disorder is frequently misdiagnosed initially, this aspect of Model 1 is especially significant (Lewis and Vornik, 2003).

In model II we considered the effect of cortisol secretion on the mood variation of bipolar II disorder patient. Cortisol is the main byproduct of HPA axis activities. Stress situations trigger the HPA axis, which is essential in raising the concentration of cortisol that leads to release of energy to the organism. Stress, both acute and chronic, has been identified as an essential etiological factor of depression. We observed that hypercortisolism and hypocortisolism have significant effect on the mood variation of bipolar II disorder patient. HPA axis hyperactivity or hypoactivity can be termed as HPA axis dysregulation that might partly mediate the increased risk of BD relapse following intense psychosocial stress(Weiss et al. 2015). HPA axis hyperactivity predicted clinical relapses and hypoactivity is associated with a higher number of mood episodes (Ellenbogen et al. 2013). Relative hypercortisolism were common among younger and more often females while hypocortisolism is common among older patients; must often inherent in patients that was not on Lithium (Havermans et al. 2011). Since hypercortisolism is more peculiar among younger BD patients, we can suggest that hypocortisolism results from accumulated stress load from physiology, environmental and severe ailment episodes. This view is buttressed by (Maripuu et al. 2017) with studies performed on stress – related disorder and general population samples that collectively point at increased chronic stress and increased accumulated stress load as central to the development of the phenomenon. BD has a multifactorial etiology, depending on both genetic and environmental factors. Lately Craddock and Sklar (2013) estimated that monozygotic twin show concordance between 40 and 70%, and a heritabitity of around 90%. Enormous research has been conducted on the genetic risk factors of BD, genes related to

HPA axis activity were not found to be significant risk factors for BD. Common polymorphisms of HPA – related genes are associated with different clinical features of BD. Variants of "clock" genes confer a vulnerability to circadian rhythms instability and to BD itself (Gonzalez, 2014). Environmental stressors such as parental neglect can lead to a vertical, intergenerational transmission of HPA axis abnormalities; Ellenbogen et al. (2013) suggested that it might occur as a result of childhood trauma and dysregulated parenting style. Recently (Perroud et al. 2014) showed that childhood traumatic experiences can determine epigenetic modifications of the glucocortisolic receptors (GR) gene in patients with BD, HPA axis dysfunction might act as a mediator, on the basis of gene – environmental interactions. Summarily, HPA axis hyperactivity or hypoactivity can be considered as an endophenotype, i.e. an etiological factor of BD but rather as a pathogenetic mechanism that can contribute to shape the clinical presentation of the disorder, on the ground of genetic – environmental interplay.

Numerous generalizations of our models can be considered to further examine mood disorders using limit cycle oscillators. For example, one can incorporate the fact that the medication administered to bipolar II individuals typically takes several days to reach therapeutic levels in the blood stream by adding a time-delay to the treatment function. One can also gain further mathematical and biological insight by directly examining the bifurcations that occur in our models.

Limit cycle oscillators can also be used to study behavioral cycling in mood disorders besides bipolar disorder; as such phenomena are of considerable interest to both psychologists and psychiatrists (Ferrier et al. 2001). Individuals suffering from cyclothymia disorder rapidly flip back and forth between depressed and euphoric moods. Their high and low periods, which are relatively short, are much less intense than those of bipolar individuals.

Although it is not known precisely what leads individuals from one pole to the other, possible causes include psychosocial stress, disrupted sleep patterns, or some endogenous or internal biological mechanism that is not connected to environmental stimuli. It is also not known what happens to cycling over time. It is speculated that an individual's cycling may slow down with age. From a mathematical perspective, we wish to highlight that the effects of disrupted sleep patterns can be studied by coupling a cyclothymic (or bipolar) individual with a limit cycle oscillator representing the human sleep–wake cycle.

Another important issue to consider is the threshold for flipping poles. It has been theorized, for example, that the threshold for depression (and for flipping poles) gets lower over time. It has been speculated (Robert and David, 2009) that the longer one is ill, the more autonomous or disconnected episodes become from the environment. This is termed ‘‘kindling theory" and is believed to be analogous to what happens in epilepsy, in which there is a gradual kindling of biological disturbances in the brain that eventually surpasses the threshold for a seizure.

In model III we considered a case that the damping is fractional – ordered because of the continuity of the body's attempt to resist abnormalities in mood and other morphological, physiological and psychological trends. The main contribution of this model seems to be suggesting the idea that the clinical course of bipolar disorder, which is characterized by repeated erratic cycles of mania and depression, may be understood based on the concept of fractional-ordered derivative models. It is observed that as the fractional parameter increases, the curve shifts to the ideal amplitude which in this work we considered as unity. We discover that increment of this parameter i.e. the pharmacotherapy under the prescription of a physician enables the mood variation to stabilize. Patient are always exposed to stressors that have the tendency of exhausting the resources that are normally available for contending with

more adverse health outcomes; hence patients have to take their medication promptly for backup interventions.

Bipolar II disorder patients have a relatively high rate of non – adherence to pharmacotherapy (Buckjohn, 2010). Psychosocial therapy in addition to prescribed medication may reduce the number and length of relapses, improve quality of life, and reduce hospitalization. Psychosocial therapeutic approaches like concomitant support, educational, family and group therapy is usually indicated, since it can help to reduce the rate of relapse and recurrence (McEwen, 2010). The development of interventions that aims on the quality of parent – child relationships, could be essential in the treatment of bipolar II disorder, not neglecting symptom management. Family therapy can be enhanced by training families in communication skill that will enable functional family relationships. In addition, they should be taught the relapse signs so that they can identify the signs and symptoms of relapse. Family therapy could be divided into three stages: an assessment stage, communication enhancement training, and problem solving training (Buckjohn, 2010). The urgency for gross education about bipolar II disorder will curtail the resultant negative effects in the society. Patients and families should be provided with the knowledge about the dangers of the misnomer. The main focus of psychoeducation is the side effects of treatments, the course of the illness and barriers to recovery (Rothbaum and, Astin, 2000)

Recent literatures have it that group therapy educates patients about the treatment compliance; the number of relapses can be reduced by 15% by decreasing the stigma associated with psychiatric illness (Rothbaum and, Astin, 2000). Society should also be educated that psychiatric illness is like any other malfunction in the morphology and physiology of human system. Research has proven that patients that combine prescribed medication and psychosocial therapy can have less severe course of disease than patients who receive medication and is faced with marital failures, poor family interactions, alcoholism or

related substance addictions, and unemployment. Hence expatiates on the need of joining groups as directed by the psychiatrist such acts as a shock absorber, in preventing depressive and hypomanic recurrences, stabilizing symptoms. The main purpose of such group or education is to manage stressors or daily hassles that induces mood swings and promote family – oriented society that everyone is recognized and appreciated.

6.2 PSYCHOSOCIAL THERAPY

Reviewing the data on the usefulness of psychosocial intervention in BD is rather disappointing. It seems that only psychoeducation is efficacious for the relapse prevention of mood episodes but only in a selected subgroup of patients at an early stage of the disease who have very good if not complete remission of the acute episode. CBT and IPSRT could have some beneficial effect during the acute phase, but more data are needed. Mindfulness interventions could only decrease anxiety, while interventions to improve neurocognition seem to be rather ineffective. Family and Friends therapy seems to have benefits during onsets, acute episode, neurocognition, anxiety, relapse etc.

The mechanisms responsible for the efficacy of the psychosocial treatments are unknown and poorly studied. Opinions suggest that the effect could be mediated through enhancement of treatment adherence (Colom et al. 2010); improving the lifestyle and especially biological rhythms, food intake and social zeitgebers (Frank et al. 2005); the changing of dysfunctional attitudes (Ball et al. 2006); but also through the improvement of family interactions (Simoneau et al. 1999). The enhanced ability for the early identification of signs of relapse may play an important role too (Perry et al. 1999). As in any trial concerning any psychological intervention, the methodological issues hampering research are cardinal. The blindness problem together with the impossible task to have a valid placebo group limits the value of the data. Because of these methodological drawbacks, often small studies of this

kind have an unexpectedly high effect size, while at the same time there is a lack of replication of the same treatment by different research groups under the same conditions.

Psychosocial interventions suffer from an additional drawback themselves. The training of the therapist and the setting itself might play an important role and it is quite different to apply the same intervention in specialized centres than in real-world settings in the everyday clinical practice. Furthermore, the gathering of the data is far from systematic; adverse events are not routinely registered, outcomes are not hierarchically stated a priori and too many post hoc analyses are published without being stated as such.

The best timing for the implementation of psychological interventions is still uncertain, but it seems that they function better in subjects which are at an early stage of the disease and who were euthymic when recruited (Scott et al. 2012). It is highly possible that a higher number of previous episodes (Colom et al. 2010; Scott et al. 2006) as well as a higher psychiatric morbidity and more severe functional impairment (Reinares et al. 2014) might reduce treatment response although the data are not conclusive (Lam et al. 2009). In addition, it has been suggested that in the early phases, the intervention should be simpler, with a focus on neuroprotective strategies (Kapczinski et al. 2009). At later stages, the emphasis could focus more on rehabilitative interventions dealing with the specific disabilities of the patients (Berk et al. 2010).

FFT, IPSRT and CBT might be also efficacious during the acute episodes, but this is far from clear (Frank et al. 2005 ; Scott et al. 2012). Specific characteristics of the family environment have also been shown to influence the response to treatment (Miklowitz et al. 2009). Probably there were subpopulations who will especially benefit from these treatments (Scott et al. 2012), but these assumptions are based on post hoc analyses alone. It should be mentioned that most of research concerns pure and classic BD – I patients although there are some rare data concerning special populations like BD – II (Swartz et al. 2012),

schizoaffective disorder (Murru et al. 2012), patients with high suicide risk (Fountoulakis et al. 2014) and patients with comorbid substance abuse (Weiss et al. 2009). The literature includes reports which suggest that the benefits of psychosocial interventions if achieved can last for up to 5 years (Gonzalez-Isasi et al. 2012) although some patients might need booster sessions (Lam et al. 2003 ; Ball et al. 2006, Abulseoud et al., 2017). The complete range of the effect these interventions have is still uncharted. It is reasonable to expect a beneficial effect in a number of problems, including suicidality, but research data on these issues are virtually non- existent (Fountoulakis et al. 2014).

Overall, there are some data in the literature supporting the notion that adjunctive specific psychological treatments can improve specific illness outcomes which is supported by our analytic approach. It seems reasonable that FFT and any such intervention should be applied as early as possible and should always be tailored to the specific needs of the patient in the context of personalized patient care, since it is accepted that both the patients and their relatives have different needs and problems depending on the stage of the illness.

CHAPTER 7

SUMMARY AND CONCLUSION

7.1 CONCLUSION

The three models studied in this work is concern with the emotional variation of Bipolar II disorder patients; its quantitative representation, and the effect of psychosocial therapy in the general treatment. Our research did not involve the method of diagnosis, which is a challenging clinical labyrinth; we instead concentrate on the dynamics of our models under the proposed, which involves a combination of Pharmacotherapy and psychosocial therapy. The purpose of our modeling efforts is not to recommend a specific treatment for bipolar individuals but rather to provide some insight into the complicated dynamics of bipolar disorder. Our intent is to provide a mathematical framework that ultimately leads to the development of more detailed models of bipolar disorder that incorporate clinical data. With this work, we hope to motivate the collection of time-series data from clinical trials that will lead to refinements of our model that incorporate such data. In our view, dynamical systems theory and mathematical modeling in general can lead to important advancements in the understanding of bipolar disorder.

Our work has the following assertions

- From the analysis of the solutions obtained, we observed that when the medication parameter (Pharmacotherapy and Psychosocial therapy) is increased considerably, the limit cycle or the stable mood variation of the patient is achieved faster.
- Our results indicate that the fractional – order damping oscillator allows for the better and quicker trend observation.
- The amplification of the mood can be curtailed when the damping parameter (family and friends harmonization, stable and favourable economic system, serene environmental aperture, peaceful political and government structures etc.) is increased

because the body system naturally develops a shock – absorber to contain the under secretion of cortisol and other endocrine secretions responsible for the mood swing.

- The stressors represented as the forcing function has adverse effects on the mood variation, succinctly leads to unbounded amplitude increase; which is checkmated by increasing the damping coefficient and the nonlinearity parameter or medication parameter.

- The present work illustrates real – world outcomes for quality of Life (QoL) under guided BD treatment – pharmacotherapy and focusing on FFT: improves the mental quality of life and even physical QoL which is supported by Morton et al. 2018. Psychosocial therapy in addition to prescribed medication can reduce the number and length of relapses, improve quality of life, and reduce hospitalization. FFT can be enhanced by training families in communication skill that will enable functional family relationships and families should be provided with the knowledge about the dangers of the misnomer in addition to the onset signs.

7.2 SUMMARY

This work addresses bipolar II disorder in terms of its peculiar mood variation. It considers modeling of this mood variation by mathematical approach which is purely analytic using a dynamical oscillator that has the ability to depict the trend in the disorder when the parameters are varied. The parameter that represents medication (pharmacotherapy and psychosocial therapy) is of tremendous interest. Psychosocial therapy considered in this work is the FFT, which is observed that the stability in mood variation of the patient is achieved faster when the parameter is increased under prescribed pharmacotherapy and conducive environment both endocrine and epiendocrine. We also examine the effect of HPA axis with reference to cortisol to the episodes in bipolar II disorder; it is observed that cortisol is not a

state marker to the inflammation of the episodes. Since the etiology of BD is continuous we modeled the disorder with fractional calculus that indicates that in our view, our work is another step in developing mathematical models of the mood variations of bipolar II patient. We are bent on providing a new mathematical framework that ultimately leads to the development of more exhaustive models of bipolar II disorder that incorporate clinical data.

7.3 LIMITATION AND FUTURE WORK

There are several limitations of this study. First, clinical data that was used for validation of our results were not sufficient to account for general speculations. Hence they should be regarded as empirical. However, a similar method was used in recent works by researchers (Nana, 2009, Goldbeter et al., 2013) and yielded results that were consistent with a larger study (McIntyre et al., 2013). The solutions to the proposed models are asymptotical and may include some notable approximation errors.

On the basis of this review, future studies on this topic should examine the role of hypothalamic dysfunction in Bipolar II disorder, assessing the role of clock genes; examine the effect of psychosocial stress and its relation to ailment progression, explore more on the effect of the fractional parameter to the relapse and recovering of BD patient. Additional information on the effects of psychotropic drugs on the HPA axis as well as the psycho – physiology of the patients.

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