Liénard Oscillator Modeling of Bipolar Disorder
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Abstract
Bipolar disorder, also known as manic-depression, is a disorder in which a person has mood swings out of proportion or totally unrelated to the events in their lives. Bipolar disorder affects as many as 1 percent of the adults in the United States. We focus in particular on Bipolar II disorder, which is characterized by alternating hypomanic and depressive episodes. We model a person affected with bipolar II disorder using a Van der Pol oscillator, which is an example of a Liénard oscillator. We then generalize the Van der Pol oscillator to represent the patient after they receive medication. In this paper we analyze the size and stability of limit cycles and support this analysis with numerical simulations.

1 Introduction
There are 5 different diagnoses for bipolar disorder: bipolar I disorder, schizoaffective disorder, bipolar type, bipolar II disorder, bipolar disorder NOS (not otherwise specified), and cyclothymia [1]. We closely examine bipolar II disorder, which is characterized by alternating hypomanic and depressive episodes. Symptoms of hypomania include a decreased need for sleep, increased confidence and energy, impulsive behavior, and poor judgement. Symptoms of depression include loss of motivation, slowing of speech, increased need for sleep, and recurring thoughts of suicide [1].
Bipolar II is often misdiagnosed as either unipolar depression or a severe personality disorder. In order to be correctly diagnosed, a patient seeking treatment must give an accurate description of their past behavior. Due to the nature of the hypomanic episodes (more energy, decreased need for sleep, etc.) patients do not describe these to doctors and are therefore diagnosed with unipolar depression [1]. According to the Results of the National Depressive and Manic-Depressive Association 2000 survey of people with bipolar disorder, over one third of those that responded sought professional help within a year of onset of symptoms [2]. However, it took up to 10 years and 4 physicians for some patients to be correctly diagnosed [2].

This paper builds on reference [3], whose authors modeled a bipolar individual with a negatively damped oscillator (1), and a medicated patient with a Van der Pol oscillator (2) [3]. In their paper the authors analyzed calculations of (1) and (2) and observed differences in the days it took to reach a functional state, and also analyzed two bipolar patients interacting.

\[
\ddot{x} - \alpha \dot{x} + \omega^2 x = 0 \quad (1)
\]

In this paper we will begin with the Van der Pol oscillator [4] to represent a patient, then modify the oscillator to show the effect of the medication on the patient. The Van der Pol oscillator is given by:

\[
\ddot{x} + \omega^2 x - \epsilon(\alpha - x^2)\dot{x} = 0 \quad (2)
\]

where \(\omega\) is the frequency of the oscillator when \(\epsilon = 0\), \(x\) is the emotional state, \(\alpha\) is the damping coefficient, \(\epsilon\) determines the departure linearity (more linear as \(\epsilon -> 0\)), and \(\dot{x}\) is the rate of mood change. Everyone one has mood swings, so we characterize moods with this oscillator. Bipolar Patients have an amplitude of emotional state above a 'normal' level which is determined arbitrarily. We then use a Van der Pol oscillator in the form of

\[
\ddot{x} + \omega^2 x - \alpha \dot{x} - \beta x^2 \dot{x} = g(x) \quad (3)
\]

were \(g(x)\) represents the medication given to the patient:

\[
g(x) = \gamma x^4 \dot{x} + \delta x^2 \dot{x}
\]

and use the method of averaging [5], to determine criteria for 'medication' to affect a patient desirably. We only used \(\delta = 0\) in our representations, but
one can apply a medication of this generalized form to change the coefficient \( \beta \) by applying medication.

### 2 Untreated Patient

We model an untreated bipolar II patient using a Van der Pol oscillator (2).

The patient (modeled by the function) has mood swings that oscillate between two points, forming a limit cycle. Depending on the parameters in (2) we can determine the amplitude and shape of the limit cycles. We can evaluate the amplitude and stability of the limit cycle using the method of averaging. Taking into account that everyone has mood swings we can choose an arbitrary 'normal' range for the emotional state \( x \). We will choose .1 to be the threshold of a hypomanic episode, and -.1 for a depressive episode. A healthy person can be modeled by (2), provided the limit cycle has an amplitude less than .1. For our model, we use \( \alpha = .1 \), \( \beta = -100 \), and \( \omega = 5 \). This creates the graph shown in Figure 1, producing a limit cycle with amplitude .067, which is within our normal range. Figure 1 thus represents a healthy person. The figure represents someone still oscillating between higher and lower states, just within our given boundaries. Figure 2 is a graph of the limit cycle. Using this information we adjust our parameters to form a model for an untreated patient. Figure 3 and Figure 4 represent an untreated bipolar II patient. The parameters here are \( \alpha = .36 \), \( \beta = -100 \), and \( \omega = 5 \).

### 3 Treated Patient

Starting with the Van der Pol oscillator caricature of the untreated patient, we apply a forcing function \( g(x) \) to represent medication. We now have the following equation for a medicated patient:

\[
\ddot{x} + \omega x^2 - \alpha \dot{x} - \beta x^2 \dot{x} = \gamma x^4 \dot{x} + \delta x^2 \dot{x}
\]

(4)

The medication function \( g(x) \), can take several possible forms. Medications used to treat bipolar disorder include the mood stabilizer lithium and anticonvulsants such as, divalproex sodium, and carbamazepine [1]. Finding
Figure 1: Time series of the behavior of a healthy person, parameters used: $\alpha = .1$, $\beta = -100$, and $\omega = 5$, creating a limit cycle with amplitude of .067, which is within the healthy range.

Figure 2: Limit cycle corresponding to Figure 1
Figure 3: Time series representing the behavior of an untreated patient. The parameters are $\alpha = .36$, $\beta = -100$, and $\omega = 5$, creating a limit cycle with an amplitude of .12, which is above 'normal'.

Figure 4: Limit cycle corresponding to Figure 3
the correct way to treat a given patient may take as many as 10 to 15 trials on different medications. The most comprehensive treatment, however, involves medication treatment and psychotherapy [1].

We use (4) to represent a treated bipolar II patient. The treated patient will have an unstable, larger limit cycle, greater than .1 (our threshold for ‘normal’ behavior), that changes to a stable smaller limit cycle. If we chose $\alpha = .1, \beta = -100, \gamma = 5000$, we get the plots in Figures 5 and 6.

By using the method of averaging, we obtain information regarding the limit cycles of equation (4), which is of the form:

$$\frac{d^2x}{dt^2} + \omega^2 x = \epsilon F \left( x, \frac{dx}{dt}, t \right).$$

We will then seek a solution in the form:

$$x = a(t) \cos(\omega t + \psi(t))$$

$$\frac{dx}{dt} = -a(t)\omega \sin(\omega t + \psi(t))$$

When $\epsilon=0$, as is sensible for bipolar II disorder, limit cycles are nearly circular, so the ansatz (6) is reasonable. We can then determine dynamical equations for $a(t)$, the amplitude of the limit cycle, and $\psi(t)$, the phase shift of the limit cycle [5]. By differentiating (6) and holding (7) true, and differentiating (7) and substituting into (5) we get

$$-\frac{da}{dt} \sin(t + \psi) - a \frac{d\psi}{dt} \cos(t + \psi) = \epsilon F(a \cos(t + \psi), -a \sin(t + \psi), t)$$

We solve for $d\psi/dt$ and $da/dt$. We then make approximate for $a$ and $\psi$ in the following form

$$a = \bar{a} + \epsilon \omega_1(\bar{a}, \bar{\psi}, t) + O(\epsilon^2)$$

$$\psi = \bar{\psi} + \epsilon \omega_2(\bar{a}, \bar{\psi}, t) + O(\epsilon^2)$$

Where $\bar{a}$ and $\bar{\psi}$ are the averaged values and $\omega_1$ and $\omega_2$ are chosen to remove all the $O(\epsilon)$ terms [5]. The resulting equation for $a(t)$ gives the amplitude of the limit cycles for the original equation. After averaging the system of equations we get
\[
\frac{d\tilde{\psi}}{dt} = 0; \quad \frac{d\tilde{a}}{dt} = \tilde{a} \left( -\alpha - \frac{\beta \tilde{a}^2}{4} - \frac{\gamma \tilde{a}^4}{8} \right) \tag{11}
\]

where the condition \(d\tilde{a}/dt = 0\) determines the radii of the limit cycles.

In order to solve for \(\tilde{a}^2\), we use the quadratic formula. This yields conditions that must be met in order to have zero, one, or two limit cycles. When we solve for \(\tilde{a}\), we obtain positive and negative solutions but the negative answer will not be relevant, as one cannot have a negative radius. The solution for \(\tilde{a}\) is:

\[
\tilde{a}^2 = \frac{\beta \pm 4\sqrt{\frac{\beta^2}{16} - \frac{\alpha^2}{2}}}{-\gamma} \tag{12}
\]

Once we find the values of the limit cycles we compute the second derivative to determine their stability:

\[
\frac{d^2\tilde{a}}{dt^2} = -\frac{1}{2} \left( \alpha + \frac{3\beta \tilde{a}^2}{4} + \frac{5\gamma \tilde{a}^4}{8} \right). \tag{13}
\]

We now evaluate these equations to obtain conditions based on the values of \(\alpha, \beta,\) and \(\gamma\). We note that there will always be an equilibrium at \(\tilde{a} = 0\). Our conditions for the limit cycles and their stability are:

1. One limit cycle:
   - When the \(\beta^2/16 - \alpha \gamma/2 = 0\), \(\beta/\gamma\) is positive. We obtain the conditions: \(\beta/\gamma > 0\) and \(\beta^2 = 8\alpha \gamma\). There is a bifurcation at this point and the stability cannot be determined by this method.
   - When \(\beta^2/16 - \alpha \gamma/2 = 0\) is large enough for the positive root in (12), and small enough for negative root to yield one negative answer. We obtain the condition: \(0 < -\alpha \gamma\). Such a limit cycle is always unstable.
   - When one root is zero which occurs when \(\alpha = 0\), there will always be one limit cycle. Then \(d^2\tilde{a}/dt^2 = -2\beta^2/4\gamma\) so the limit cycle is stable if and only if \(\gamma > 0\).

2. Two limit cycles: We get one condition: \(\beta^2 > 8\alpha \gamma > 0\). The smaller limit cycle is stable if and only if \(2\beta^2 > 8\gamma\alpha\) is satisfied. The larger limit cycle always has the opposite stability as the smaller one. The
Figure 5: Treated Patient, the parameters are $\alpha = 0.1, \beta = -100$, and $\gamma = 5000$, which yields a transition between a limit cycle with amplitude greater than 0.1, to a stable limit cycle with amplitude less than 0.1.

Equilibrium at $(0,0)$ generically has the same stability as the larger limit cycle. For example, in Figures 5 and 6 we used the parameters $\alpha = 0.1, \beta = -100$, and $\gamma = 5000$. This gives us the condition $10000 > 4000 > 0$, therefore we know we have two limit cycles, and the stability of the smaller is stable because $20000 > 4000$.

3. Zero limit cycles will be produced when none of the above conditions are met.

The patient represented in Figure 5 begins to receive treatment at about the age of 5 to 10 years the patient starts to receive treatment. The age of onset of bipolar disorder is most often between 10 and 29 years, but bipolar disorder can start in early childhood [1]. There is currently not a dearth of data concerning bipolar disorder, one of the reasons for this is a lack of agreement on a well suited trial design. Therefore, bipolar disorder is a very difficult to study, using clinical trials [6].
4 Conclusion

After averaging (2) we established criteria for the existence of zero, one, or two limit cycles. We also calculated their amplitudes and the stability. We use this information to model a treated and untreated bipolar II individual.

5 Future Work

As modeled in this paper the medication takes up to 10 years to start working. Ideally this model should be adjusted to a more reasonable time frame. Work can also be done to add more biology to better define the parameters $\alpha$, $\beta$, and $\gamma$ and develop a better, more complicated differential equation model. Another aspect for future work is coupling of bipolar disorder individuals to sleep-wake cycles, as clinical doctors know this to be important. An appropriate model to study this is coupled Van der Pol-like oscillators. Work can also be done to represent a medication function in the form $g(x,t)$ to have an explicit time dependent forcing.
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References


