Computing and Informatics, Vol. 44, 2025, 961–982, doi: 10.31577/cai_2025_4_961

MODELING AND ANALYZING HORMONAL EFFECTS OF DEPRESSION BASED ON PETRI NETS AND MACHINE LEARNING

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Abstract. Depression has become a common mental illness, and the number of patients has shown a noticeable rising trend. However, the exploration of the connection between hormone levels and physical state changes in depression patients is still open. Hormone levels are complex and play a key role in regulating multiple body systems and functions, directly or indirectly influencing overall health and physical state. This work utilizes Petri nets to establish a corresponding model for the transition of hormone levels and states in depression, focusing on the association between different hormone levels and states in depressive patients. At the same time, machine learning methods offer a new approach to predicting the reachability of depression patients' states. This work enables healthcare professionals to quickly assess patients' emotional changes and their impact on outcomes, improving resource allocation.

Keywords: Petri nets, machine learning, process modeling, depression

Mathematics Subject Classification 2010: 68T05, 92C50

1 INTRODUCTION

Depression can have adverse effects on both the psychological and physical health of patients, significantly disrupting their daily life, professional development, and social interactions. Its onset is influenced by various factors, encompassing genetic,

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physiological, social, and psychological elements [1]. In recent years, changes in lifestyle have led to a dramatic increase in the prevalence of depression [2]. The World Health Organization (WHO) reports that depression is the most widespread mental illness globally, about 1 billion people worldwide suffer from mental disorders, and more than 95 million people in China will suffer from depression[1]. The magnitude of this problem has prompted many researchers to refocus their efforts on this field [3]. Considering the gravity of the situation, it is crucial to develop a model that accounts for the effects of multiple biological hormone levels on the physical condition of patients. Although some scholars [4] previously established relevant models to examine the pathophysiological impacts and underlying mechanisms of depression-related hormones, the descriptions of the associated biochemical reactions and pathways in the models are not comprehensive enough. Given that depression is a recurring process. Individuals who have been treated for depression are prone to experiencing it again. Therefore, to enhance our understanding of patients' conditions and the recurrence of depression, we require a more comprehensive model that can better analyze these aspects.

As a graphical language, Petri nets can be used for modeling and also allow researchers to effectively analyze the dynamic behavior and structural characteristics of systems [5]. They enable genuine concurrency rather than relying solely on interleaved semantics. Petri nets can describe the structure and the dynamic behavior of the system [6]. There are currently some studies applying Petri nets technology in the field of medicine. For example, colored Petri nets are combined with machine learning methods to model and analyze the multi-factor disease evolution process, and apply Petri nets to study the effects of related factors on essential hypertension, and hierarchical Petri nets can be utilized to study the modeling of patient flow and the optimization of staffing level in ED [7, 8, 9]. Some scholars [10] have proposed a depression recognition method that combines EEG feature transformation and machine learning techniques. Using EEG data from 28 participants, they extracted power spectral density and activity features and employed ensemble learning (Deep Forest + SVM) and deep learning (CNN) methods for depression classification. Experimental results showed that the ensemble learning method achieved the best classification accuracy of 89.02% on the total frequency band, while the deep learning method performed well on the Alpha frequency band with an accuracy of 84.75%. Some scholars [11] have utilized weather data and physiological sensor data to study methods for predicting depression and emotional states. By performing correlation analysis to identify significant predictive attributes, they employed machine learning algorithms such as Random Forest, Support Vector Machine (SVM), and LogitBoost to classify the severity of bipolar disorder and depression, while optimizing model performance through feature selection. So far, most depression studies have primarily focused on the identification and severity prediction of depression. While a few studies [4, 7] have utilized Petri nets to examine the mechanisms of monoamine hormones in depression, and modeling relevant model, while there

[1] `http://yn.people.com.cn/health/n2/2023/0710/c228588-40487592.html`

is currently no research on combining Petri nets and machine learning methods to predict the reachability of patients' mental and physical states.

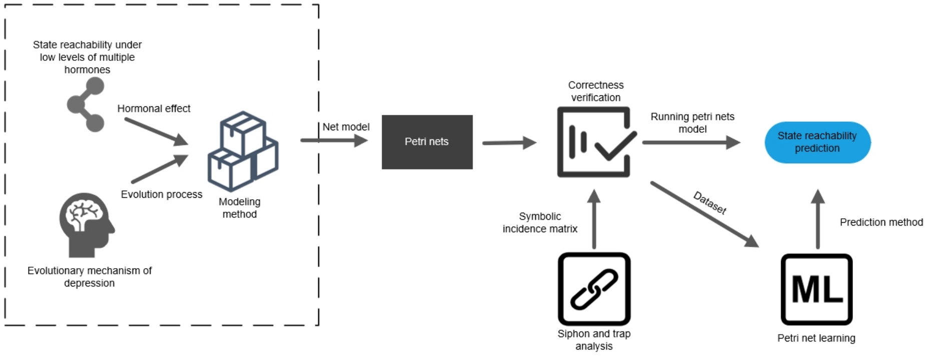

Figure 1. The overall process framework for studying depression

Based on previous research, although Petri nets technology has been applied in the realm of medical information and has contributed to biopathology, the work regarding its use in modeling and analyzing depression is still open. Our primary focus is to use Petri nets modeling technology to develop a model that examines how different hormone levels and emotional regulation mechanisms affect patients' physical states. Additionally, we aim to predict the reachability of patients' states using machine learning method [12]. This approach allows us to reliably forecast the condition of patients with depression and promptly assess the influence of different hormone levels on their physical well-being. Our method facilitates doctors in efficiently analyzing and managing extensive patient data, contributing to a more efficient allocation of medical resources and efforts. At the same time, compared to existing studies, we not only focus on the prediction of depression states but also explore the dynamic mechanisms of hormone effects. Moreover, leveraging the unique advantages of Petri nets in dynamic modeling and system analysis, our research goes beyond the limitations of classification problems and further investigates the interactions within complex physiological mechanisms.

We propose the framework as illustrated in Figure 1. The primary contributions of this paper include: Considering the changes in neurotransmitter levels (such as dopamine and norepinephrine), we construct a disease process model based on Unbounded Petri Nets (UPNs). This model can be used to analyze various mental health disorders and other conditions affecting emotional and cognitive functions. By simulating the changes in neurotransmitter levels and emotion regulation mechanisms, medical professionals can achieve a deeper insight into the pathogenesis and development of these diseases, providing valuable information and guidance for research and clinical practice in related fields. We utilize the machine learning method to swiftly and accurately predict the reachability of the patients' physical states. We substantiate the effectiveness of this method by validating the prediction results. This allows doctors to have a clearer understanding of the impact of different hormone levels on a patients' health status, providing more solid support for clinical diagnosis and treatment. The framework proposed in this paper depicts the process of modeling and analyzing the evolution of the disease. Additionally, this framework integrates methods such as marking generation software, modeling method using Petri nets, and machine learning for prediction to gain a clearer understanding of the disease's pathogenesis and progression. Finally, we apply this approach to research on depression, enabling medical professionals to better understand the pathophysiology of depression caused by changes in multiple hormone levels.

The remainder of this paper is organized as follows: Section 2 elaborates the relevant definition and modeling process of the multihormone level analysis model. Section 3 shows the method of machine learning prediction. Section 4 discusses the advantages and disadvantages. Finally, Section 5 makes a comprehensive summary of this paper.

2 MODELING SCHEME

2.1 Related Concept

We delve into the pertinent definitions of original Petri nets, the related concepts of machine learning. By introducing Petri nets, we aim to enhance our understanding of information transmission and state transition in the modeling process of depression. In the process of discussing machine learning, we explore how these approaches can be utilized to analyze models and unveil the intricate relationship between patient hormone levels and their status. Ultimately, we offer a comprehensive analysis of the specific modeling steps and methodologies for depression process, thereby laying the groundwork and offering guidance for future research.

2.2 Petri Nets

Petri nets can describe and analyze diverse systems [13]. Its characteristics include concurrency, asynchronous, distributed, parallel, uncertainty and randomness [14]. Using token flow, Petri nets simulate the system's dynamic and concurrent activities [15, 16, 17]. Furthermore, as a mathematical tool, it can also establish some equations to effectively manage the operational behavior of systems [18]. The following are relevant definitions of Petri nets.

Definition 1 ([19])**.** A Petri net $N = (P, T, F, W)$, where P is a places set, T is transitions set, F is directed arcs set, which connects the place and transition, and describes the flow of resources. W is the weight on the arc. When the resource of preceding place is less than $W(f)$, the transition cannot occur.

Definition 2 ([19])**.** The transition firing rules: For any $p \in \cdot t$, $M(p) > W(p, t)$, then $t \in T$ is enabled. When all input places of a transition have sufficient resources (meeting the weight requirements), the transition can occur, and releasing resources to output places (based on weights). This flow rule ensures that a transition is triggered only when all prerequisites are met. If multiple transitions are connected to the same place, these transitions should be mutually exclusive, meaning only one transition can occur at a time.

$$M'(p) = \begin{cases} M(p) - W(p,t), & \text{if } p \in \cdot t - t\cdot, \\ M(p) + W(t,p), & \text{if } p \in t \cdot - \cdot t, \\ M(p) - W(p,t) + W(t,p), & \text{if } p \in \cdot t \cap t\cdot, \\ M(p), & \text{if } p \notin \cdot t \cup t \cdot . \end{cases} \tag{1}$$

Definition 3 ([19])**.** Let N be a network system and $M = \{M_0, M_1, \ldots, M_k\}$ be a non-empty set of markings, where M_0 describes the distribution of resources.

$\alpha = \{t_1, t_2, \ldots, t_k\}$ represent a sequence of transitions, and having a series of markings $M_1, M_2, \ldots, M_k$ such that $M_0[t_1 > M_1[t_2 > M_2[t_3 > \ldots > M_{k-1}[t_k > M_k$ (i.e., $M_0[\alpha > M_k)$, we say that M_k can be reached from M_0.

Definition 4 ([12])**.** In the net system N, boundedness refers to the existence of a positive integer k that provides a ceiling for the number of tokens $M(p)$ for any reachable marking M and every place p within the system. If such k exists, the system is said to be bounded, indicating that the number of tokens in the system will not exceed this limit. In the absence of such a limit, the system is considered unbounded, suggesting that the number of tokens could grow indefinitely.

Definition 5 ([12])**.** Consider a Petri net $N = (P, T, F, W)$. A marking refers to a function $M : P \to \mathbb{N}$, which assigns a non-negative integer to each place in the Petri net.

The marking can also be expressed as a vector of natural numbers with a length of $|P|$. For any place $p \in P$, $M(p)$ represents the token count in p.

2.3 Machine Learning

Some scholars [12] have proposed using machine learning combined with BaggingPU algorithm to train reachable markings and unknown markings in Petri nets, a method known as Net Learning, thereby predicting the reachability of UPNs. For discrete event systems, the problem of rapidly increasing state combinations due to their extremely large state space makes it exceedingly difficult to conclusively determine state reachability within a finite time. Therefore, the purpose of machine learning is to achieve probabilistic prediction of unknown marking reachability by training the known marking reachability of UPNs. The new marking's reachability is gradually approached by using finite time and known reachability states. Additionally, the Net learning method is not only applicable to UPNs but also to large bounded Petri nets. For some bounded Petri nets, their reachability graphs or coverability trees are difficult or even impossible to generate. Therefore, the Net learning method can effectively address these issues.

In our paper, data labeled as 0 does not necessarily indicate unreachable markings, but rather data that is a mixture of reachable and unreachable markings. This is because, in an unbounded Petri net, it is impossible to determine whether a marking is unreachable, making direct judgment unattainable. However, reachable markings are known, and therefore, we can effectively address this issue using the BaggingPU algorithm. For the baseline machine learning algorithm, the data needs to have clearly defined positive and negative sample classifications. In our case, the positive samples are reachable markings, while the negative samples include both reachable and unreachable markings. Due to the specificity of this classification, the baseline machine learning algorithm cannot be directly applied to our experiments. The comparison between BaggingPU and the baseline machine learning algorithm is shown in Table 1.

Comparison Item	**BaggingPU Algorithm**	**Baseline Machine Learning Algorithm**
Data Requirements	Requires reachable markings and unknown markings, can utilize unknown markings	Requires clearly reachable markings and unreachable markings
Labeling Cost	Low (no need to label a large number of unknown markings)	High (requires clearly reachable markings and unreachable markings)
Adaptability to Specific Data Types	Suitable for large amounts of unknown markings	Adaptability to such specific data types is poor
Marking Reachability Prediction	Yes	No

Table 1. Comparison of BaggingPU and baseline machine learning algorithm

Definition 6 ([12])**.** For an unbounded network system N and a training dataset (TD), suppose a marking M is given. A classifier is a scoring function f learned from *TD*: $M \to [0,1]$. $Dr(M)$ is a decision function:

$$D_r(M) = \begin{cases} 1, & \text{if } f(M) \geq \varepsilon, \\ 0, & \text{else}, \end{cases} \tag{2}$$

where ε serves as the threshold for probability reachability. When $Dr(M) = 1$, it indicates that M can probabilistically reach from M_0.

Definition 7 ([12])**.** Let $\Sigma = (N, M_0)$ as an UPNs. The definition of triplet (M, l_M, s_M) is as follow: $M \in \mathbb{N}^{|P|}$ represents a marking that contains the number of resources in all places. l_M indicates whether M is reachable from M_0. If M is within the reachability relation $R(N, M_0)$, then $l_M = 1$; otherwise, $l_M = 0$. And s_M denotes whether M is labeled. If M is labeled, then $s_M = 1$; otherwise, $s_M = 0$.

Consequently, positive samples are denoted as $(l_M = 1, s_M = 1)$ and negative samples are denoted as $(l_M = 0, s_M = 1)$. Respectively, the unlabeled sample is denoted as $(s_M = 0)$.

2.4 Model Research

To enhance our understanding of the characteristics of depression and to create a model that captures these states. We achieve this by analyzing the interplay between dopamine and norepinephrine levels in patients with depression. Additionally, we consider how mood regulation influences their psychological status. We present the necessary definitions of Petri nets and essential analysis methods required for Petri nets analysis. Following that, we delve into the specific modeling process. We establish a Hormone Level Cascade Model (HLCM) by considering the disease evolution process and the impact of monoamine hormones on patient states. This model explains the state changes caused by low dopamine and norepinephrine levels, as well as the influence of mood regulation on patient states. This model is illustrated in Figure 2.

In HLCM, besides the state changes resulting from variations in a single hormone's level, changes induced by the simultaneous interaction of two hormones are also noted. When a patient's physical condition is suboptimal, the introduction of emotional regulation mechanisms can induce certain changes in the patient's state, facilitating a more accurate analysis of their condition. In cases where a particular state is induced by a low level of a specific hormone, further reduction in that hormone's level may occur, creating a circular feedback loop that constitutes an UPN. For example, p_7 (decreased intelligence) caused by p_0 (low norepinephrine levels) and p_4 (mental anxiety) caused by p_1 (low dopamine levels) together contribute to t_4 (low mood). After the appearance of p_8 (low mood), the norepinephrine and dopamine levels drop again. This creates a closed loop, the UPNs. The meanings of places are shown in Table 2. In our model, only the places have actual meanings, while the transitions merely serve as intermediaries for occurrences. Therefore, transitions do not carry any meanings.

The HLCM model incorporates various control architectures, such as sequential and parallel architectures. The sequential structure elucidates how decreased hormone levels initiate ongoing alterations in the patient's physical state. In instances of selective state changes, parallel structures are employed to delineate this regulatory mechanism. These architectures operate based on deterministic decision rules that drive state evolution. Assigning biological significance to each place and transition, we develop further analysis techniques to simulate hormonal interactions [20].

The paper explores a range of changes in patient physical states linked to biological hormones. Reduced levels of pertinent hormones can result in feelings of

Place	**Meaning**
P_0	Low norepinephrine
P_1	Low dopamine
P_2	Cognitive decline
P_3	Energy depletion
P_4	Anhedonia
P_5	Bradykinesia
P_6	Decreased immune function
P_7	Decreased intelligence
P_8	Feeling down
P_9	Emotional regulation
P_{10}	Slow thinking
P_{11}	Emotional regulation

Place	**Meaning**
P_{12}	Emotional stability
P_{13}	Restless
P_{14}	Lack of concentration
P_{15}	Reduce irritability
P_{16}	Emotional regulation
P_{17}	Normal state
P_{18}	Depressive state
P_{19}	Boring
P_{20}	Decision misery
P_{21}	Reduced anxiety
P_{22}	Low norepinephrine

Table 2. Places meaning

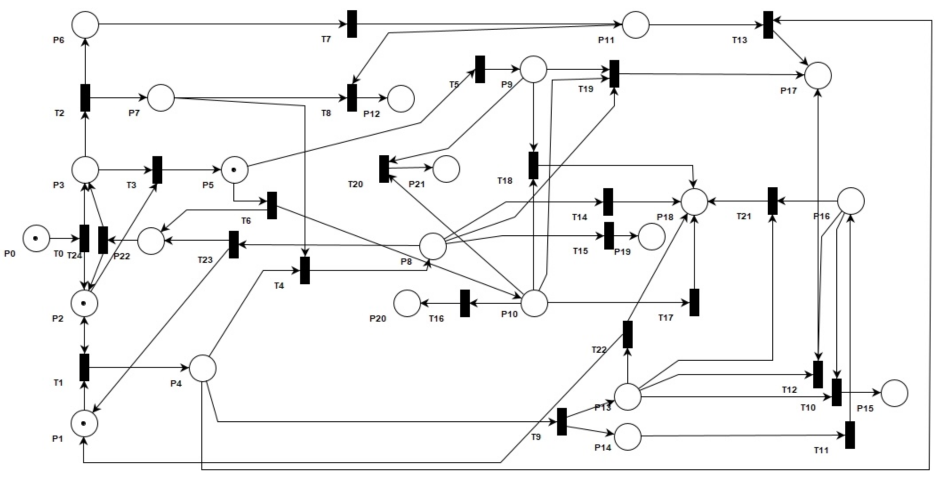

Figure 2. HLCM (Hormone Level Cascade Model)

agitation, diminished pleasure, decision-making challenges, and fatigue. Individuals with depression may additionally encounter sensations of worthlessness and guilt, difficulties with concentration and decision-making, and an increased risk of suicide and mortality [21].

Low levels of norepinephrine, widely distributed throughout the brain, result in reduced activity of the α_1 receptor, leading to decreased energy and cognitive decline. This is evidenced by low energy levels, sluggish movement, and diminished willpower [4]. Concurrently, diminished activity of the α_2 receptor also contributes to a loss of motivation and reduced vitality, reflected in slower thinking speed [22]. Furthermore, decreased activity of the β receptors may lead to feelings of low mood, closely related to symptoms of depression.

Dopamine is primarily concentrated in the prefrontal cortex, where its neural projection is highly sensitive to stress [23]. This area responds more intensely to stress compared to the basal ganglia. Chronic stress has been associated with potential harm to this system, leading to insufficient dopamine levels in the prefrontal cortex. This deficiency might reduce appetite and pleasure, ultimately contributing to the onset of depression. Some scholars [24] developed a chronic stress model in rats to mimic human depression. In their model, rats were subjected to repeated mild stresses in response to environmental changes. Through testing the rats' consumption of saccharin-containing solutions, researchers observed a decline in the animals' activity, appetite, and pleasure drive. Reduced appetite is often associated with decreased functioning of dopamine receptors, and the dopamine system in regulating appetite and other fundamental motivations. The dopamine system is intricately linked to the reward mechanism, aiding in our adaptation to new stimuli and the development of corresponding behavioral patterns [25]. Impairment of the reward system can result in irritability, apathy, and anhedonia, symptoms reminiscent of depression. This altered physical and mental state due to reduced dopamine levels can be reversed and improved with standard antidepressants, such as TCAs and selective serotonin reuptake inhibitors (SSRIs) [26].

In response to the changes in hormone levels mentioned above, we can alleviate symptoms of depression by employing emotion regulation strategies. Emotion regulation encompasses a series of intentional or unintentional physiological responses, behavioral adjustments, and cognitive processes aimed at lowering, maintaining, or enhancing an individual's emotional level [27]. Emotion regulation can assist patients in better understanding and managing their emotions, leading to improved emotional experiences and alleviation of depressive symptoms [28].

2.5 Model Process

In order to construct this model, we start from the requirements analysis in the system design phase to extract the key functional features in the progression of depression. We then follow these steps to build the model:

Symbol definition for the Hormone Level Cascade Model (HLCM): based on medical literature and clinical research reports, we precisely define the clinical parameters and other potential influencing factors, declaring the necessary elements and their connections for the model construction.

Constructing the local HLCM: we identify factors such as hormonal changes and psychological states that affect the evolution of depression. Following key clinical observations and design standards, we establish the critical events and interactions that lead to the worsening and change of depressive symptoms.

Construction of the local behavior model for hormonal levels: we analyze the interactions between different hormonal levels and their effects on the progression of depression. Key factors affecting depression, such as fluctuations in hormone levels, stress responses, and emotional regulation, are identified, and their input and output channels are defined through cause-and-effect logical relationships, represented by directed arcs.

Fusion operation of HLCM: based on clinical evidence and the definitions in the previous steps, we integrate to form a comprehensive behavioral model of depression (HLCM). At the initialization of the model, we introduce indicative data that represent the onset stage of the illness, such as baseline hormone levels and initial psychophysiological states.

3 MODEL ANALYSIS AND PREDICTION

3.1 Model Running Rules

We construct an original Petri net-based model to explore the interaction of hormones and intrinsic interventions in depression. To ensure that the model works efficiently, we need to mention some supporting rules. Below, we elaborate on the operational rules of the HLCM model to deepen understanding of the simulation process. In our HLCM model, p_0 (low norepinephrine level) and p_1 (low dopamine level) constitute the initial input places of the model. These input places receive resources to form the initial marking M_0. In this initial state, there are multiple transitions that can be activated. By randomly selecting and triggering a transition, we obtain a new marking M_1. Continuing this process, in the M_1 state, there are multiple transitions that can be triggered. After randomly selecting and executing a transition, the next new marking M_2 is generated. The operational process of the HLCM model involves a continuous sequence of changes in markings and transitions, illustrating the dynamic evolution process as the simulation progresses.

3.2 Model Prediction

A major challenge in analyzing UPNs is dealing with infinite states [29]. The vast number of numbers in ω within the finite reachability tree makes it difficult for existing reachability analysis methods to deliver precise results. This is particularly challenging without excessive computing time and space requirements. As a result, this concept has led to the development of a machine learning approach, which can partially address the reachability problem in UPNs. By initially defining the probabilistic reachability of markings, the machine learning approach redefines the UPNs reachability challenge as a problem of predicting markings. This method combines machine learning with the BaggingPU algorithm to train on the reachable markings generated by Petri nets and the unknown markings produced according to specific rules, thereby predicting the reachability of unknown markings. By designing an iterative strategy to continuously update the classifier, the reachability of samples beyond the training and testing sets can be predicted. Experimental results demonstrate that the proposed method performs well in terms of accuracy and time efficiency.

The core idea of Bagging PU (Positive-Unlabeled) is to construct multiple classifiers using Positive-Unlabeled (PU) data and reduce model variance through the Bagging method. Bagging works by repeatedly sampling from the training dataset to create multiple subsets, training multiple base learners on these subsets, and finally obtaining the final prediction through voting or averaging.

Assume there are T base learners, where each learner h_t is trained on a sampled training set. The final prediction is obtained through the weighted combination of all the learners:

$$H(x) = \frac{1}{T}\sum_{t=1}^{T} h_t(x). \tag{3}$$

In Bagging PU, random sampling is performed on unlabeled samples and combined with all positive samples to form the training set. The sampling process is completed using the Bootstrap method. For the dataset D, a subset D_t is generated through sampling with replacement, where its size is at most max_samples times the original dataset. The process is represented as:

$$D_t \sim \text{Bootstrap}(D, \text{max\_samples}), \tag{4}$$

where max_samples represents the sampling ratio. Bootstrap refers to randomly sampling from D with replacement.

We can utilize machine learning methods to predict the reachability of marking in the HLCM model, enabling us to quickly determine whether a patient is likely to transition to other states under certain specific conditions. This approach provides strong support for clinical decision-making, allowing doctors to better formulate personalized treatment plans. Through the dynamic analysis of patient states, we gain a deeper understanding of the disease progression, thereby improving the effectiveness of prevention and intervention strategies.

Theorem 1 ([12])**.** The probability calculation formula for the reachability of a new sample is shown as follows:

$$P_r(l_M = 1 \mid M) = \frac{P_r(s_M = 1 \mid M)}{P_r(s_M = 1 \mid l_M = 1)}. \tag{5}$$

Our team developed a reachability marking generation software primarily designed to automate the generation of data or information related to markings, aiming to improve the efficiency and accuracy of the data labeling process. By using intelligent algorithms and rule engines, it can automatically identify and generate markings based on predefined standards. The software is widely applied in data analysis, machine learning model training, and information management, among other fields. It not only significantly reduces the time and cost of manual labeling, but also enhances the consistency and reliability of the markings, which is crucial

Place	**Value**					
P_0	1	1	0	0	0	0
P_1	1	1	1	1	0	0
P_2	1	1	2	2	2	1
P_3	0	0	1	0	0	0
P_4	0	0	0	0	1	0
P_5	1	0	0	0	0	1
P_6	0	0	0	1	1	0
P_7	0	0	0	1	1	0
P_8	0	0	0	0	0	1
P_9	0	1	1	1	1	1
P_{10}	0	0	0	0	0	0
P_{11}	0	0	0	0	0	0
P_{12}	0	0	0	0	0	0
P_{13}	0	0	0	0	1	0
P_{14}	0	0	0	0	1	1
P_{15}	0	0	0	0	1	0
P_{16}	0	0	0	0	0	0
P_{17}	0	0	0	0	0	0
P_{18}	0	0	0	0	2	0
P_{19}	0	0	0	0	0	0
P_{20}	0	0	0	0	0	0
P_{21}	0	0	0	0	0	0
P_{22}	1	1	1	1	1	0
Label	1	1	1	1	1	0

Table 3. Part of the data sample

for accelerating data preparation and improving model performance. Furthermore, the software is not only suitable for generating reachability markings for original Petri nets but also supports the generation of reachability markings for transition priority Petri nets, temporal Petri nets, and other types of Petri nets. The main interface of the software is shown in Figure 4.

We use the custom-developed software and certain specific rules to generate 10 000 markings, including both reachable and unreachable markings. Due to the diversity of the markings, we were only able to generate a subset of them. Some of the data samples are illustrated in Table 3. By applying the bagging strategy in Net learning for training and predicting the data, we found that this method significantly improved the overall accuracy of the model. The bagging algorithm works by aggregating the results from multiple base learners, effectively reducing overfitting and enhancing the model's generalization ability. To further validate the effectiveness of this strategy, we compared five different machine learning models: Support Vector Machines (SVM), Decision Tree (DT), Multi-Layer Perceptron (MLP), Random Forest (RF), and Extreme Gradient Boosting (XGB). The experimental results indicate that the DT model demonstrated the highest overall accuracy among all the models while also requiring the least training time, highlighting its efficiency and effectiveness for the specific task in this study. By comparing the performance of different models, we found that while other models (such as MLP and XGB) also exhibited certain predictive capabilities, the Decision Tree model significantly outperformed them in terms of accuracy and training efficiency. The advantages of the Decision Tree model are not only reflected in its ability to quickly capture patterns in the data but also in its intuitive and interpretable decision rules, making it highly applicable to complex system modeling and optimization. The results show that the Decision Tree model excels at identifying critical patterns in the data, providing stable, accurate, and efficient predictions for this type of task. The comparison results of different models are shown in Figure 3, further emphasizing the comprehensive advantages of the Decision Tree model.

Machine learning models calculate evaluation metrics such as Precision, Recall, Accuracy, and F1-score for classification results using the following formulas:

$$\text{Precision} = \frac{\text{TP}}{\text{TP} + \text{FP}}, \quad \text{Recall} = \frac{\text{TP}}{\text{TP} + \text{FN}}, \quad F_1 = \frac{2 \cdot \text{Precision} \cdot \text{Recall}}{\text{Precision} + \text{Recall}}. \tag{6}$$

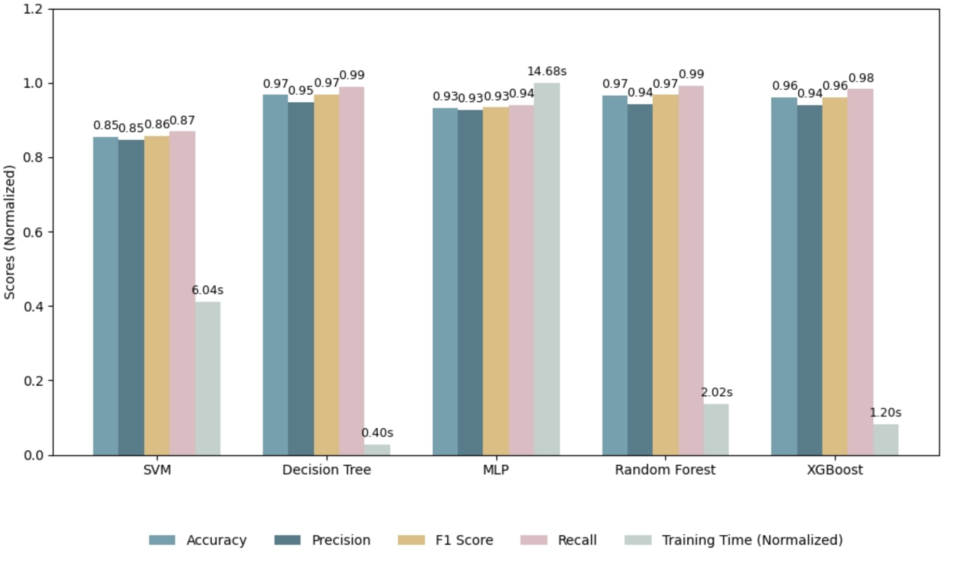

Figure 3. Performance comparison of machine learning models

It is assumed that in the initial state, p_0, p_1, p_2, and p_5 each contain one resource, which reflecting the patient's low levels of norepinephrine and dopamine, cognitive decline, and bradykinesia. Through repeated iterative training of the data, we can predict the specific identifier. For example, the state of p_1 with one resource, p_2 with two resources, and p_5 and p_{12} with one resource each is predicted. The result is positive, indicating that the state is reachable. This means that patients with low levels of norepinephrine and dopamine, cognitive decline, and bradykinesia have the potential to return to an active state after undergoing mood regulation. The model verification shows that this state can be achieved by undergoing transitions t_0, t_2, t_7 and t_8.

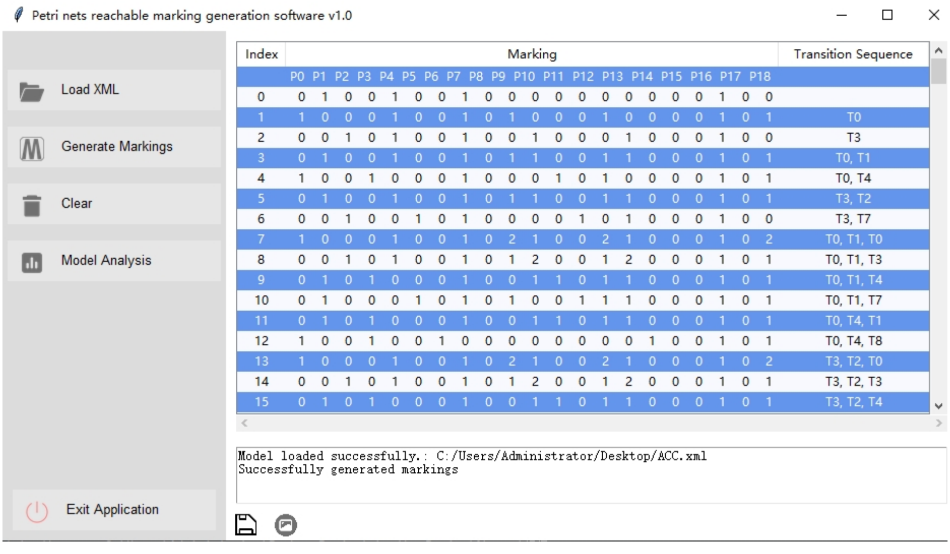

Figure 4. The marking generation software

By training machine learning model with a sufficient amount of data, the models can digitize the connections between places and transitions, thereby achieving precise reachability prediction for markings. The prediction based on the data suggests that under the condition of relatively low initial markings for norepinephrine and dopamine levels, after transition t_0, the patient's energy begins to diminish, and following transition t_2, this manifests further as reduced immune function and decreased vigor. After transitions t_7 and t_8, with the introduction of emotional regulation, the patient's mental state shows a restoration of vitality. Petri nets, with their intuitive graphical representation, allow us to convert intricate biological problems into mathematical models, thereby facilitating mathematical analysis and problem-solving [30].

Finally, we predict whether the randomly generated data outside the label is reachable, and running the Petri net to verify the correctness of the prediction results. After manually running the HLCM model, we found that the predicted state reachability was accurate. This indicates the strong predictive capability of our model. A predicted state of 1 signifies that the patient may reach that mental state under the given input conditions. The prediction result is shown in Figure 5.

```
Prediction results:
marking [0, 0, 1, 0, 0, 0, 0, 0, 0, 2, 0, 0, 0, 1, 0, 0, 1, 0, 0, 0, 0, 0, 0] prediction result: [1]
marking [1, 0, 1, 0, 1, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0] prediction result: [1]
marking [1, 0, 1, 0, 1, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 1] prediction result: [1]
marking [1, 0, 1, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 1, 1, 0, 0, 0, 1, 0, 0, 0, 0] prediction result: [1]
marking [0, 1, 2, 1, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0] prediction result: [1]
marking [1, 0, 1, 0, 1, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0] prediction result: [1]
marking [1, 0, 1, 0, 1, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 1] prediction result: [1]
marking [1, 0, 1, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 1, 1, 0, 0, 0, 1, 0, 0, 0, 0] prediction result: [1]
marking [0, 0, 2, 1, 1, 0, 0, 0, 0, 1, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0] prediction result: [1]
marking [1, 0, 1, 0, 1, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0] prediction result: [1]
marking [1, 0, 1, 0, 1, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0] prediction result: [1]
marking [1, 0, 1, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0] prediction result: [1]
marking [1, 0, 1, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0] prediction result: [1]
marking [0, 0, 2, 0, 0, 0, 0, 0, 0, 0, 2, 0, 0, 1, 1, 0, 0, 0, 0, 0, 0, 0, 1] prediction result: [0]
marking [0, 0, 3, 0, 0, 0, 1, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0] prediction result: [0]
marking [0, 0, 3, 0, 1, 0, 0, 1, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0] prediction result: [0]
marking [0, 0, 3, 0, 0, 0, 1, 1, 0, 0, 0, 0, 0, 1, 1, 0, 0, 0, 0, 0, 1, 0, 0] prediction result: [0]
marking [0, 0, 2, 0, 1, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0] prediction result: [0]
marking [0, 0, 2, 0, 1, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 1] prediction result: [0]
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Figure 5. Prediction result

4 DISCUSSION

This paper proposes a method that combines Petri nets with Net learning for modeling and analyzing the hormonal influences in depression. The innovation of this method lies in integrating the formal modeling capabilities of Petri nets with the predictive power of machine learning, enabling the modeling and prediction of state transitions in complex systems. The core innovation of this research is the combination and application of these methods. Compared to existing approaches, such as the analysis of invariants in monoamine hormones in depression and the multi-factor modeling and analysis of disease evolution by combining Petri nets with machine learning, our research offers the following advantages:

1. These methods typically lack the ability for dynamic prediction via machine learning, or are limited to binary classification predictions of depression outcomes. Our research not only focuses on predicting depression outcomes, but also extends to predicting multiple states.

2. We have developed dedicated software for generating reachability markings, supporting automated marking generation and prediction, significantly improving work efficiency.
3. With the help of Net learning methods and self-developed software, we effectively solve the state space explosion problem. The advantages of Petri nets in dynamic modeling and system analysis enable us to break through traditional classification problems and explore interactions within complex physiological mechanisms.

However, our research has not fully considered external environmental factors (such as weather, social activities, and lifestyle) and has not fully leveraged multimodal data and large-scale data sources.

In conclusion, this method offers a different perspective for the use of artificial intelligence in depression treatment research. Although there are still many areas for improvement, it has demonstrated the potential of Petri net analysis techniques in predicting the treatment effects of depression through machine learning. Therefore, further research and exploration in this field are crucial.

5 CONCLUSION

The main contribution of this paper is to apply machine learning to the medical field of depression, and predict the state of patients through the method of reachability marking, which can reduce unnecessary medical examination and treatment, thus reducing medical costs and improving the efficiency of medical services. The HLCM model reveals the changes in physical state triggered by low norepinephrine and low dopamine levels, and explores the positive effects of mood regulation on patient recovery.

Additionally, this paper propose a framework regarding depression, which enhances the clarity and visualization of the disease's evolution process and method usage. Combined with the predictive ability of machine learning, this study broadens the application of intelligent technology in the medical field and advances the understanding of the treatment mechanism of depression. However, there are some aspects that require improvement. In the future, we intend to enhance the accuracy of the model to accurately represents the real impact of low dopamine and norepinephrine levels on patient states, and to validate whether the model covers all pertinent biochemical reactions and pathways. Furthermore, we will explore utilizing similar dynamic analysis methods to conduct more thorough research on Petri net models, thereby enhancing the model's comprehensiveness and reliability.

Acknowledgements

Funding: This work was in part supported by the Natural Science Foundation of Shaanxi Province, China under Grant No. 2021JM-205, the Fundamental Research Funds for the Central Universities, China under Grant No. GK202205039, and the Open Research Fund of Anhui Province Engineering Laboratory for Big Data Analysis and Early Warning Technology of Coal Mine Safety, China under Grant No. CSBD2022-ZD05, in part by the Open Research Fund of Key Laboratory of Embedded System and Service Computing (Tongji University), Ministry of Education, China, under Grant No. ESSCKF2023-02, and this work was also supported by the China Scholarship Council.

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