ABSTRACT
Major depressive disorder or clinical depression is a mental disorder characterized by daily low moods, which occur across many situations. Individuals suffering from depression are typically treated with counseling and antidepressant medication. This paper presents a computing approach for visualizing the dynamics of pairwise interactions of moods in personalized depression under and without medication. The methods of fuzzy cross recurrence plots of time series and their tensor decomposition offer a new way for gaining insight into the causality of the complex behavior of depression and its treatment.

Index Terms— Personalized depression, causality, medication stopping, time series, nonlinear dynamics, fuzzy cross recurrence plots, tensor decomposition.

I. INTRODUCTION

Medications are usually recommended to people with depression that is chronic or severe. Treatment by antidepressants are commonly carried out for many weeks to minimize the chance of recurrence and even up to one year [1]. People with chronic depression may need to take medication indefinitely to avoid relapse if a patient’s remission cannot be sustained.

This study was motivated by the public availability of a time-series dataset of a personalized depression [2, 3] created for investigating momentary affective states in the daily life of an individual suffering from major depression before, during, and after the double-blind phase in which the dosage of antidepressant medication was gradually reduced. The authors of this dataset have suggested that the utilization of methods for analysis of nonlinear dynamics may provide a new direction for better evaluation of the personalized risk of gradual transitions of medication for depression. In fact, major depression has been suggested as a nonlinear dynamic system [4]. Chaos and nonlinear time-series analysis have been applied to characterize patients with mental disorders [5], [6].

A recent prior work [7], [8] has applied methods of fuzzy joint recurrence plots and networks, which were developed in chaos and nonlinear dynamics, to elucidate if the individual would develop a new episode of depression when the antidepressant medication was gradually reduced to complete stopping. Analysis of the dynamics of recurrence underlying nonlinear time series fits well into the study of depression because recurrence plays a major role in the disorder symptoms [9].

It is well known that one of the most challenging tasks in medicine is the understanding of causality. Medical researchers are interested in determining if a given time series is being controlled or driving another time series. If the question can be answered, then the nature of the control can be potentially explained. One way for studying causality in medical problems using time series is that two time series can be cross-correlated to examine their relationships [10]. The work presented in this paper attempts to apply the methods of fuzzy cross recurrence plots of time series of depression and tensor decomposition of the recurrences to visualize the causality of depression and dynamics of the spatial correlations of several mental states in different drug trial phases.

II. PERSONALIZED DEPRESSION DATA

The time series were obtained from a male participant at the age of 57 years, who was diagnosed with major depressive disorder and had been using anti-depressants for 8.5 years at the time of the experiment [11].

The dataset consists of time series of 12 affective items: 1) unresting, 2) agitated, 3) irritated, 4) anxious, 5) lonely, 6) guilty, 7) enthusiastic, 8) cheerful, 9) content, 10) strong, 11) worrying, and 12) suspicious. There are 5 phases associated with the data. Phase 1 is the baseline period. Phase 2 is a double-blind period in which the anti-depressant dosage was not yet reduced. Phase 3 is a double-blind period in which the anti-depressant dosage was gradually reduced. Phase 4 is the post-assessment period. Phase 5 is the period after the gradual stopping of the medication.

In this study, the time series of unresting, worrying, and suspicious moods for phase 1 and phase 5 were used and denoted as the negative mental state; whereas time series of enthusiastic, cheerful, and strong moods for phase 1 and phase 5 were used and denoted as the positive mental state. These time series were measured on a 7-point Likert scale,
ranging from 1 (not) to 7 (very). The lengths of the time series vary from 176 (phase 1) to 1472 (phase 5).

III. METHODS

III-A. Fuzzy cross recurrence plots

Let \( X = (x_1, \ldots, x_N) \) and \( Y = (y_1, \ldots, y_M) \) be the collections of phase spaces of two time series, and \( V_X = \{v_1(X), \ldots, v_c(X)\} \) and \( V_Y = \{v_1(Y), \ldots, v_c(Y)\} \) be the sets of distinct \( c \) fuzzy cluster centers of \( X \) and \( Y \), respectively. A fuzzy cross recurrence plot (FCRP) of \( X \) and \( Y \), denoted as \( C_{XY} \), can be visualized as a grayscale image in the range \([0, 1]\) with a maximum intensity of \( \mu(X) \), \( \mu(Y) \), and \( \mu(x_i, y_j) \), where \( \mu \) denotes the membership grade of \( X \) and \( Y \) in \( \{0,1\} \) and \( \mu(X) \), \( \mu(Y) \), and \( \mu(x_i, y_j) \) are fuzzy membership grades of similarity between \( X \) and \( Y \), respectively, and the \( \wedge \) stands for the minimum operator.

The computation of the fuzzy membership function \( \mu_X(x_i, y_j) \in [0, 1] \), which quantifies the similarity between the two phase-space vectors can be inferred using two properties of the fuzzy relation [13] as follows:

1) Reflexivity:
\[
\mu_X(x_i, y_j) = 1 \text{ if } x_i = y_j, i = 1, \ldots, N, j = 1, \ldots, M.
\]

2) Transitivity:
\[
\mu_X(x_i, y_j) = \vee_{v_c(X)}(\mu(x_i, v_k(X)) \wedge \mu(y_j, v_k(X))),
\]
with \( v_c(X) \), which is called the max-min composition, where the symbol \( \vee \) stands for the maximum operator.

The procedure for determining the fuzzy membership of \( x_i \) assigned to a cluster center \( v_k \) of \( X \), \( \mu(x_i, v_k(X)) \) or denoted as \( \mu_{ik} \), can be performed using the fuzzy c-means (FCM) algorithm [14] that assigns \( N \) elements of \( X \) into \( c \) fuzzy clusters, \( 1 < c < N \). The details of the computational procedure were described in [12]. As a result, an FCRP is visualized as a grayscale image in the range \([0, 1]\) by taking the complement of \( C_{XY} \), which displays a black pixel if \( x_i = y_j, i = 1, \ldots, N, j = 1, \ldots, M \), otherwise a grayscale pixel.

III-B. Tensor decomposition of FCRPs

The depression data in this study can be modeled as a three-mode tensor that is arranged in the following way:

\[
\text{Subject} \times \text{States} \times \text{Recurrence},
\]
where the number of subjects = 1 (an individual), number of states = 2 (negative and positive), and the recurrence dynamics consists of the vectorized FCRPs of the moods associated with each of the two mental states.

Tensor decomposition using the parallel factor analysis (PARAFAC) model, which is considered as a generalization of bilinear principle component analysis [15], was used in this study. The PARAFAC model of a three-mode tensor for the recurrence dynamics of the two mental states in two phases can be mathematically expressed as [16]

\[
\mathbf{X}_k \approx \sum_{f=1}^{F} \mathbf{a}_f^{(1)} \otimes \mathbf{a}_f^{(2)} \otimes \mathbf{a}_{f,k}^{(3)},
\]
where \( \mathbf{X}_k \) stands for the tensor of phase \( k, k = 1, 2 \), \( \mathbf{a}_f^{(1)} \) is the first-mode vector whose length is equal to the number of subject = 1 (single participant), \( \mathbf{a}_f^{(2)} \) is the second-mode vector whose length is equal to 2 (number of mental states), and \( \mathbf{a}_{f,k}^{(3)} \) is the third-mode vector whose length is equal to the length of the corresponding vectorized fuzzy cross recurrence plot computed for phase \( k \).

The PARAFAC model tries to find 3 factor matrices \( \mathbf{a}_f^{(1)}, \mathbf{a}_f^{(2)}, \) and \( \mathbf{a}_{f,k}^{(3)} \) by using the alternating least squares method (ALS) whose solution was addressed in literature [17]. Figure 1 shows the \( F \)-component PARAFAC model of a third-order tensor.

![Fig. 1: PARAFAC model of multi-way data \( \mathbf{X} \).](image_url)

IV. RESULTS AND DISCUSSION

The FCRPs were computed with the embedding dimension = 3, time delay = 1, and number of clusters = 3. For other FCM parameters: fuzzy exponent \( m = 2 \), maximum number of iterations = 100, and convergence tolerance = 0.00001.

Figure 2 shows the visualizations of FCRPs of the negative mental states (unresting and worrying, unresting and suspicious, worrying and suspicious) computed for phase 1 (base line: prior to medical reduction) and phase 5 (post medical reduction). The degrees of co-occurrences indicated by the mean fuzzy membership grades (\( \bar{\mu} \)) of the FCRPs suggest that the dynamics of the worrying and suspicious states occurs most simultaneously (\( \bar{\mu} = 0.90 \) for phase 1 and 0.59 for phase 5), next is the unresting and suspicious (\( \bar{\mu} = 0.68 \) for phase 1 and 0.55 for phase 5, and least the unresting and worrying (\( \bar{\mu} = 0.64 \) for phase 1 and 0.47 for phase 5). The FCRPs not only can show the recurrent
relationship or spatial correlation of the mental state pairs, but also the time of the relationship. For example, in Figure 2 (e), the gray horizontal lines indicate some weak relationship of the worrying and suspicious states at certain times. Once again, the mean fuzzy memberships of the three FCRPs in both phase 1 and phase 2 suggest that suspicion is the main cause of the personalized depression among the mental states of unrest, worry, and suspicion during antidepressant medication and after the complete reduction of the drug.

\[
\begin{align*}
\text{Fig. 2: FCRPs of negative mental states of a personalized depression, where } \bar{\mu} \text{ is the mean fuzzy membership grade, (a) and (b): unresting and worrying, (c) and (d): unresting and suspicious, and (e) and (f): worrying and suspicious.}
\end{align*}
\]

Figure 3 shows the visualizations of FRCPs of the positive mental states (enthusiastic and cheerful, enthusiastic and strong, cheerful and strong) computed for phases 1 and 5. In comparison with the FCRPs for the negative states, the pairwise relationships of the three positive states in both phases, which can be visualized from the corresponding FCRPs, are generally weaker. The maximum average fuzzy membership grade is 0.57 (FCRP of the cheerful and strong in phase 5). In phase 1, the relationship between enthusiastic and strong states has the largest mean fuzzy membership (0.50), and next is the cheerful and strong (0.48). These fuzzy membership grades suggest that, during the medication, feeling strong is the main causality for being positive among cheerful, enthusiastic, and strong factors. In phase 5, the relationship between cheerful and strong states has the largest mean fuzzy membership (0.57), and next is the enthusiastic and cheerful (0.54). Thus, the suggestion is that, after the complete stopping of the antidepressant drug, the cheerful state is dominant among being enthusiastic, cheerful, and strong. However, the causality in both phases is weak.

\[
\begin{align*}
\text{Fig. 3: FCRPs of positive mental states of a personalized depression, where } \bar{\mu} \text{ is the mean fuzzy membership grade, (a) and (b): enthusiastic and cheerful, (c) and (d): enthusiastic and strong, and (e) and (f): cheerful and strong.}
\end{align*}
\]
A study of causality in personalized depression by visual computing of time series using fuzzy cross recurrence plots has been presented and discussed. Such a finding would be useful for targeted treatment and management of mental disorders. The ability to identify causality that is the relationship between a cause and its effect allows the accurate diagnosis of causes and prediction of future events. Understanding main factors that lead to mental disorders can be useful for recognizing the causes of symptoms, predicting the future course, and providing optimal interventions [18]. Furthermore, the use of tensor decomposition of fuzzy cross recurrence plots can reveal several interesting features of the dynamics of depression with and without antidepressant medication. The study reported herein opens doors to a new way for understanding drug effects on depression.

Future study will include other mental states and trial phases to explore in depth the causality and nonlinear behavior of depression. Furthermore, quantification of the impact of interactions between many mental states associated with depression would be important for studying major depressive disorders to elucidate the cause that is believed to be a combination of genetic, environmental, and psychological factors.

VI. REFERENCES