Models of Negatively Damped Harmonic Oscillators: the Case of Bipolar Disorder

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August 9, 2002

Abstract

Bipolar II disorder is characterized by alternating hypomanic and major depressive episodes. A negatively damped harmonic oscillator is used to model the periodic mood variations of a single bipolar II individual. Treatment is modeled via an autonomous forcing function that is capable of stabilizing, within some boundaries, the mood variation of the patient. In this

paper we study the dynamics of two individuals with bipolar II disorder who interact with each other. The interaction of two subjects living together who experience bipolar II disorder is modeled via two weakly-coupled, weakly-damped harmonic oscillators.

1 Background

Bipolar disorder affects about one percent of the general population [5]. This disorder presents many unique problems to current clinical practitioners, such as the difficulty in diagnosing the disorder, patient non-adherence to treatment and/or medication, and the fact that most drugs, if taken individually, have a toxic level of efficacy [8]. Psychiatrists have established a broad range of criteria for classifying this disorder in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM IV) [1]. The disorder has a variety of characteristics which may or may not be present in all patients, including mixed episodes, in which it is possible to simultaneously experience symptoms of both mania and depression, and rapid cycling, where a patient experiences at least 4 cycles per year [5]. Bipolar Disorder can be separated into several distinct groups. Bipolar I disorder is characterized by a combination of manic and depressive episodes with the possibility of mixed episodes, while bipolar II disorder is characterized by a combination of hypomanic and depressive episodes [1], [3]. Patients with bipolar II disorder tend to be more prone to rapid cycling especially if initially treated only with antidepressants [8].

Treatment for bipolar disorder ideally includes a combination of medication and therapy. The typical drug treatment includes mood stabilizers, antipsychotics, antidepressants, and other drugs found to be effective (i.e.,some select anticonvulsants). Some names for a few of the more commonly used drugs are Lithium, Valproate (also know as Depakote), Carbamazepine (also known as Tegretol), and Prozac. The mood controlling drugs such as Lithium take 4 to 10 days to reach therapeutic levels in the blood stream, so initially treatment is likely to include antidepressant and antipsychotics [3]. During the maintenance state antidepressant or antipsychotics are likely to be used in addition to mood stabilizers. Monotherapy (single drug therapy) is generally avoided by clinicians due to the strong side effects of some of the drugs used. Other drugs that can be used are selective serotonin reuptake inhibitors (SSRI) and monoamineoxidase inhibitors (MAOI) both of which are generally used for depression [3]. In some cases, special care must be taken to ensure that the individual does not fall into a pattern of rapid cycling or become addicted to some of the medication because substance abuse is an associated problem with bipolar disorder [3].

Bipolar II disorder is highly heritable. It has been reported that for people with bipolar II disorder there is a 35 percent chance that offspring will also be bipolar II. We know that family units do exist with more than one individual with bipolar II disorder. We seek to examine the dynamics of a closely interacting pair of bipolar individuals

2 Introduction

For the purpose of our model some simplifying assumptions need to be clarified. First, while bipolar II disorder can be somewhat erratic, there exist patterns of recurrence to the episodes. For a group of patients with the disorder, there is a periodicity which governs the manic and depressive episodes [9]. Also, it is a common assumption that if the disorder is left untreated it will severely progress. Therefore, the negatively damped harmonic oscillator is one possible model that captures qualitatively the mood variations of a single patient diagnosed with bipolar II disorder. Hence, the governing equation is

$$\ddot{x} - \alpha \dot{x} + \omega^2 x = 0, \tag{1}$$

where x is the emotional state of the patient, $\dot{x}$ is the rate at which mood changes between hypomania and severe depression, and $\alpha > 0$ and ω are parameters. In order to establish a biologically reasonable scale for mood variations we consider values $|x| \leq 10$, where $x = 10$ arbitrarily represents the most severe hypomania while $x = -10$ represents the most severe depression.

Since all individuals experience some mood variation, we will establish a threshold of ± 1 in mood variations to indicate the clinical diagnosis of bipolar II disorder. That is, a patient is classified as having bipolar II disorder when x ranges beyond ± 1. We realize that many considerations actually go into the proper diagnosis of the disorder. In our model, by the time the oscillator is able to reach an x value of ± 1, a sufficient number of the classifying criteria are assumed to have been met to be able to diagnose the individual with the disorder. The emotional state where a patient is able to perform everyday activities without the hindrances normally associated with bipolar II disorder is arbitrarily define to be $|x| \leq 0.3$. Since we are seeking a qualitative analysis, our scales are chosen only as a caricature of the general behavior.

3 Typical Untreated Bipolar II Patient

The typical bipolar II patient is expected to experience fewer than four cycles per year and is usually diagnosed between the ages of 18 and 24 [5]. Also, a typical bipolar II patient is usually diagnosed when they are in a depressive episode rather than in a hypomanic episode [9]. Setting the parameters $\alpha = 1/2$ and $\omega = 20$ with initial conditions $t_0 = 0$, $x(0) = 0$, and $\dot{x}(0) = 0.07$, allows for the modeling of such a patient (see Figure 3.1). There are many initial conditions that we can consider, but the qualitative behavior that occurs when medication is applied remains the same, for any biologically reasonable initial conditions. Also, the time at which we choose to apply the medication function will be arbitrary up to the point that the amplitude is greater than ± 1, this means the patient can be diagnosed during either a manic or a depressive episode. Equation (1) can solved exactly for $x(t)$ [7]. The solution is

$$x(t) = \exp\left(\frac{t}{4}\right)\left[A\sin\left(\frac{9\sqrt{79}}{4}\,t\right) + B\cos\left(\frac{9\sqrt{79}}{4}\,t\right)\right] \tag{2}$$

where A and B are determined by the initial conditions. Substituting $t = 0$ into Equation (2) we obtain $B = 0$. To find A, we differentiate Equation (2) with respect to t to obtain

$$\begin{aligned} \dot{x} &= \exp\left(\frac{t}{4}\right)\left(\frac{1}{4}A - B\right)\sin\left(\frac{9\sqrt{79}}{4}\,t\right) \\ &\quad + \exp\left(\frac{t}{4}\right)\left(\frac{9\sqrt{79}}{4}A + \frac{1}{4}B\right)\cos\left(\frac{9\sqrt{79}}{4}\,t\right) \end{aligned} \tag{3}$$

Substituting $B = 0$ and $t = 0$ into Equation (3) we obtain $A = \frac{7\sqrt{79}}{17775}$. Using our chosen values for α, ω, A, and B we have

$$x(t) = \frac{7\sqrt{79}}{17775}\exp\left(\frac{t}{4}\right)\sin\left(\frac{9\sqrt{79}}{4}\,t\right) \tag{4}$$

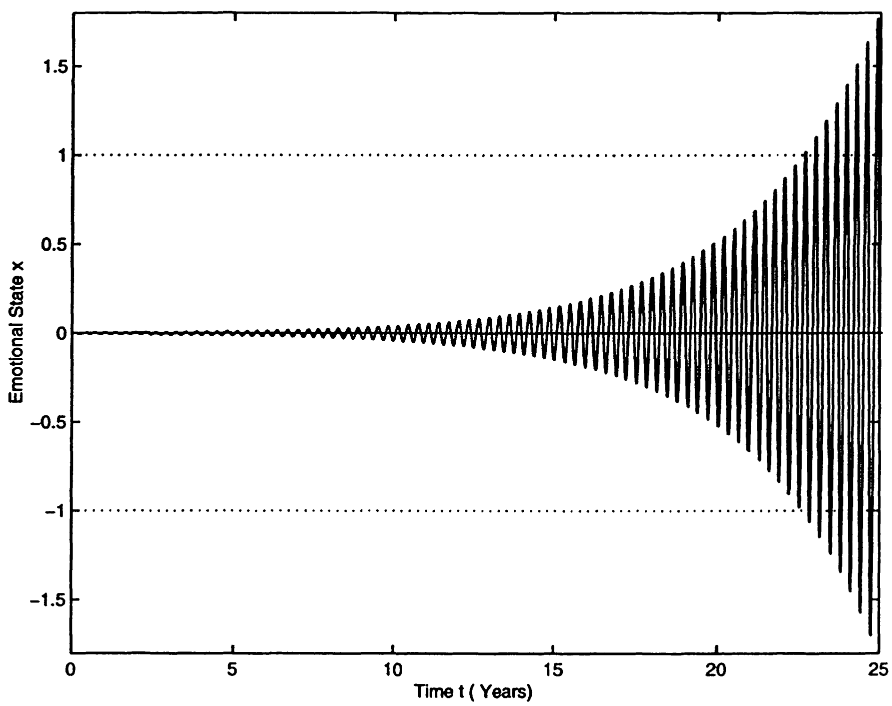


Figure 3.1: Typical patient: mood variations with onset of bipolar II disorder

and

$$\dot{x} = \frac{7\sqrt{79}}{71100} \exp\left(\frac{t}{4}\right) \left[\sin\left(\frac{9\sqrt{79}}{4}\, t\right) + 9\sqrt{79} \cos\left(\frac{9\sqrt{79}}{4}\, t\right) \right]. \tag{5}$$

We are interested in calculating the approximate age at which a typical patient has the first episode of hypomania and severe depression. This can be obtained by solving Equation (4) for t_1 such that $x(t_1) = 1$ and t_2 such that $x(t_2) = -1$, respectively. In this system, $x(t_1) = 1$ at about $t_1 \approx 22.69$ and $x(t_2) = -1$ at about $t_2 \approx 22.84$ (see Figure 3.2).

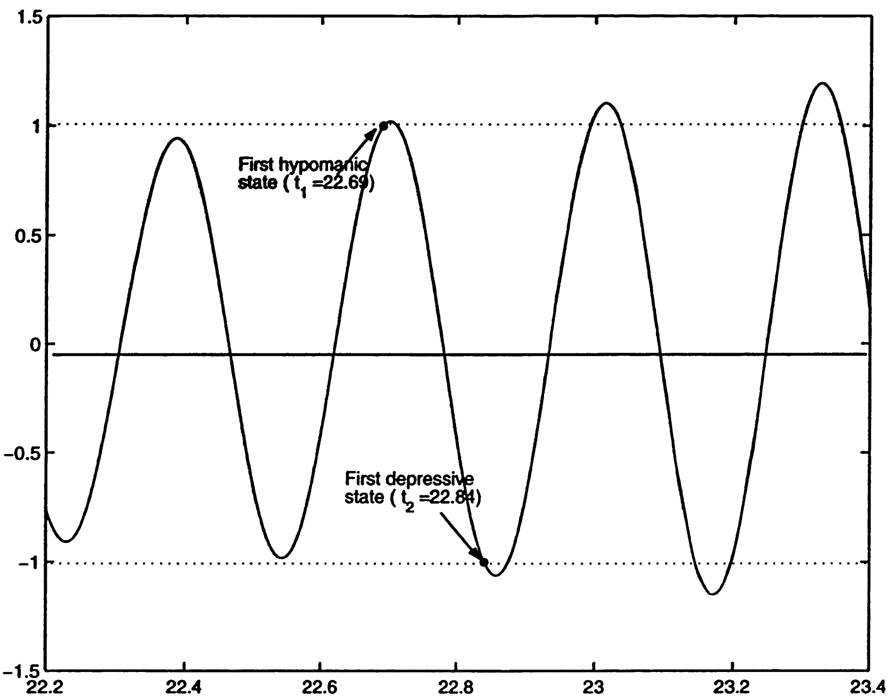


Figure 3.2: Typical patient: first hypomanic and depressive episodes

Thus, a typical patient experiences the first episode of hypomania and severe depression at approximately age 22.69 and 22.84 respectively.

We are also interested in approximating the ages at which the typical patient reaches the most extreme level of severe depression, exits the severe depression level, and reaches a reasonable functional state. Setting Equation (2) equal to -1 and t from 22.85 to 23 we obtain $t_3 \approx 22.87$. This implies that at about age 22.87 the typical patient will reach the most extreme level of severe depression. We anticipate that the most extreme level of severe depression will occur between the ages 22.84 to 22.87 (approximately 11 days). We found that the system reaches a minimum when $x \approx -1.06$ and

$t_4 \approx 22.86$. This implies that at about age 22.86 a typical patient reaches the most extreme level of severe depression. Setting Equation (2) equal to -0.3 and allowing t to vary from 22.85 to 23 we obtain $t \approx 22.92$, which implies that at about age 22.92 the patient reaches a reasonable functional state (see Figure 3.3).

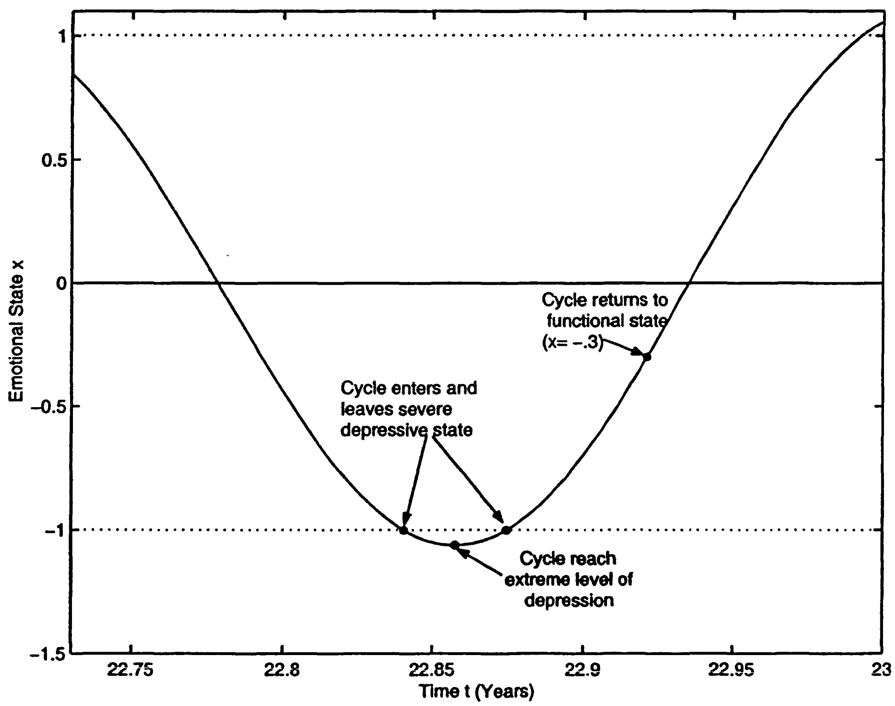


Figure 3.3: Typical patient with onset of bipolar II disorder: Depressive episode

4 Typical Treated Bipolar II Patient

Most patients with bipolar II disorder are diagnosed when they are in a depressive episode because hypomania usually does not prevent the normal function of individuals. In many cases hypomania enhances functionality in the short term [5]. For this reason, we assume treatment begins at approximately age 22.84. Autonomous forcing functions, which will represent the treatment of the patient, are introduced into the negatively damped harmonic oscillator, Equation (1), to obtain

$$\ddot{x} - \alpha\dot{x} + \omega^2 x = \beta x^2 \dot{x} \tag{6}$$

The autonomous forcing function $\beta x^2 \dot{x}$ represents overall treatment which includes a combination of antidepressant, mood stabilizers, psychotherapy, and either antipsychotics or tranquilizers, to control the mood variations of bipolar II patients. We have chosen this particular autonomous forcing function because treatment is dependent upon the severity of the mood and the rate at which they vary. This particular autonomous forcing function with $\beta = -50$ is a caricature of the effects of the overall treatments given to bipolar II patients. Successful treatment is characterized by limiting the mood variation where $|x| \leq 0.3$.

We are interested in finding the time the patient spends in a severe depressive state (t_5 - t_2), the time it takes to reach a reasonable functional state ($t_6 - t_2$), and the time and degree of the next peak in the cycle of mood variations (t_7, x_7). The ODE45 function in MatLab (see Appendix A) facilitated these calculations. It was determined that the patient exits the severe depressive state at time $t_5 \approx 22.868$, so $t_5 - t_2 \approx 0.028$ (approximately 10.22 days). The patient then enters a reasonable functional state at $t_6 \approx 22.951$, so $t_6 - t_2 \approx 0.112$ (approximately 40.88 days). Finally, the peak is reached at time $t_7 \approx 23.05$ with a maximum value of $x_7 \approx 0.561$.

4.1 Limit Cycle

After examining the numerical simulations of our model we observed that adding the forcing function generates a limit cycle (see Figure 4.1).

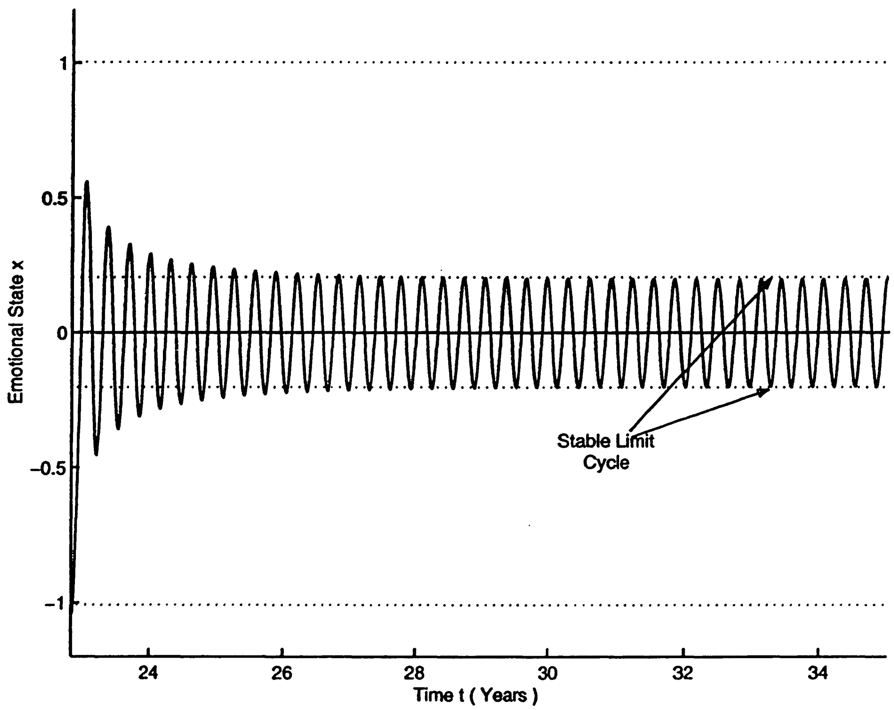


Figure 4.1: Mood variations of a treated bipolar II patient; limit cycle achieved $\beta = -50$, $\alpha = \frac{1}{2}$, $\omega = 20$

To prove the stability of this limit cycle we re-write our model with treatment as

$$\ddot{x} + (-\beta x^2 - \alpha)\dot{x} + \omega^2 x = 0. \tag{7}$$

If we let $f(x) = -\beta x^2 - \alpha$ and $g(x) = \omega^2 x$, then Equation (7) satisfies all the criteria required by Liénard's Theorem.

Liénard Theorem:[10]

Suppose that $f(x)$ and $g(x)$ satisfy the following conditions:

(1) $f(x)$ and $g(x)$ are continuously differentiable for all x;

(2) $g(-x) = -g(x)$ for all x (i.e., $g(x)$ is an odd function);

(3) $g(x) > 0$ for all $x > 0$;

(4) $f(-x)$=$f(x)$ for all x (i.e., $f(x)$ is an even function);

(5) The odd function

$$F(x) = \int_0^x f(u)du$$

has exactly one positive zero at $x = a$, is negative for $0 < x < a$, is positive and nondecreasing for $x > a$, and

$$F(x) \to \infty \text{ as } x \to \infty$$

Then the system has a unique, stable limit cycle surrounding the origin in the phase plane.

Therefore, Equation (7) has a unique, stable limit cycle surrounding the origin in the phase plane. This indicates that after our patient is given treatment the patient's mood variations will oscillate within a range of x values to be determined by the parameter. To approximate the amplitude of this limit cycle we will look at the first harmonic of the Fourier Series that will represent $x(t)$, a technique also known as harmonic balance.
Let

$$x(t) = A\sin(\Omega t) \tag{8}$$

Substituting Equation (8) into Equation (7) we obtain

$$\begin{aligned} -A\Omega^2\sin(\Omega t) - \frac{1}{4}A^3\Omega\beta\cos(\Omega t) + \frac{1}{4}A^3\Omega\beta\cos(3\Omega t) \\ -A\Omega\alpha\cos(\Omega t) + \omega^2 A\sin(\Omega t) = 0 \end{aligned} \tag{9}$$

We collect all the terms with $\sin(\Omega t)$ and set

$$\left(-A\Omega^2 + \omega^2 A\right)\sin(\Omega t) = 0 \tag{10}$$

Solving Equation (10) for Ω we obtain

$$\Omega = \pm\omega. \tag{11}$$

We then collect all the terms with $\cos(\Omega t)$ and set

$$\left(\frac{1}{4}A^3\Omega\beta - A\Omega\alpha\right)\cos(\Omega t) = 0. \tag{12}$$

Thus,

$$\text{A=0}, \ \pm 2\sqrt{\frac{\alpha}{-\beta}} \tag{13}$$

The amplitude $A = 2\sqrt{\frac{\alpha}{-\beta}}$ in Equation (13) is an approximation of the true amplitude.

5 Two Bipolar II Patients Interacting

Now that we have examined the situation of an individual undergoing treatment, we will look at the interactions between two bipolar II patients. We are interested in modeling the possible effect two patients will have on each other while undergoing treatment. Consider our two individuals, each separately given by Equation 7 in polar coordinates as such

$$\begin{aligned}
\dot{r_1} &= -\beta r_1^3(\cos\theta_1)^2(\sin\theta_1)^2 \\
&\quad +r_1\sin\theta_1\left[\alpha\sin(\theta_1)+\cos(\theta_1)-\omega^2\cos(\theta_1)\right]+K_1(r_2-r_1) && (14)\\
\dot{\theta_1} &= \alpha\sin(\theta_1)\cos(\theta_1)-(\sin\theta_1)^2- \\
&\quad \omega^2(cos\theta_1)^2-\beta r_1^2(\cos\theta_1)^3\sin(\theta_1)+K_2(\theta_2-\theta_1) && (15)\\
\dot{r_2} &= -\beta r_2^3\cos{\theta_2}^2(\sin\theta_2)^2 \\
&\quad +r_2\sin\theta_2\left[\alpha\sin(\theta_2)+\cos(\theta_2)-\omega^2\cos(\theta_1)\right]+K_3(r_1-r_2) && (16)\\
\dot{\theta_2} &= \alpha\sin(\theta_2)\cos(\theta_2)-(\sin\theta_2)^2- \\
&\quad \omega^2(cos\theta_2)^2-\beta r_2^2(\cos\theta_2)^3\sin(\theta_2)+K_4(\theta_1-\theta_2), && (17)
\end{aligned}$$

where K_1, K_2, K_3, K_4 represent the coupling coefficients.

We use polar coordinates in order to facilitate the adding of coupling terms which will represent interaction between two patients. We assume that the phase difference will only affect the phase terms and the amplitude difference will only affect the amplitude terms. We propose that the purpose of these coupling functions is to average out, between the 2 individuals, the difference in the magnitude of the mood variations and the difference in the rate at which the episodes are occuring. One important detail to note is that in Equations (15) and (17) we use coupling terms of θ without any limitation on the phase angle. That is, in this system, if the difference in θ_1 and θ_2 were to increase beyond 2π then our model would be invalid. This consideration is unnecessary, however, when we convert back into rectangular coordinates, because the coupling terms remain bounded due to our terms of $\sqrt{x_i^2 + \dot{x_i}^2}$ and $\arctan\left(\frac{\dot{x}}{x}\right)$. For the program we use the numerical integration will only return values between $-\pi/2$ and $\pi/2$ for arctan. Even though the arctangents in our rectangular equations create a discontinuous vector field, we feel that the behavior seen near the discontinuities still models the biology seen in cases where 2 patients with bipolar disorder are interacting (fluctuation near in-phase and out-of-phase modes). When we couple two similar individuals, they have the same values of α, ω, and β, then the four dimensional system of equations that involves $\dot{x_1}$, $\dot{y_1}$, $\dot{x_2}$, and $\dot{y_2}$ are

$$\begin{aligned}
\dot{x_1} &= y_1 - K_2 y_1\left[\arctan\left(\frac{y_2}{x_2}\right) - \arctan\left(\frac{y_1}{x_1}\right)\right] \\
&\quad + K_1 x_1\left(\frac{\sqrt{x_2^2 + y_2^2}}{\sqrt{x_1^2 + y_1^2}}\right) - K_1 x_1 \qquad (18) \\
\dot{y_1} &= \beta_1 x_1^2 y_1 + \alpha_1 y_1 - \omega_1^2 x_1 + K_2 x_1\left[\arctan\left(\frac{y_2}{x_2}\right) - \arctan\left(\frac{y_1}{x_1}\right)\right] \\
&\quad - K_1 y_1 + K_1 y_1\left(\frac{\sqrt{x_2^2 + y_2^2}}{\sqrt{x_1^2 + y_1^2}}\right) \qquad (19) \\
\dot{x_2} &= y_2 - K_4 y_2\left[\arctan\left(\frac{y_1}{x_1}\right) - \arctan\left(\frac{y_2}{x_2}\right)\right] \\
&\quad + K_3 x_2\left(\frac{\sqrt{x_1^2 + y_1^2}}{\sqrt{x_2^2 + y_2^2}}\right) - K_3 x_2 \qquad (20) \\
\dot{y_2} &= \beta_2 x_2^2 y_2 + \alpha_2 y_2 - \omega_2^2 x_2 + K_4 x_2\left[\arctan\left(\frac{y_1}{x_1}\right) - \arctan\left(\frac{y_2}{x_2}\right)\right] \\
&\quad - K_3 y_2 + K_3 y_2\left(\frac{\sqrt{x_1^2 + y_1^2}}{\sqrt{x_2^2 + y_2^2}}\right). \qquad (21)
\end{aligned}$$

5.1 Qualitative Behavior for the Simplest Model of the Coupled System

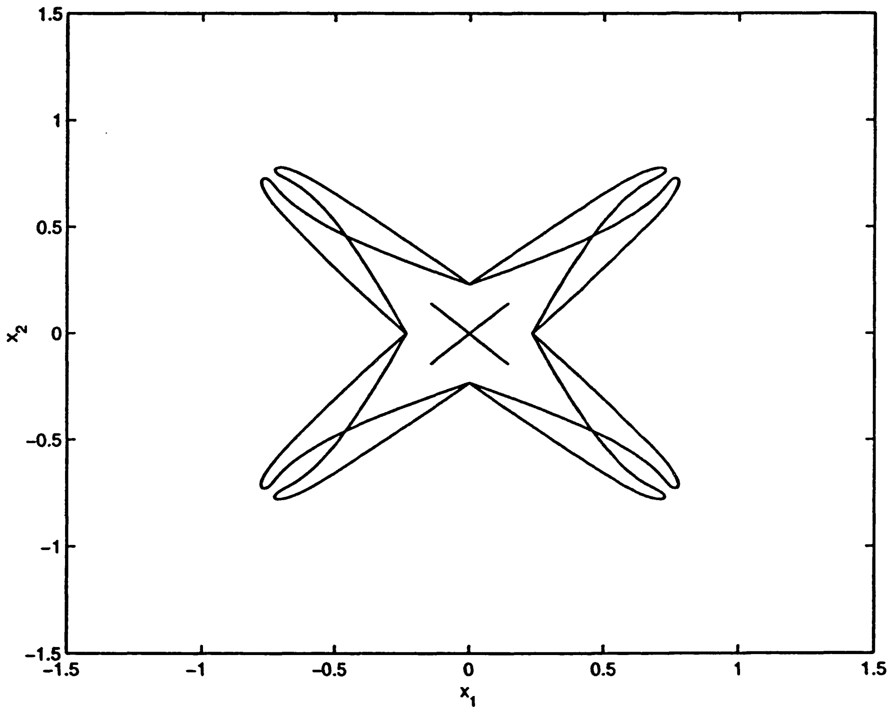


Figure 5.1: Simplest case periodic orbits

We consider the interaction of two patients in order to determine any joint behavioral patterns. For our system of coupled equations, we chose, for our simplest case,

$$\beta_1 = \beta_2 = 100 \tag{22}$$

$$\alpha_1 = \alpha_2 = \frac{1}{2} \tag{23}$$

$$\omega_1 = \omega_2 = 20 \tag{24}$$

$$K_1 = K_2 = K_3 = K_4 = 1. \tag{25}$$

The important qualities of this particular system are that the patients are the same in terms of their oscillations and in terms of their individual treatment functions. Something else to note about the system is that their interactions are the same, Patient 1 and Patient 2 affect each other equally. When integrated numerically we find 4 predominant orbits for small values of x's and y's. Two important solutions are the in-phase mode and out-of-phase mode, which will be analyzed later. There are also 2 similar 4-point periodic oscillations. The patients go from near in-phase to near out-of-phase and then back again. These solutions appear stable because a solution will tend toward these 4-point oscillations if the initial conditions are outside the relatively small basin of attraction for the in-phase and out-of-phase modes and far enough away from the equilibria, (see Figure 5.2). The initial conditions used for our figures are as follows:

4-point curve 1: $x_1 = -0.291$, $y_1 = -7.68$, $x_2 = 0$, and $y_2 = -9.5$.

4-point curve 2: $x_1 = 0.743$, $y_1 = 0.743$, $x_2 = 0.7115$, and $y_2 = -7.65$.

In-phase curve: $x_1 = 0.1$, $y_1 = 0$, $x_2 = 0.1$, and $y_2 = 0$.

Out-of-phase curve: $x_1 = 0.1$, $y_1 = 0$, $x_2 = -0.1$, and $y_2 = 0$.

We also looked for equilibria in our system. We know there must be some unstable equilibrium inside the in-phase and out-of-phase modes [10]. Using DSTool, we observed numerically a saddle point at the origin [6]. It also calculated 4 additional saddle points and 8 sink points, (see Figure 5.2).

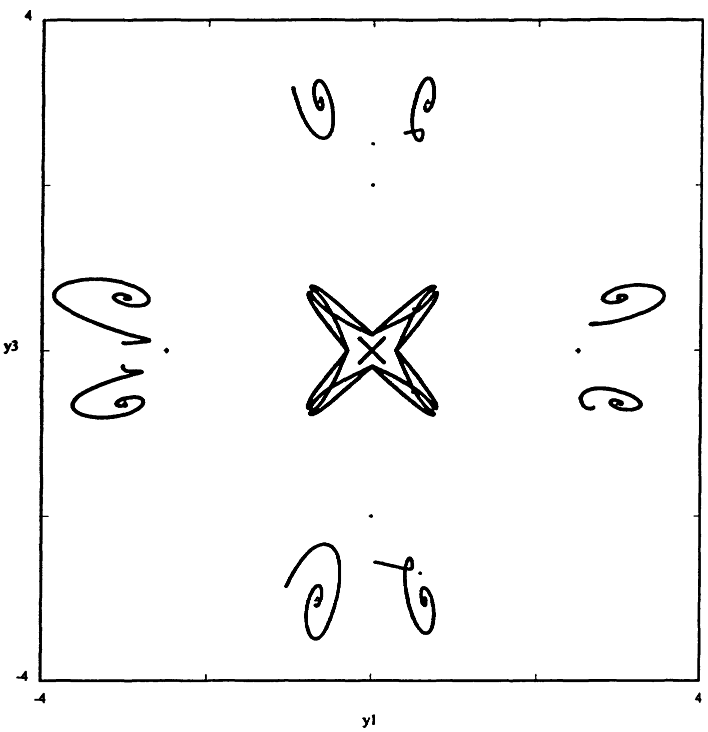


Figure 5.2: Simplest case periodic orbits with equilibrium points

These equilibrium points cause our model to have very interesting mathematical behavior, but we can say very little about the biological applications, so we must leave mathematical analysis to later work. Due to the symmetry in our system and the presence of 4 other saddle-sink pairs, we believe that there are 4 other saddle points in our system, even though we have not yet succeeded in finding them.

5.2 In-Phase/Out-of-Phase Mode

To examine the in-phase mode, let $x_1 = x_2$, and $y_1 = y_2$. Then our model simplifies to a two dimensional system of either x_1 vs y_1 or x_2 vs y_2, depending on which way we take our substitution. Without loss of generality, we consider x_1 vs y_1. We can then apply Liénard's theorem to see that the in-phase mode exists and is stable in the 2-dimensional invariant manifold, which sits in our 4-dimensional space. We also observed numerically that our in-phase mode appears to be stable in the 4-dimensional system. We can see that if we make our substitution for the out-of-phase mode, $x_1 = -x_2$ and $y_1 = -y_2$, then the same analysis applies and therefore the out-of-phase mode also exists and is stable within a 2-dimensional invariant manifold. Due to the other periodic motions in the system, specifically the 4-point oscillations (which occur for small values of k), the in-phase and out-of-phase modes, even though they are stable, have relatively small basins of attraction

This means that when we couple our two individuals, if they have close to similar values for x_1 vs x_2 and y_1 vs. y_2 (similar moods and rates of change) then they will tend towards remaining in-phase. This is to say that as time progresses they will both tend towards entering a hypomanic phase together and both tend towards entering a depressive episode together. Since the same argument works for the out-of-phase mode, if the two individuals are coupled at a time when their moods and rates of change are almost completely out-of-phase, then they will tend to stay out-of-phase, where one individual enters a hypomanic phase while the other is entering a depressive phase, and vice versa.

5.3 Degrading Orbits

The 4-point oscillations have some very interesting behavior. We can see that for the simplest case scenario there are definitely stable orbits. A case study we undertook was to model a specific orbit (see Figure 5.3) with initial

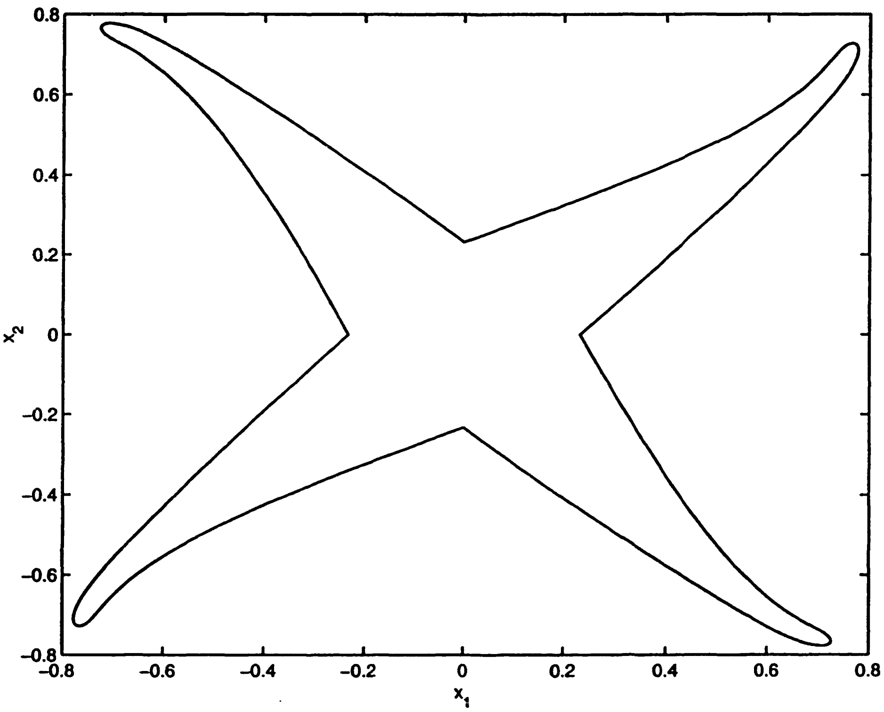


Figure 5.3: Increasing K=1 values

conditions $x_1 = 0.743$, $y_1 = 0.743$, $x_2 = 0.7115$, and $y_2 = -7.65$. We increase the amount of interaction by increasing all of the K values ranging from 2 to 6. At the end of every stable orbit, we used the last points as the new initial conditions for the next orbit (see Figures 5.4 through Figure 5.6)

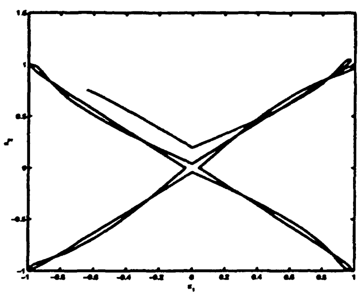
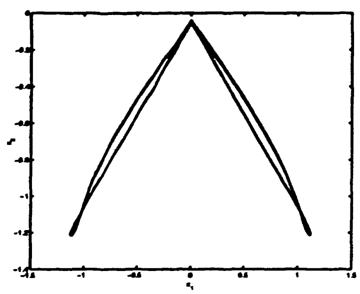


Figure 5.4: Increasing K=2



Increasing K=3

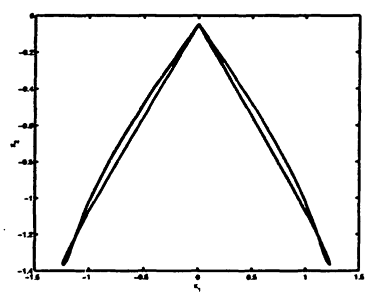
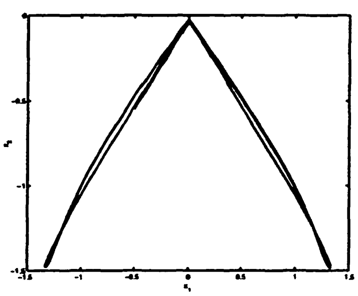


Figure 5.5: Increasing K=4



Increasing K=5

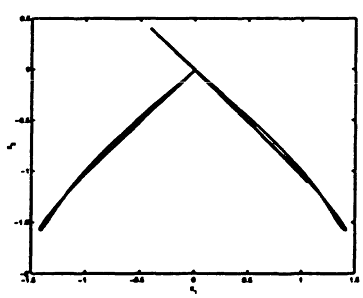
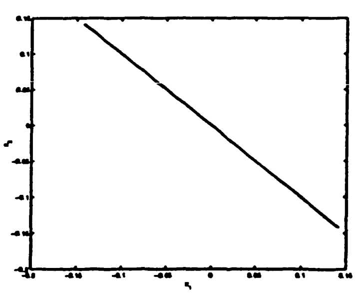


Figure 5.6: Increasing K=6



Increasing K=6 second time

It appears that the basins of attraction for the in-phase and out-of-phase modes becomes larger for larger K values. For large values of K (10 through 100) the system tends toward either the in-phase mode or out-of-phase mode. For large values of K, our initial conditions can be farther from the origin and still generate solution curves that will tend towards either the in-phase or out-of-phase modes.

5.4 Varying of Parameters

Up to this point, our two patients have been assumed to be identical (same α and β). We now vary α and β, while keeping $K_1 = K_2 = K_3 = K_4 = 1$, we see the following behavior
(see Figures 5.7 and 5.8)

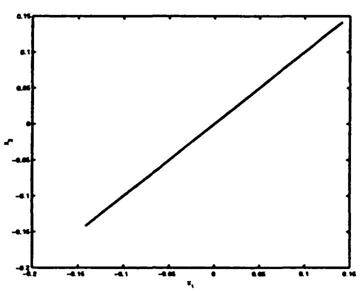
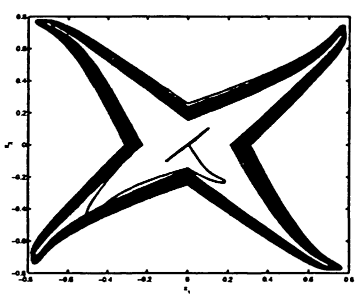


Figure 5.7: Tendency to chaos



Tendency to chaos

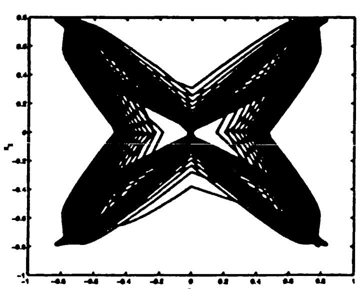
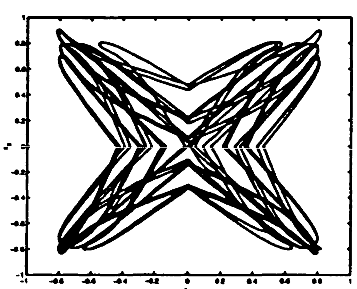


Figure 5.8: Tendency to chaos



Tendency to chaos

These figures seem to suggest that our system becomes chaotic by detuning some of our parameters.

6 Discussion

After analyzing the calculations of an untreated patient and those of a treated patient, a noticeable difference is observed. In the untreated patient, it takes 0.081 years $\approx$ 29.57 days from the time the patient enters a severe depressive episode to when the patient reaches a functional state. On the other hand, the treated patient takes 0.111 years $\approx$ 40.52 days to go from the first sign of severe depression to a reasonable functional state. Initially, it appears that the treatment is prolonging the depressive episode, but in reality the cycle is undergoing a phase shift. The phase shift only prolongs the depressive episode an additional 0.03 years $\approx$ 11 days during the initial cycle, but in return manages to reduce the amplitude of the cycle to $x_2 \approx 0.561$ where x would have exceeded 1 in the hypomanic state if left untreated. Overall, the autonomous forcing function causes a phase shift and diminishes the amplitude of the mood cycles to be within functional state (see Figure 6.1). As a result of the relatively simple nature of our two dimensional system, we can see that it is relatively easy to model a single patient with the disorder. When we couple two patients with the disorder there is a major consideration, that being the equilibria. The sink points in particular, are not biologically reasonable. We were not able to find documented cases where a patient asymptotically approached some emotional state far above the required amount to be considered bipolar. This happens in eight distinct places in our model and makes analysis for the behavior in a weakly coupled system difficult for large values of x and y. For small values of x and y, however, our coupled system seems adequate. The two patients experience periodic mood variations, and depending on what we vary, our model can achieve behavior ranging from stable oscillations, to apparently chaotic mood variations in other parameter regimes.

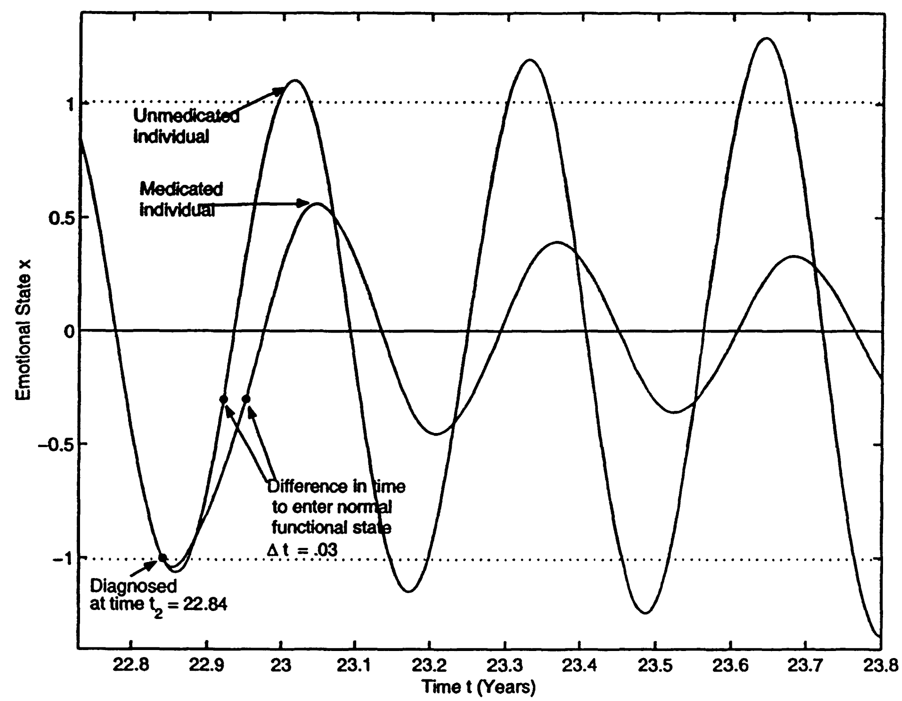


Figure 6.1: Mood variations a bipolar II patient

7 Future Work

The medications administered to bipolar II patients take days to reach therapeutic levels in the blood stream. The model can be modified by adding a time-delay function to the treatment in order to better model the delayed effect of the medication. Another way of improving the model is to do an analysis of the equilibria in the system for the simplest model with an additional search for new equilibria. By analyzing the symmetry of the system we might find whether or not more saddle points exits. The last recommendation is to analyze the bifurcations of the equilibria by varying the parameters.

If we vary several parameters we might gain insight on how these equilibria were born.

8 Acknowledgments

Special thanks to those who supported us through this study: Stephen Wirkus, Michael Stubna, Carlos Castillo-Chavez, Richard Rand, Mason Porter, Abdul-Aziz Yakubu, John Franke, Roxana Lopez-Cruz, Terry Kupers, and Dane Quinn.

This research has been partially supported by grants given by the National Science Foundation, National Security Agency, and the Sloan Foundation (through the Cornell-Sloan National Pipeline Program in the Mathematical Sciences). Substantial financial and moral support was also provided by the Office of the Provost of Cornell University, the College of Agriculture & Life Science (CALS), and the Department of Biological Statistics & Computational Biology. The authors are solely responsible for the views and opinions expressed in this research; it does not necessarily reflect the ideas and/or opinions of the funding agencies and/or Cornell University.

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Appendix A

Integration Script

```
function [t,y,te,ye,ie]=
              integration_script(tstart, tfinal, y0, val)
% [t,y,te,ye,ie]=integration_script(tstart, tfinal, y0, val)
% is the calling statement
% where tstart = initial time;      tfinal = final time;
% y0 = a vector of initial conditions (ie y0=[ x-initial;
% y-initial]);
% val= is the values of x where MatLab will note for recalling
% t-values and y-values
% Note to recall t-values and y-values use: (  te; and ye;  )
global xval
xval=val;
options = odeset('Events',@events, 'AbsTol', 1e-8, 'RelTol', 1e-8);

[t,y,te,ye,ie] = ode45(@f,[tstart tfinal],y0,options);
% -------------------------------------------------------------------
function dydt = f(t,y)
global xval
dydt = [y(2); .5*y(2)-400*y(1)-0*y(1)^2*y(2)];

% -------------------------------------------------------------------
function [value,isterminal,direction] = events(t,y)
global xval
% Locate the time when height passes through zero in a decreasing
% direction
% and stop integration.
value = [y(1)-xval, y(2)];     % detect when height = xval
isterminal = [0, 0];   % stop the integration
direction = [0, 0];   % both neg/pos direction (replace (0) with
%(-) for neg direction only
%                  and (+) for pos direction only.
%*******************************************************************
```