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# INVESTIGATING THE ROLE OF SLEEPING TIME IN DEPRESSIVE MOOD DISORDERS USING SIMULATION-BASED QUANTITATIVE METHODS

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**Abstract.** Recent studies support that self-regulation can play a prominent role as a beneficial strategy to treat affective disorders. Manipulating the amount of sleeping time during the days and nights can be considered as one of such useful self-regulation strategies. Although it has been significant progress to treat mood disorders using self-regulation methods, the details related to exact mechanism is still unknown. Therefore, it is essential to investigate the role of self-regulation methods in mood related disorders by finding the possible relation among entities involved in depressive mood using statistical methods, and analyze it as a psychological system using quantitative modelings. The present study uses Fuzzy Stochastic Hybrid Functional Petri nets as a mathematical tool to model and simulate the relationship between mood and the amount of sleeping time based on the questionnaire completed by 153 volunteers. We perform 40000 stochastic runs of the model at a 95 percent confidence level and then find average mean of the stochastic runs. Average behavior of the model shows that sleeping time more than 8 hours at night time, and less than 2 hours at the day time leads to maximum positive effect on mood states. This study is limited to young adults, and can be extended in future studies. The data was gathered using questionnaire, not clinical experiments. The results showed that proper amount of sleeping time during the day and night can be considered as a self-regulation strategy to treat depressive mood disorders.

**Keywords**: depressive mood, self-regulation, petri nets, sleeping time.
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## 1 Introduction

Depression is a frequent disorder that negatively affects emotions, actions, and an individual's way of thinking. Surveys in the World Mental Health (WMH) indicated that the prevalence of major depressive disorders (including bipolar types of depression) in a lifetime is about 53 percent (Kessler et al., 2013). Psychotherapy, drug-based therapy, and electroconvulsive therapy (ECT) are possible strategies to to manage or significantly treat depressive mood disorders. However, the effectiveness of a treatment of each type differs from one individual to another. This necessities the use of personalized treatment of depression related disorders which would be based on a function of regularity system described in detail for each individual. One of the factors which relates to different types of depression could be the amount of sleep time of an individual during the day and night. It was revealed that patients who are suffering from bipolar depression have a longer amount of sleeping time comparing to control healthy group, while major depression patients often experience insomnia (Bowden, 2001). Thus, the amount of sleep time of an individual can play an important role in depressive mood disorders, and it can be considered as a target parameter of self-regulation techniques in treatment of depression.

In the last few decades, there have been studies discussing perspectives of considering depression as a self-regulatory disorder (Strauman, 2002). So, creating a model based on entities involved in regularity system function of depression can be helpful to predict potential treatments for the depressive mood disorder. Mathematical modeling approaches and computer simulations can be used to reach this goal. Modeling complex psychological system is challanging problem. Such a project starts with understanding how objects, agents, and events are appraised based on individual's personality. OCC is first such model which is named after its developers Ortony, Clore and Collins (Ortony et al., 1990). On the other hand, Mehrabian in his model partitioned mood states to three almost independent components being Pleasure, Arousal, and Dominance (PAD) (Mehrabian, 1996). The linkage between OCC and PAD was introduced in Alma's approach by a mapping from OCC emotions to PAD mood components (Gebhard, 2005). These models made it possible to construct models, which can predict mood and emotion states in different individuals using time series as a statistical method (Mehraei et al., 2017) and stochastic Petri nets as a mathematical tool (Mehraei, 2017). These models can be used to predict potential treatments for mood related disorders by manipulating the entities and process rates in the proposed cognitive psychological system.

The current study extends the stochastic Petri nets model proposed by Mehraei (2017) to fuzzy stochastic hybrid functional Petri nets (FSHFPNs) to investigate the role of sleeping time as a self-regulation factor in depressive mood disorders Mehraei (2018) by analyzing the computer simulation results in young adults with or without depression.

# 2 Method

## 2.1 Sampling and data collection

The sample in this study included 153 volunteers, all of which were students at Eastern Mediterranean University. About 59 percent of the sample were female, and the age range was from 18 to 30 years old for both genders. These international students were born in different countries, and they could represent individuals with different background and personalities. A questionnaire was desingned to receive information about Openness, Conscientiousness, Extroversion, Agreeableness, and Neuroticism (OCEAN) personality traits (Goldberg, 1992), average amount of sleeping time of individuals during days and/or nights, the most significant emotion type of individuals before and after sleep time, and whether they have ever been diagnosed by professional psychologists for having mild or severe depressive mood or not. These individuals were asked to fill the questionnaire anonymously to make their answers trustworthy. The initial sample size was 200 students, but 153 of the volunteers were considered in the study because 47 of filled questionnaires contained either missing data or not accurate answers.

## 2.2 Fuzzy logic

The theory of fuzzy was introduced by Zadeh (1965). In this theory, a fuzzy set is defined on a universal set by its membership function. The membership degrees can be defined in [0,1] interval. Thus, fuzzy sets are the subsets of crisp numbers which can be defined only in the mentioned interval membership degree. There are different types of fuzzy numbers such as triangular and trapezoidal types. A triangular fuzzy number can be defined by three components (a, b, c), where a is smaller than b, and b is smaller than c. The crisp number b in the fuzzy number represents the value with membership 1, which is the highest possible membership value. Therefore, a set of fuzzy numbers can be defined as numbers with membership degrees greater than 0. The $\alpha$-cut of a fuzzy set for a level of $\alpha$ which can take values between 0 to 1 of membership function contains all the elements whose membership degree is greater than or equal to a given $\alpha$. Thus, a fuzzy number can be considered as a special convex with its corresponding $\alpha$-cut convex sets normalized fuzzy set defined on the set of real numbers (Liu et al., 2016).

### 2.3 Quantitative modeling with Petri nets

A Petri net is a directed graph including of places, transitions, and arcs which connects places/transitions to transitions/places (Murata, 1989). Each arc has a weight which indicates the number of parallel arcs between any two places/transitions. A place can represent any entities, and the flow of tokens among places of a Petri net describes the dynamic behavior of a Petri net. A marking of a Petri net is the distribution of tokens in all the places at a specific Petri time (pt). Many properties have been added to a classical Petri net (Murata, 1989) in the last few decades to describe distributed systems. To include continuous places and transitions into a Petri net, Continuous Petri nets were introduced (David & Alla, 1987). Continuous Petri nets solved a common problem in classical Petri nets, named state explosion problem. The state explosion problem happens when markings in places of classical Petri nets grow exponentially. To create a model for most of the systems, both discrete and continuous places are needed. Therefore, Hybrid Petri nets were introduced to overcome this problem (David & Alla, 2001). Firing rules are the conditions in a Petri net, which allows a transition to be activated or not. If the corresponding places, which are connected to a certain transition through arcs hold the conditions, then the transition has the permission to "fire", that is the flow of tokens from input places to output places of a certain transition. The continuous Petri nets which have functional firing rules on their transitions are called Hybrid Functional Petri nets (HFPNs) (Matsuno et al., 2003). Deterministic HFPNs could shed light on how complex systems might work, but it is not clear how accurate and significant the simulation results are in such deterministic quantitative modeling (Mehraei et al., 2016). So, some extended properties have been added to Petri nets, such as time, color, stochastic, and fuzzy extensions to overcome this problem (Liu et al., 2016).

In the last two decades, various types of Petri nets as mathematical tools have been used to create quantitative models to describe and analyze complex biological systems, such as Hybrid Functional Petri nets to model biological signaling pathways. It was shown that Petri nets can be also used as an appropriate quantitative model to describe complex psychological systems (Mehraei, 2017). The analysis of simulation results by manipulating the process rates of such Petri net models makes it possible to identify novel strategies to treat psychological disorders.

### 2.4 Creating Fuzzy Stochastic Hybrid Functional Petri nets model

In the current study, Fuzzy Stochastic Hybrid Functional Petri nets were used to model the role of sleeping time in mood regulation. Hybrid and functional properties were needed for this model since there exist both discrete and continuous places in the proposed Petri nets, and there are some transitions which need specific firing rules. Psychological systems are typically governed by stochastic aspects as biological systems (Mehraei, 2017), so stochastic property should be added to Hybrid Functional Petri nets to model such systems (Heiner et al., 2008). The most challenging part of creating such Petri nets models is the determination of the exact kinetic parameters of the transition rates. Unfortunately, most of the kinetic parameters in psychological systems are unknown or different for each individual. Thus, Fuzzy property can be added to Stochastic Petri nets to overcome this problem (Liu et al., 2016).

The Amygdala is a section of the brain that its activity plays important role in memory, attention, mood, and emotion. One of the neurotransmitters which is known to be responsible for activating Amygdala is 5-hyrdoxytryptmane (5-HT), known as Serotonin. The section of the proposed FSHFPN model in this study related to the role of Serotonin in PAD mood components is illustrated in Figure 1. On the other hand, as explained in section 2.1, all 153 volunteers in this study were asked to give information about their most significant emotion types before and after sleeping time. The logistic regression analysis with 95 percent confidence level showed that after sleeping time, disappointment, resentment, and distress emotion types were changed significantly to hope, joy, and relief emotion types, respectively. Therefore, only these emotion types were included in the proposed FSHFPN model. The simplified emotion interaction segment of the proposed Petri net model is illustrated in Figure 1 as well. In this Figure, only relief and distress emotion types are shown as examples. These emotion types are represented as discrete places, which can have either 0 or 1 markings. For instance, when marking of distress place is 0, it means that the individual is experiencing distress and the inhibitory arcs which connect distress place to continuous transitions can't prevent the firing of these transitions anymore. The rates of these continuous transitions are determined based on ALMA's emotion types to PAD mood components mapping (Gebhard, 2005). The two transitions of "sleeping" and "waking up" change the status of the emotion types, which can lead to an effect of emotion types on PAD mood components. On the other hand, Serotonin increases Amygdala activity using a stochastic transition which leads to increase of PAD levels.

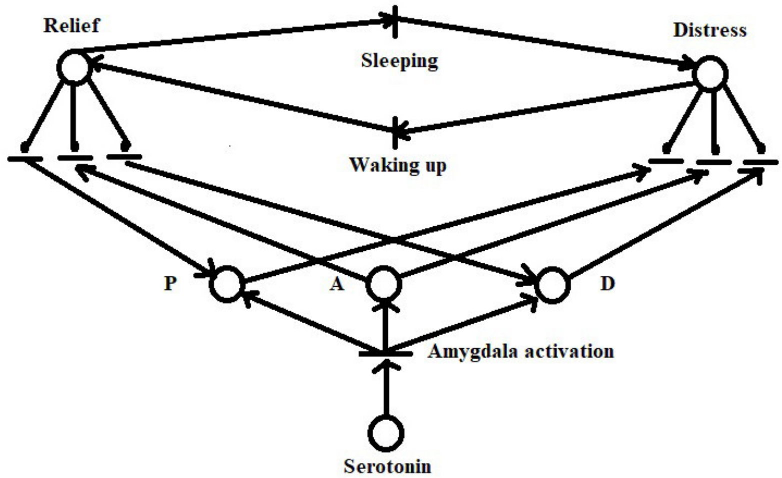


**Figure 1:** The role of emotion types and Serotonin on PAD mood components

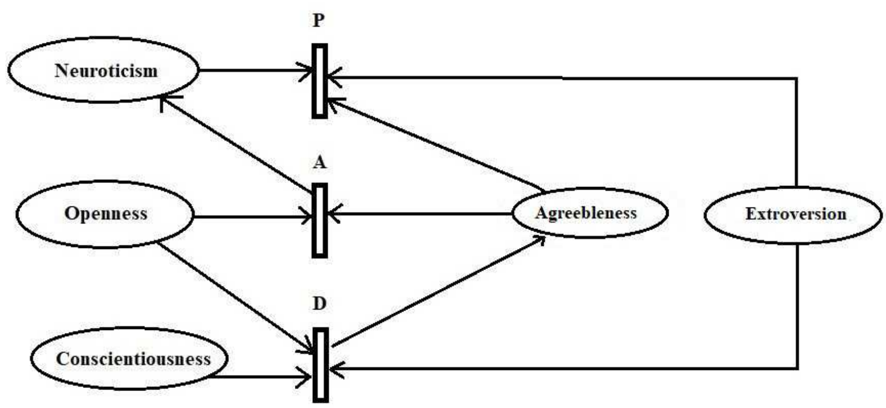


**Figure 2:** OCEAN personality traits to PAD mood components in FSHFPN model

The initial marking of Pleasure, Arousal, and Dominance(PAD) places in the proposed Petri nets can be considered using OCEAN personality traits of each individual (Mehraei, 2017). However, considering personality as an initial marking of places in Petri nets neglects the long effect of personality on mood components. So, a segment was added to the proposed FSHFPN model to consider the long effect of personality traits on the PAD mood components. This added segment is illustrated in Figure 2. The OCEAN personality traits of each individual were measured using the filled questionnaire in this study. The transition rates were determined using the mapping from OCEAN personality traits to PAD mood components (Gebhard, 2005).

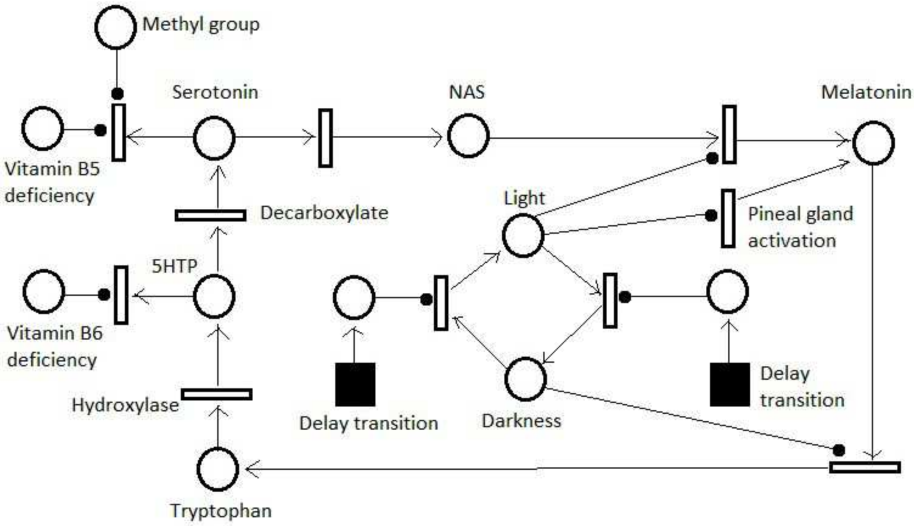


**Figure 3:** Serotonin and Melatonin secretions based on light-dark cycle in FSHFPN model

N-acetyl-5-methoxy tryptamine (Melatonin) and 5-hyrdoxytryptmane (Serotonin) are known as sleeping hormones, which regulate the sleeping patherns in various species including human beings (Andrews et al., 2015). The level of secretion of these hormones depends on dark-light cycle (Thor et al., 2007). Therefore, the levels of Serotonin and Melatonin increase and decrease during day time, respectively. The level of melatonin secretion increases in darkness to help animals and human beings to sleep (Dawson et al., 1993). Thus, we have considered serotonin and melatonin secretion cycle based on dark-light cycle in the proposed model. This segment of FSHFPN model is illustrated in Figure 3.

The production of Melatonin from Serotonin is possible with the help of an enzyme named hydroxyindole-o-methyl transferase through N-acetylserotonin (NAS), which is a chemical precursor. On the other hand, Melatonin hormone is secreted by the Pineal gland in the absence of light since it has light-sensitive cells and nervous connection from the eyes. Therefore, when the eyes are exposed to the light, the level of Melatonin decreases and Serotonin can be produced by an amino acid, named Tryptophan. Tryptophan is also a precursor to Melatonin and Serotonin (Slominski et al., 2002). The segment of FSHFPN model related to the cycle of Serotonin and Melatonin production is illustrated in Figure 3. There exist places in this Petri net model which are connected to stochastic transitions by an inhibitory arcs. For example, lack of Vitamin B5 and B6, which can lead to decrease in Serotonin level to be produced by Tryptophan. The delay transitions are defined in this FSHFPN model to simulate dark-light cycle. The initial marking of darkness place has a token at the beginning of the simulation. The light place can have a token at 50 Petri time (pt) and dark place can have a token at 100 pt. This cycle can go on based on the number of days in the study. The information related to the transitions in the proposed FSHFPN is summarized in Tables 1-3.

**Table 1:** Transition rates in the proposed FSHFPN model

| Transition with its Type | Kinetic Parameter | Delay Time |
|---|---|---|
| Activation (Stochatic) | K1 = (0.05, 0.1, 0.15) | 0 |
| Natural Degradation (Stochastic) | K1 | 0 |
| Day-nigt cycle (Discrete) | 1 | 0 |
| Light-dark cycle (Discrete) | 1 | 0 |
| Darkness (Deterministic) | 1 | 50 |
| Light (Deterministic) | K1=(0.09, 0.1, 0.11) | 100 |
| Day time sleep (Deterministic) | 1 | Personalized |
| Night time sleep (Deterministic) | 1 | Personalized |

**Table 2:** Transition rates in the proposed FSHFPN model for emotion states and PAD mapping

| Transition | Type of Transition | Kinetic Parameter |
|---|---|---|
| Relief emotion to Pleasure | Stochastic | K2 = (0.15, 0.2, 0.25) |
| Arousal to Relief emotion | Stochastic | K3 = (0.25, 0.3, 0.35) |
| Relief emotion to Dominance | Stochastic | K4 = (0.35, 0.4, 0.45) |
| Joy emotion to Pleasure | Stochastic | K4 |
| Joy emotion to Arousal | Stochastic | K2 |
| Joy emotion to Dominance | Stochastic | K1 = (0.05, 0.1, 0.15) |
| Hope emotion to Pleasure | Stochastic | K2 |
| Dominance to Hope emotion | Stochastic | K1 |
| Pleasure to Disappointment emotion | Stochastic | K3 |
| Disappointment emotion to Arousal | Stochastic | K1 |
| Dominance to Disappointment emotion | Stochastic | K4 |
| Pleasure to Distress emotion | Stochastic | K4 |
| Arousal to Distress emotion | Stochastic | K2 |
| Dominance to Distress emotion | Stochastic | K5 = (0.45, 0.5, 0.55) |
| Pleasure to Resentment emotion | Stochastic | K2 |
| Arousal to Resentment emotion | Stochastic | K3 |
| Dominance to Resentment emotion | Stochastic | K2 |

Generally, biological systems are governed by stochastic aspects. Thus, to model biological systems, stochastic property should be added to hybrid functional Petri nets (Heiner et al., 2008). In the proposed model, the processes related to activation, transcription, translation, natural degradation, and binding were considered using stochastic transitions. All mRNAs and proteins in this model are following the central dogma of biology, and their levels are kept steady using natural degradation. The central dogma of biology and natural degradations in the Petri net model are illustrated in Figure 2.

**Table 3:** Transition rates in the proposed FSHFPN model

| Process | Type of transition | Rate of transition |
|---|---|---|
| Transcription | Stochastic | K1=(0.09, 0.1, 0.11) |
| Translation | Stochastic | K1 |
| Activation | Stochastic | K1 |
| Binding | Stochastic | K1 |
| mRNA degradation | Stochastic | K1 |
| Protein degradation | Stochastic | K2=(0.009, 0.01, 0.011) |
| Perifosine process | Continuous | K3=(0.05, 0.06, 0.075) |
| PTEN-mutation process | Continuous | K4=(6.5, 7, 7.8) |
| shAkt process | Continuous | K5=(999.2, 1000, 1001) |

# 3 Results

The proposed FSHFPN model was conducted on the Snoopy platform (Heiner et al., 2012) and the simulation results were obtained by calculating the average of 40000 stochastic runs, and by manually considering three alpha levels of each fuzzy number (boundary points and the value with membership 1). The confidence level of these simulation results were set at 95 percent based on the formula proposed by Sandmann et al. (2008). The number of simulation runs was considered the way to have the ratio of the standard deviation and the mean tending to 1. The big size of simulation runs avoids sacrificing the accuracy of the results (Liu et al., 2016). The simulation results are based on Petri times (pt). The interval of 0 pt to 50 pt is the warm up stage of the simulations. Then each 100 pt interval represents day-night cycle.

Each of PAD components can take values between -1 to 1. When the mood swing of an individual for all PAD components falls often between -0.35 to -0.7 or -0.7 to -1, it indicates that the individual is having mild or major depressive disorder, respectively. Therefore, the individuals in this study were categorized based on the simulation results of their PAD components to healthy, minor depression, and major depression groups. This categorization based on simulation results from 50 pt (Petri times) to 150 pt is illustrated in Figure 4. Since Petri nets can't accept negative markings for their places, a mapping was used to receive results for levels of PAD components between -1 to 1 (Mehraei, 2017). The simulation results with 95 percent confidence show that 55 out of 153 individuals in this study should be categorized in either mild or major depression groups. These simulation results are in line with what these individuals claimed in the questionnaire whether they often experience a depressive mood or not.

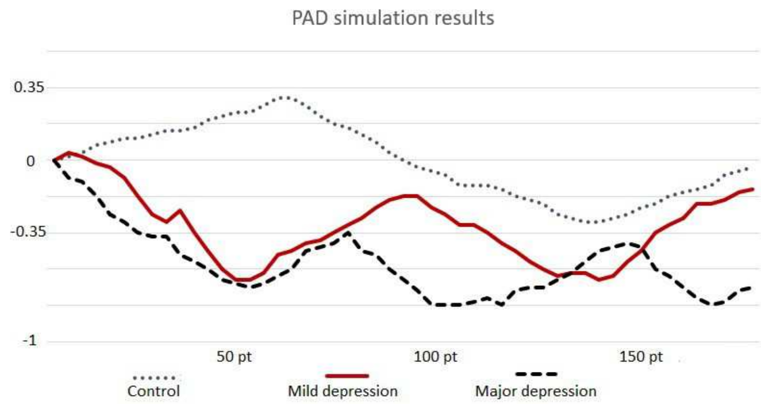


**Figure 4:** Example of categorizing based on PAD simulation results.

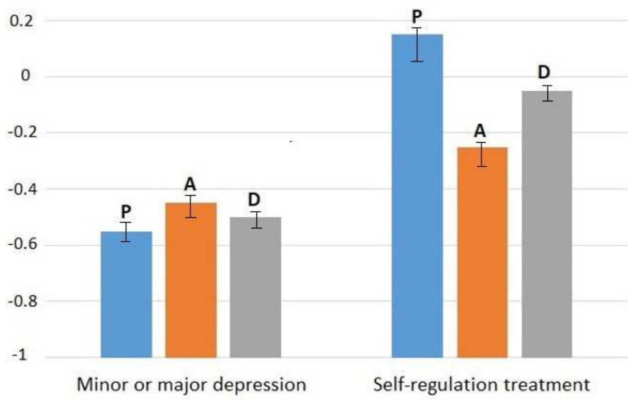


**Figure 5:** Levels of PAD components in depressive mood subjects versus treated ones.

Logistic regression tests of filled questionnaire with 95 percent confidence showed that those who sleep between 6 to 10 hours at night, and less than two hours in day time significantly belong to the group with rare depressive mood. The simulation results of the proposed FSHFPN model are in line with these results as well. So, the role of time of sleeping time in experiencing depressive mood is important. However, is it possible to manipulate the amount of sleeping time as a self-regulation strategy to treat depressive mood disorders?

As it was shown in Table 1, the amount of sleeping time during the day and/or night can be personalized for each individual. Based on the results obtained by both the statistical method for logistic regression and the computer-based simulation on the FSHFPN model, 8 hours and 1 hour sleeping time were determined for individuals in either group of mild depression or major depression as process rates of "day time sleep" and "night time sleep" deterministic transitions, respectively. The simulation results of these two groups by finding the average mean of 55 subjects by running 40000 simulation runs revealed that the level of PAD components significantly increased by considering p-value less than 0.05. The comparison of levels of PAD components for the average mean of 55 subjects in either mild or major depression groups is illustrated in Figure 5. To compare the effect of amount of sleeping time on PAD components independently, it can be concluded that the proper amount of sleeping time has the most and the least positive influence on Pleasure (P) and Arousal (A) of PAD components, respectively. Thus, this self-regulation strategy can be also beneficial for patients who suffer from anxiety.

# 4 Conclusion

Self-regulation strategy as one of the various treatments of depressive mood disorders has been discussed in recent years. However, the exact mechanism is still unknown. In this study, a FSHFPN model was introduced to shed light on how mood regulation, possibly works when it comes to amount of sleeping time in the day-night cycle. In addition, the amount of sleeping time was manipulated for those groups who claimed to suffer from either mild or major depressive mood. Both logistic regression test results and FSHFPN simulation results on Snoopy were in line. Data analysis with 95 percent confidence of the data obtained by filled questionnaires of 153 individuals showed that the group who doesn't experience a depressive mood frequently have at least 6 hours sleep time at night, and less than 2 hours sleep time in daytime. Therefore, the process rates of amount of sleep time for the subjects in the groups of either minor or depressive mood disorders were manipulated and changed to an average of 8 hours sleeping at night, and 1 hour sleeping in day time. The average of 40000 stochastic simulation runs on the proposed FSHFPN showed that the level of PAD mood components was increased significantly with p-value less than 0.05. Thus, manipulating the amount of sleeping time during the day or night can be used as a self-regulation strategy to treat depressive mood disorders. These results are in line with previous studies in the sense of using statistical methods such as time series (Mehraei et al., 2017) and mathematical modeling such as Petri nets (Mehraei, 2017) to describe and analyze mood regulation. These results validate the coefficients used in OCEAN personality traits to PAD mood components mapping (Mehrabian, 1996) and emotion traits to PAD components (Gebhard, 2005) as reliable estimation of fuzzy kinetic parameters.

The age of the volunteers in this study was in the range from 18 to 30. So, all results could be discussed only for young adults. The sample of subjects can be extended to cover all ages in future studies. The data in this study was gathered using questionnaire, not clinical experiments. Thus, clinical experiments can be run by clinical psychologists to validate the results obtained by simulation results and statistical analysis in this study. In future studies, the current FSHFPN model can be extended to identify new gene therapies or drug-based therapies by integrating genetic and environmental factors in the model, and then manipulating the estimated fuzzy kinetic parameters which are known to be missing or vague. Such mathematical modelings can be helpful to describe the mechanism of psychological systems and then analyze them to identify potential treatments for various psychological disorders before running tests on patients physically.

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