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Equilibrium-Based Bipolar Neurological Modeling

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Abstract—**This work introduces an equilibrium-based dynamic model for the characterization, classification, and diagnostic analysis of bipolar disorder, a psychiatric syndrome with manic and depressive phases. The new model extends the traditional spectrum model of mood states from a static and closed world to a dynamic open-world of equilibria with a bipolar universal modus ponens (BUMP). The utility of the new model is illustrated in diagnostic analysis of depression and clinical psychopharmacology of different phases of this disorder.**

***Keywords*: YinYang Bipolar Equilibrium; Depression and Bipolar Disorder; Bipolar Neurological Modeling; Bipolar Diagnostic Analysis**

I. INTRODUCTION

According to the NIMH (National Institute of Mental Health) more than 20 million children and adults are affected by major depression or bipolar disorder in the US, and depression has been shown to be a leading cause of disability world wide. Understanding the differences in how people respond to medications is one of the most important goals of drug therapy. Progress in this area, especially for psychiatric medications, has been slow because of the complexity of the disorders. Mathematical modeling and analysis of such neuropsychiatric disorders undoubtedly bear great significance in bioengineering and clinical psychopharmacology.

Traditionally bipolar disorder is characterized and classified based on a one-dimensional spectrum as depicted in Fig. 1. The spectrum has a number disadvantages in the characterization and classification of depression and bipolar

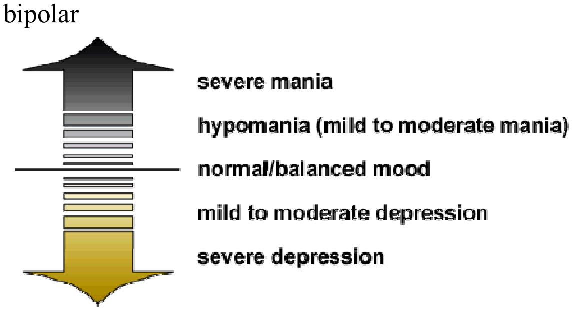

Fig. 1. Mood states in bipolar disorder [1]

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disorders including: (1) it does not support bipolar coexistence for bipolar logical reasoning; (2) As a static model it does not support energy and stability analysis; (3) It can not show time-variant series of symptoms.

This work presents a YinYang bipolar neurophysiological model for depression and bipolar mania with illustrations in bipolar diagnostic analysis and clinical psychophar-macology. Secion II introduces a mathematical basis. Section III illustrates bipolar neurophysiological modeling with an example. Section IV presents a unified outcome model. Section V draws a few conclusions.

II. YinYang Bipolar Logic

With YinYang bipolarity the two opposing sides of an equilibrium (including quasi- or non-equilibrium) are considered negative and positive elements that lead to the concepts of bipolar logic and sets [8-14]. An NP bipolar poset $(B,\geq\geq)$ [14] is defined as a set of bipolar bindings $\{(x,y)\}$ or bipolar equilibria with a negative pole and a positive pole, where x is negative and y is positive, and $\geq\geq$ is a bipolar partial order relation and for $\forall(x,y),(u,v)\in B$ we have

$$(x,y)\geq\geq(u,v), \text{ iff } |x|\geq|u| \text{ and } y\geq v, \quad (1)$$

where $|x|$ stands for "the absolute value of x."

Equations (2)-(6) define a number of bipolar logical functions as neurophysiological operators.

$$blub((x,y),(u,v)) \equiv (x,y)\oplus(u,v)\equiv(-(|x|\vee|u|),|y|\vee|v|); \quad (2)$$

$$bglb((x,y),(u,v)) \equiv (x,y)\&(u,v)\equiv(-(|x|\wedge|u|),|y|\wedge|v|)); \quad (3)$$

$$cglb((x,y),(u,v))\equiv (x,y) \otimes (u,v)$$
$$\equiv (-(|x|\wedge|v|\vee|y|\wedge|u|), (|x|\wedge|u|\vee|y|\wedge|v|)). \quad (4)$$

In the above definitions, $\oplus$ is a bipolar disjunctive; & is a bipolar linear conjunctive, and $\otimes$ is a cross-pole non-linear conjunctive.

A bipolar lattice B (crisp or fuzzy) is **bounded** if it has both a unique minimal element denoted (0,0) and a unique maximal element denoted (-1,1) (Note: (0,0)–bipolar false or non-existent; (-1,1)–bipolar true or full equilibrium). A bounded bipolar lattice B is **complemented** if, $\forall(x,y)\in B$, we have the **bipolar complement** $\neg(x,y) \in B$.

$$\neg(x,y) \equiv (\neg x,\neg y) \equiv (-1-x,1-y); \quad (5a)$$

Note that bipolar complement induces bipolar implication. Thus, a bounded and complemented bipolar lattice B (crisp or fuzzy) can be denoted as $(B,\equiv,\oplus, \otimes, \&, -, \neg,\rightarrow)$ with $-$ and $\rightarrow$ defined in the following:

Implication:

$$(x,y)\rightarrow(u,v) \equiv (x\rightarrow u,y\rightarrow v) \equiv (\neg x\vee u, \neg y\vee v); \quad (5b)$$

Negation:

$$-(x,y) \equiv (-1,0)\otimes(x,y)=(-y,-x); \quad (5c)$$

where the negation operator is derived from ⊗.

Further, we define the negation of ⊗ as $\otimes^-$ and the negation of ∅ as $\varnothing^-$.

$$\text{cglb}^-((x,y),(u,v)) \equiv (x,y) \otimes^- (u,v) \equiv -(x,y) \otimes (u,v). \quad (6a)$$

$$\text{club}^-((x,y),(u,v)) \equiv (x,y) \varnothing^- (u,v) \equiv -(x,y) \varnothing (u,v). \quad (6b)$$

Fig. 2 shows the hasse diagrams of two bipolar lattices; and Fig. 3 lists a number of bipolar laws.

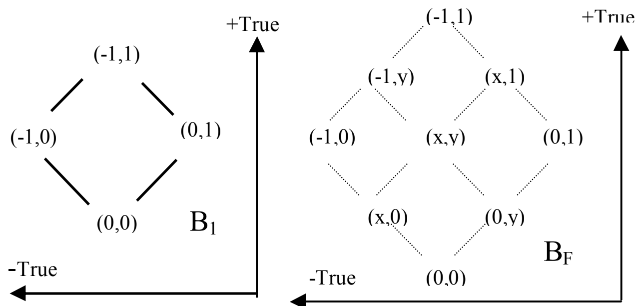

Fig. 2 Hasse diagrams of $B_1=\{-1,0\}\times\{0,1\}$ and $B_F=[-1,0]\times[0,1]$

Excluded Middle	$(x,y)\oplus\neg(x,y)\equiv(-1,1),\ \forall(x,y)\in B_1$.	
Non-Contradiction	$\neg((x,y)\&\neg(x,y))\equiv(-1,1),\ \forall(x,y)\in B_1$.	
Linear Bipolar DeMorgan's Laws on B_1 and B_F	$\neg((a,b)\&(c,d))\equiv \neg(a,b)\oplus\neg(c,d)$	$\neg((a,b)\oplus(c,d))\equiv \neg(a,b)\&\neg(c,d)$
Non-Linear Bipolar DeMorgan's Laws on B_1 and B_F	$\neg((a,b)\otimes(c,d))\equiv \neg(a,b)\varnothing\neg(c,d)$	$\neg((a,b)\varnothing(c,d))\equiv \neg(a,b)\otimes\neg(c,d)$
	$\neg((a,b)\otimes^-(c,d))\equiv \neg(a,b)\varnothing^-\neg(c,d)$	$\neg((a,b)\varnothing^-(c,d))\equiv \neg(a,b)\otimes^-\neg(c,d)$

Fig. 3 Bipolar Equilibrium Laws [16]

III. BIPOLAR NEUROPHYSIOLOGICAL MODELING

Based on the notion of bipolar lattice we have the notion of bipolar L-sets [14]. A **bipolar L-set $B=(B^-,B^+)$ in a bipolar set X over to a bipolar lattice B_L** is a bipolar equilibrium function (including quasi- or non-equilibrium [14] through this work) or variable or mapping $B{:}X\rightarrow B_L$. If B_L is crisp we call B a **bipolar L-crisp set**; if B_L is fuzzy we call B a **bipolar L-fuzzy set**. Bipolar L-sets polarize Boolean logic [2] and L-fuzzy sets [3,6]. Based on bipolar L-sets classical modus ponens has been extended to a YinYang bipolar universal modus ponens (BUMP) [13,14] (Fig. 4).

Fig. 5 shows the 2-D space of B_F [15] after converting it to the 4th quadrant following the convention of graphical user interface (GUI) design. The (0,0) corner region can be best described as "Negative Small and Positive Small" (NS,PS); the (-1,1) corner region can be best described as "Negative Large and Positive Large" (NL,PL); the (-1,0) corner region can be best described as "Negative Large and Positive Small" (NL,PS); the (0,1) corner region can be best described as "Negative Small and Positive Large" (NS,PL); the center (-0.5,+0.5) can be best described as "Negative Medium and Positive Medium" (NM,PM); where [NL,NM,NS,0] × [0,PS,PM,PL] form a bipolar linguistic fuzzy lattice. Any bipolar threshold α, for instance, (-0.6, +0.35), divides the 2-D space into four regions. Each bipolar value in the figure can be fuzzified with a bipolar linguistic fuzzy sets that generalize Zadeh's extension principle from [0,1] to B_F [15]. For instance, (-0.6,+0.35) can be described as (NL(0.2)-NM(0.8), PS(0.3)-PM(0.7)) as in Fig. 5.

In Fig. 5, the (0,1) corner characterizes symptoms of **bipolar mania (I)**. The (-1,0) corner characterizes symptoms of **bipolar depression (II)**. The vacillation amplitude and frequency with respect to the (0,0) — (-1,1) diagonal characterizes **cyclothymic disorder (III).** (-1,1) is the healthy equilibrium state (or **mental balance**). (0,0) is the zero energy or cease-to-exist state. (Note: **Mixed states** are not discussed in this work and addressed in a future paper.)

Bipolar lattices, L-sets, and BUMP generalized unipolar cognition to YinYang bipolar cognition that have a wide range of potential applications including bipolar neurological modeling, diagnostic analysis, and data mining.

With the bipolar approach, a psychopathologic symptom set, a drug set, or a treatment set can all be bipolar L-sets over B_F, and the outcome of a treatment can be dynamically modeled. We illustrate the use of BUMP in bipolar neurological modeling with the following sentential facts and rules:

Facts: *"Negative medication provides a negative trigger to un-excite the nervous system of a bipolar disorder patient; positive medication provides a positive trigger to un-depress the nervous system."*

"Patient A is a child with depression located at (-0.9, 0) and became manic (0, 0.9) after taking pediatric antidepressant M with strength (0,0.9)."

$$((\phi^-,\phi^+) * (\psi^-,\psi^+))$$
$$[((\phi^-,\phi^+)\rightarrow(\varphi^-,\varphi^+)),\ ((\psi^-,\psi^+)\rightarrow(\chi^-,\chi^+))]$$
$$\overline{\rightarrow((\varphi^-,\varphi^+) * (\chi^-,\chi^+))}$$

where ∗ can be bound to &, ⊕, ⊗,∅,$\otimes^-$, and $\varnothing^-$ or any applicable bipolar neurophysiological operators

Fig. 4 BUMP [14,16]

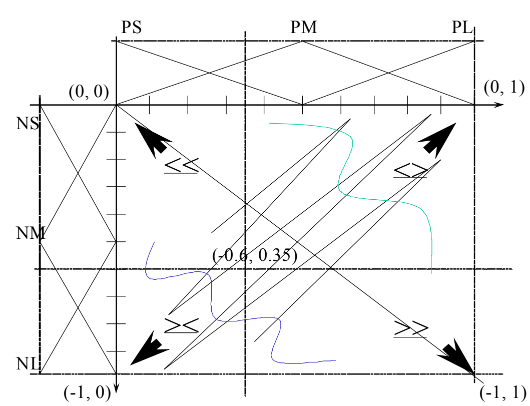

Fig. 5 The metal square B_F = [-1,0]×[0,1]

Neurological questions: *"For patient A, which neurological function (balaner ⊕, oscillator ∅, oscillator ⊗, and/or minimizer &) is working or did work with the medication?"; "Which function is not working or did not work?"*

The above question can be answered with bipolar inference using BUMP with bipolar L-crisp sets, where ij does not make a difference for $\&_i$, $\otimes_{ij}$, $\oplus_i$, or $\varnothing_{ij}$. If bipolar L-fuzzy sets are used, different ij will lead to different granularities [16]. In any case, bipolar fuzzy T-norms and T-co-norms provide a granular mathematical basis for open-world dynamic reasoning with BUMP [16].

Let p be any bipolar disorder patient and let $(\varphi^-,\varphi^+)(p)$ = (negative-trigger, positive-trigger)(p) that maps p to B_F; let $(\phi^-,\phi^+)(p)$ = (sad-mood, happy-mood)(p) that maps p to B_F. We have $\forall p$, $(\varphi^-,\varphi^+)(p)\rightarrow(\phi^-,\phi^+)(p)$ which is a bipolar knowledge fusion of the sentential rules. We then can represent the sentential facts as

$(\psi^-,\psi^+)(A)$ = (self-negation, self-assertion)(A) = (-0.9,0) and $(\varphi^-,\varphi^+)(M) = (0,0.9)$ ((Note: (-0.9,0) indicates depression and (0,0.9) indicates antidepressant medication as a positive trigger).

Since we have $\forall p\ [(\varphi^-,\varphi^+)(p) \rightarrow(\phi^-,\phi^+)(p)]$ and $[(\psi^-,\psi^+)(p) \rightarrow (\psi^-,\psi^+)(p)]$, using BUMP for patient A we have

$[(\psi^-,\psi^+)(A) \oplus_\vee (\varphi^-,\varphi^+)(M)=(-0.9,0) \oplus_\vee (0,0.9)(A)]$
$\rightarrow[(\psi^-,\psi^+)\oplus_\vee (\phi^-,\phi^+)(A)=(-0.9,0) \oplus_\vee (0,0.9)(A)=(-0.9,0.9)]$;

$[(\psi^-,\psi^+)(A)\varnothing_{11}(\varphi^-,\varphi^+)(M) =(-0.9,0)\varnothing_{11} (0,0.9)(A)]$
$\rightarrow[(\psi^-,\psi^+)\varnothing_{11}(\phi^-,\phi^+) (A)=(-0.9,0)\varnothing_{11} (0,0.9)(A)=(0,0.9)]$.

$[(\psi^-,\psi^+)(A) \&_\wedge (\varphi^-,\varphi^+)(M) = (-0.9,0) \&_\wedge (0,0.9)(A)]$
$\rightarrow[(\psi^-,\psi^+)\&_\wedge (\phi^-,\phi^+) (A)= (-0.9,0) \&_\wedge (0,0.9)(A) = (0,0)]$;

$[(\psi^-,\psi^+)(A)\otimes_{11} (\varphi^-,\varphi^+)(M) =(-0.9,0)\otimes_{11} (0,0.9) (A)]$
$\rightarrow[(\psi^-,\psi^+)\otimes_{11} (\phi^-,\phi^+) (A)= (-0.9,0)\otimes_{11}(0,0.9) (A)= (-0.9,0)$.

The four implications for A and medication M are clear and sound. The oscillator $\varnothing_{11}$ (same as $\otimes^-_{11}$ in this particular case) worked or is working because A became manic (0,0.9) after positive medication M (0,0.9). Similarly, if the mania is (0, 0.81) after the same treatment, it can be determined that $\varnothing_{12}$ worked or is working.

In another case *"Patient B has depression (-0.9, 0) and became suicidal after taking pediatric antidepressant M (0,0.9)."*

First, suicide can be diagnosed as deep depression characterized as (-1,0). Then we can determine the following compound effect:

$$(\psi^-,\psi^+)(A) \oplus_\Delta [(\psi^-,\psi^+)(A) \otimes_{ij} (\varphi^-,\varphi^+)(M)]$$
$$= (-0.9,0)\oplus_\Delta [(-0.9,0) \otimes_{ij} (0, 0.9)]$$
$$= (-0.9,0) \oplus_\Delta (x,0)$$
$$= (-1,0)$$

(Note: $(x,0)\geq\geq[(-0.9,0) \otimes_{13} (0, 0.9)]=(-0.8,0)$.)

It should be remarked that the fuzzy norm-based approach provides more granularities than a crisp approach and leads to a more robust answer with a compound effect. For instance, if we use B_1 in stead of B_F, we would have

$$[(\psi^-,\psi^+)(A) \otimes (\varphi^-,\varphi^+)(M)] = (-1,0) \otimes (0,1) = (-1,0)$$

where the compound effect $\oplus_\Delta$ would be hidden and undiscovered. Norm-based bipolar neurophsyiological modeling, analysis, and psychopharmacology are evidently suitable application areas with infinite levels of granularities.

IV. An Unified Diagnostic and Outcome Model

We summarize the above diagnostic analysis in the following.

Bipolar ⊕ Intrinsics can be inferred from symptoms whether a bipolar patient has any capability to combine the medical effects with opposing polarities and improve his/her YinYang bipolar balance. **Bipolar & Intrinsics** can be inferred from symptoms whether a bipolar patient becomes significantly weaker with certain medication. **Bipolar ⊗ and ∅ Intrinsics** can be inferred from symptoms whether a bipolar patient has oscillating episodes.

Bipolar ⊗ and ∅ intrinsics is counterintuitive which deserves special attention. $(\psi^-,\psi^+)(P) = (-1,0)$ indicates P is in deep depression. $(\varphi^-,\varphi^+)(P) = (-1,0)$ indicates a strong negative trigger like suicide attempt. $(\phi^-,\phi^+)(P)\otimes(\psi^-,\psi^+)(P)$ =(0,1) indicates that P would achieve a very positive change by killing himself. It is irrational and counterintuitive for any normal person to have a positive state with a negative trigger. Nevertheless, this observation does lead to the diagnosis that the mental or neurophysiological ⊗ intrinsic of P is correctly functioning. This may well-explain the fact that (1) any closed dynamic system tends to become an equilibrium; and (2) a person in deep depression may become suicidal or even kill his/her children to pursue a positive state. Similarly, a serious bipolar manic patient P may show no reaction to a sad event or even have a positive mood.

Open-World Reasoning. Bipolar syndrome diagnostic analysis assumes an open-world. The triggers (e.g. good and bad news, positive and negative medications) and symptoms (e.g. different episodes) are constantly changing. One type may switch to another type; a patient may gain mental balance through a treatment or become physically weaker. It can be observed, however, the two poles of a bipolar set or fuzzy set can capture both sides of symptoms, and the universal bipolar modus ponens (BUMP) can always be used to rationally explain different triggers and symptoms. With a classical unidimensional model, these would be impossible.

Unified Representations and Measures. The intrinsics unraveled provide leads for further clinical, therapeutic, and/or pharmaceutical research and application. Based on the intrinsics unified measures can be formulated as in the following for optimization, coherence, and coordination in the medical care of bipolar mania and depression.

Balancer, extinguisher, and oscillator. The intrinsics unraveled in the early analysis all involve the key concepts of bipolar balancer (⊕), extinguisher (&), and oscillator (⊗). A balancer is a neurolobiological component for bipolar fusion; an extinguisher (&) can be used to minimize excessive mania and/or depression. In the meantime, it can also extinguish life and energy. An oscillator brings dynamics to an equilibrium or quasi-equilibrium process. All three are essential neurobiological components for a bipolar patient to adapt to a bipolar (mental) equilibrium. And the medical challenge is to determine the neurobiological impairments of a patient in these aspects and to produce different biomedicines for different treatments.

A unified diagnosis for all three disorder types. Note that self-correction can be defined as negative reflexivity characterized by (-1,0). Then we have $(-1,0)\oplus(-1,0)^2 = (-1,0) \oplus ((-1,0)\otimes(-1,0)) = (-1,0) \oplus (0,1) = (-1,1)$, which is a self-adaptation to YinYang bipolar equilibrium. The key here is that an adaptive agent should have the physical and mental ability for bipolar fusion of two opposing feelings with balancer $\oplus$. Otherwise, the agent will be unstable with the vacillating sequence of symptoms $(-1,0)^N$ or $(n,y)^N$. *Therefore, all three types of disorders with certain vacillating symptoms can be diagnosed as the lack of physical or mental balancing ability.*

A unified measure for the effectiveness of different treatments. Equilibrium energy and stability in bipolar lattices [14,15] can be naturally applied as unified measures for the effectiveness of a treatment for any of the three types of bipolar syndromes. Let (ψ^-,ψ^+) = (self-negation, self-assertion), $(\psi^-,\psi^+)(P_{t0}) = (n_0,p_0)$, $(\psi^-,\psi^+)(P_{t1}) = (n_1,p_1)$, where P_{t0} indicates that the treatment starts on P at t0. We say P is **getting better** if

(1) stability(n_1,p_1) > stability(n_0,p_0) or
$(1 - |n_1+p_1|/(|n_1|+p_1)) > (1- |n_0+p_0|/(|n_0|+p_0))$; and

(2) total_energy(P_{t1}) > total_energy(P_{t0}) or
$(|n_1|+p_1) > (|n_0|+p_0)$.

Stability alone can not determine the effectiveness of a treatment. A treatment should enhance both stability and energy levels in the long run. Otherwise when a patient is getting more stable he/she may also be getting weaker (depressed). Thus, an effective treatment should move $(\psi^-,\psi^+)(P)$ toward (-1,1) in time.

V. CONCLUSION

An equilibrium-based bipolar combinatorial neurological model has been introduced. It has been shown that bipolar logic, sets, and bipolar universal modus ponens (BUMP) build a technological bridge from a linear, static, and closed world to a non-linear, dynamic, and open world of equilibria and form a basis for bipolar holistic neurobiological modeling and diagnostic analysis with added rigor to the standard spectrum model. Preliminary application examples have been presented to illustrate the basic ideas. Some seemingly paradoxical mental states have been mathematically characterized. A unified diagnosis and a unified outcome measure of different treatments have been presented.

The significance of this work is 2-fold: (1) It introduces YinYang into biomedicine for the understanding of certain neurological disorders and fosters a standard model for clinical, therapeutic, and pharmacological research and applications; and (2) It presents a bipolar mathematical basis for the characterization of neurobiological stability and regulation in individuals and/or a cohort of patients with applications in biomedical engineering and potential applications in bio-nanotechnologies for holistic and complete care of depression and other neurobiological disorders.

Equilibrium-based neurological modeling also presents a theoretical framework for the representation, visualization, and diagnostic analysis of coexisting mania-depression symptoms (or mixed states). This topic will be further discussed in a future report.

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