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## **Bipolar disorder prediction with sensor-based semi-supervised learning**



### **D4.3 – Review of existing models and methods used for scenarios of use cases**

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## **Executive summary**

This deliverable is another output of Task 4.1 and Task 4.2 activities during the first year of the BIPOLAR project, which were driven by the BIPOLAR team in cooperation with advisors representing the medical domain. It is a literature review discussing models and methods that are related to psychiatric scenarios defined in D1.1. These scenarios are the central point for the BIPOLAR project since they drive the development of the BIPOLAR package.

The review of the related work will allow for the improved design of methods to be developed within the next months of the project. Related work described in this report is divided into two parts: (1) discussion about the recently published related work related to selected semi-supervised fuzzy clustering algorithms; (2) discussion regarding the machine learning models and methods applied for monitoring of bipolar disorder using sensors. This report is aimed to review the selected main achievements and concepts in this particular field of partially labeled context of sensor-based monitoring of bipolar disorder.

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## List of acronyms

<b>Acronym</b>	<b>Explanation</b>
BIPOLAR	Bipolar disorder prediction with sensor-based semi-supervised learning project
BD	Bipolar disorder
ADP	Acoustic Data Pilot
LDP	Locomotor Data Pilot
SSFC	Semi-supervised fuzzy clustering
SSFCM	Semi-supervised fuzzy c-means algorithm
SSL	semi-supervised learning
SSMC-FCM	Algorithm with Multiple Fuzzification Coefficients
DISSFCM	Dynamic Incremental Semi-Supervised Fuzzy C-Means
S3FCM	Safe Semi-Supervised Fuzzy C-Means
CPR	Confidence Path Regularization
RPCM	Repulsive Possibilistic C-Means
PFCM	Possibilistic Fuzzy C-Means
SSPFCM	Semi-Supervised Possibilistic Fuzzy C-Means
PCM	Possibilistic C-Means algorithm
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses

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## 1.Introduction

### 1.1.About this document

The aim of this report is to review related work that can be grouped into two areas:

1. **Semi-supervised fuzzy clustering methods;**
2. **Methodological approaches for the bipolar disorder monitoring with objective data**, which is driven by the two pilots of the project, that are Acoustic Data Pilot (ADP): Acoustic data collected from smartphones of bipolar disorder patients and Locomotor Data Pilot (LDP): Locomotor data collected from sensor of bipolar disorder and unipolar depression patients.

Table 1. summarizes the keywords applied to select the related works.

**Table 1.** Keywords applied to identify the related work

Area	Keywords
Semi-supervised fuzzy clustering methods	semi-supervised learning fuzzy clustering semi-supervision partially labeled data
Methodological approaches for bipolar disorder monitoring	mental health monitoring bipolar disorder monitoring acoustic features sensor-based monitoring affective state modeling bipolar disorder depression mania voice speech acoustic

## 2. Related work

### 2.1. Semi-supervised fuzzy clustering

Semi-supervised fuzzy clustering (SSFC) is a truly cross-functional topic. It combines the knowledge from different fields, namely: fuzzy logic, cluster analysis, semi-supervised learning. Researchers contributing to the SSFC have different backgrounds, and study different aspects of semi-supervised fuzzy clustering problem. Therefore, to show the recent advances in the literature, we first put SSFC in a broader context.

First of all, semi-supervised fuzzy clustering is categorized into semi-supervised learning (SSL). [1] provide a great introduction and a general overview of SSL methods. Semi-supervised learning is often described as a setting between (completely) unsupervised and (completely) supervised learning. The key characteristic of SSL is that one has additional knowledge about a part of  $M$  observations out of all available  $N$  observations ( $M < N$ ).

This additional information may come in different forms, with two major being (i) labels and (ii) constraints. In the first case, a label  $y \in \{y_1, \dots, y_c\}$  is obtained that denotes a class observation belongs to. For example, in a problem of predicting the health status of a patient, one may distinguish between 2 classes  $\{y_1 = \text{healthy}, y_2 = \text{sick}\}$ . Constraints-based SSL provides information of a kind “observations  $x_0$  and  $x_1$  belong to the same class” or, on the contrary, “observations  $x_0$  and  $x_1$  must not belong to the same class”. The actual label of the class considered is not necessarily provided. We further refer to “partial supervision in a form of labels” as to “partial supervision”. In this case, we are effectively working with the classification problem. [1, p. 16] state that “The semi-supervised learning problem belongs to the supervised category, since the goal is to minimize the classification error (...)”. This statement applies to SSFC as well, even though it may be counter-intuitive. The term “clustering” in the name “semi-supervised fuzzy clustering” - after all - refers to one of the major unsupervised tasks. It concerns grouping unsupervised data into clusters in a way that observations in the same cluster are similar to each other, while being dissimilar to observations from other clusters. In majority of applications, “the goal is to partition the data into clusters in order to identify a latent class variable” [2, p. 232]. Even though core clustering is an unsupervised learning task, the additional information in the form of labels attached to a part of (unsupervised) patterns opens up new possibilities. One can build classifiers by applying a cluster assumption: “If points are in the same cluster, they are likely to be of the same class” [1, p. 5]. By arbitrarily establishing a one-to-one mapping between clusters and classes, one can introduce partial information into the clustering.

Regarding clustering itself, one can distinguish between two versions of it: (i) hard (crisp) clustering and (ii) fuzzy (soft) clustering. Similar categorization is applied to semi-supervised clustering models that incorporate partial supervision. Hard clustering assigns each observation

unambiguously to a single cluster. Fuzzy clustering results in soft assignment: by design each  $j$ -th observation ( $j = 1, \dots, N$ ) belongs to each  $k$ -th cluster ( $k = 1, \dots, c$ ) to some degree of membership  $u_{jk} \in [0, 1]$ . The specific name for the degree of belonging may vary between different approaches, but the idea of membership taking values in the unit interval remains the same. [3] classify SSFC models into 3 groups: (i) distance-based, (ii) constraints-based, and (iii) hybrids. The criterion used is the type of partial supervision and a method of including it. We focus on distance-based models that formalize the notion of similarity between observations and clusters using metrics (distance functions). Observations (patterns) are represented by  $p$ -vectors  $x_j \in \mathbf{R}^p$ , and clusters are represented by  $p$ -vectors called prototypes  $v_k \in \mathbf{R}^p$ . The task of SSFC is then to formulate an objective function quantifying distances between observations and patterns adjusted by memberships. Next, a minimization problem is stated, and an algorithm to minimize the objective function is proposed. An example of the objective function related with the famous unsupervised Fuzzy C-Means model as described in [4] is

$$Q_{\text{FCM}}(U, V; X) = \sum_{j=1}^N u_{jk}^m d^2(x_j, v_k), \quad (1)$$

where  $U = [u_{jk}]$  is a membership matrix,  $V = [v_k]$  is a prototypes matrix, and  $d^2(x_j, v_k)$  denotes a Euclidean distance between  $j$ -th observation and  $k$ -th prototype, and  $m \geq 1$  is a parameter called a fuzzifier corresponding to the fuzzy character of the model. The greater the  $m$ , the “fuzzier” tend to be final memberships. A frequent approach is to set  $m = 2$  for its convenient analytical properties (see [4] for detailed discussion). Distance-based SSFC introduce partial supervision by modifying the objective function appropriately. A popular technique was proposed in [5] that we call the “additive combination” technique. It modified the core objective function  $Q_{\text{FCM}}$  leading to a semi-supervised model called Semi-Supervised Fuzzy C-Means (SSFCM). [5] proposed to consider a new objective function

$$J_{\text{SSFCM}}(U, V; X, F, \alpha) = \underbrace{\sum_{j=1}^N \sum_{k=1}^c u_{jk}^2 d^2(x_j, v_k)}_{Q_{\text{FCM}}(U, V; X)} + \alpha \underbrace{\sum_{j=1}^N \sum_{k=1}^c b_j (u_{jk} - f_{jk})^2 d^2(x_j, v_k)}_{Q'_{\text{SSFCM}}(U, V; X, F)}, \quad (2)$$

where  $\alpha \geq 0$  is called a scaling factor, and  $Q'_{\text{SSFCM}}$  has a similar form as  $Q_{\text{FCM}}$ , but weighs the distances  $d^2(x_j, v_k)$  by a term  $(u_{jk} - f_{jk})^2$  rather than by a membership  $u_{jk}^2$ . Scalar  $b_j$  is a binary indicator stating whether  $j$ -th observation is supervised or not, and matrix  $F = [f_{jk}]$  contains a priori information  $f_{jk} \in \{0, 1\}$  if  $j$ -th observation is known to belong to  $k$ -th class.

The idea of  $J_{\text{SSFCM}}$  can be regarded as a penalization adjustment, pushing the membership  $u_{jk}$  towards a value of 1 for the supervised observation. Effectively, supervised observations are pushed to belong to the cluster associated with their class, but they are not necessarily forced to. Note that a supervised observation may be classified into a different cluster than the one associated with the class this observation belongs to.



The role of the scaling factor  $\alpha$  was described in [5] as to balance the impact of partial supervision on the outcomes of the clustering model. The additive combination approach became widespread and researchers over the years took inspiration from it.

Different ideas of introducing partial supervision were proposed as well. [6] recently proposed a method of “multiple fuzzification coefficients” that, instead of using the matrix  $F$  to push observations to belong to certain clusters, introduces the partial supervision by modifying the fuzzifier  $m$ . The authors called their model Semi-Supervised Fuzzy C-Means Clustering

Algorithm with Multiple Fuzzification Coefficients (SSMC-FCM). In SSMC-FCM each observation can receive different fuzzifier  $m_{jk}$ , and the supervision is implemented by adjusting  $m_{jk}$  for the supervised patterns. Note that the model does not have any parameter similar to  $\alpha$  in SSFCM responsible for adjusting the impact of partial supervision. Moving back to the additive combination, advances in the field of SSFC building on this technique covered wide range of topics. [7] and [8] adapted SSFCM to handle streaming data, as the original model works with batch data only. In particular, the

Dynamic Incremental Semi-Supervised Fuzzy C-Means (DISSFCM) model proposed in [8] is claimed to handle the evolving structure of data by means of a splitting mechanisms that generates new, more accurate clusters as time passes. Note that it overcomes a requirement of the core SSFC to associate each class with a single cluster only. [9] study a similar problem of overcoming this limitation, but using batch data. Their approach allows a one-to-many mapping between a class and clusters, but one must set the number of clusters per class. On the contrary, DISSFCM from [8] creates subclusters automatically if certain criteria are met. Semi-supervised fuzzy clustering, as already described, introduces partial supervision to the field emerging from the unsupervised learning. With the new information there come new problems. One may question the validity of the labels, and dealing with such situations receives close attention from researchers in recent years. [10] modified SSFCM to deal with incorrectly labeled data, i.e. when a part of observations is labeled with a different class than it truly belongs to. The model in [10] is called Safe Semi-Supervised Fuzzy C-Means (S3FCM). Its key mechanism is to extend the objective function in Eq. 2 in a special way, by adding the unsupervised output-based regularization term. A different usage of SSFCM was proposed in [11]. The authors applied a suggestion from the original [5] in resolving a label uncertainty problem. In certain practical problems, uncertainty may arise if the labels are equally valid. Note that one does not necessarily question their correctness, but wants to differentiate the influence of supervised observations on the outcomes of the model. In [11], SSFCM is used to build a wrapping Confidence Path Regularization (CPR) algorithm that estimates a so-called adjusted confidence factor which reflects the degree of label validity given the data  $X$ . The architecture of the CPR algorithm takes advantage of the inherent elements of SSFCM: its capability to introduce partial supervision and the soft assignment mechanism.

The additive combination technique was applied to other fuzzy clustering models than only Fuzzy C-Means. [12] used it to propose semi-supervised adaptations of: (i) Repulsive Possibilistic C-Means (RPCM) [13], and (ii) Possibilistic Fuzzy C-Means (PFCM) [14]. Note that the first one, RPCM, modifies a classical Possibilistic C-Means (PCM) introduced in [15], while PFCM combines FCM and PCM. Both Semi-Supervised Repulsive PCM and Semi-Supervised Possi used Euclidean distance. In [16], a different metric was proposed to be used in Semi-Supervised Possibilistic Fuzzy C-Means (SSPFCM), namely the adaptive distance.

## 2.2. Monitoring mental health with locomotor and acoustic sensors

In this Section, we discuss the support of monitoring and diagnosis of bipolar disorder (BD) state through the analysis of objective markers collected from sensors. Some progress has been made in the treatment of BD over the past decade; nevertheless, the diagnosis and monitoring of this disorder remain challenging. This is partially due to the still limited understanding of the nature of the disease and, consequently, the difficulty in predicting relapses. However, as stated in the recent review of Antosik-Wojcinska et al., [17]: **”the state-of-the art solutions report accuracy ranging from 67% and higher for the BD phase classification, however, it seems too early to suggest the higher adequacy of any of the approach (regression or classification) or any particular classification or regression method”**. Furthermore, such accuracy seems still not satisfactory for practical applications.

### 2.2.1. Objective markers for bipolar disorder monitoring

Speech has been already used to diagnose and manage several disorders including Parkinson’s disease, Alzheimer’s disease and major depression [18], [19]. As Kaczmarek-Majer et al. [20] summarized in the recent paper, reduced speech activity, changes in specific voice features, and pause-related measures were found to be sensitive markers of depressive symptoms [21]. On the other hand, an increased speech activity turned out to predict the manic episode [22]. The central features of BD are also the abnormalities in psychomotor and social activities, typically with psychomotor retardation, social withdrawal, paucity of speech during the depression, and increased motor, social and speech activity during mania. The changes in the manner of speaking reflect the mood state very accurately and are used intuitively by psychiatrists in everyday practice. Considering the possibility of continuous speech data collection via a smartphone app, voice analysis has a great potential in monitoring the affective state in BD patients [23]. Also, Grunerbrl et al. [31] describe the possibility of using smartphones in recognizing the state and changing the state of bipolar affective disorder. The sample consisted

of 10 of patients whose daily activity was recorded for a period of 12 weeks (in total over 800 days, 17 state changes) using smartphones with a dedicated application.

Apart from the acoustic features of speech which are regarded as promising markers, there are also other behavioural, locomotor and physiological parameters considered appealing to solve this important challenge of objective mental health monitoring. The work [27] uses the PSYCHE platform, which allows for non-invasive measurement of physiological parameters, such as heart rate dynamics. In [33], the authors propose wearable devices based on a T-shirt with integrated electrodes and sensors that allow for obtaining his electrocardiogram, respirogram and information about body posture for a given patient. This information was collected to determine patterns of physiological parameters for a given BD condition to support the diagnosis. In [34], data received from Unterberger stepping test in place with arms stretched forward as in the Romberg standing test are collected and claimed as promising markers.

Nevertheless, apart from these encouraging results, there is still a great problem with the implementation of this knowledge into clinical practice. To date, no tool for clinicians to simply transform the results of voice data or locomotor sensor data into easily understandable information was created. Further research is needed to bridge the gap between research and implementation of given solutions into clinical settings [24].

### 2.2.2. Methodological approaches in bipolar disorder monitoring

Previous studies (e.g., MONARCA [25]–[27], SIMBA, DeepMood, BDMon [28]) confirm the transformative potential of mobile and wireless technologies for monitoring of BD patients. Notwithstanding, the combination of sensor data which are the best predictors for the levels of depressive or manic symptoms is not confirmed. In terms of machine learning, supervised learning techniques are among the most common algorithms applied in this field. However, supervised techniques require labeled data, and providing accurate labels on a daily basis is almost infeasible. At the same time, unsupervised learning techniques, such as various clustering algorithms, may overcome these limitations [29]–[31]. Mainly due to the absence of labeled information on the data distribution, further research to establish links to prior BD classes is needed. To alleviate the aforementioned problems, some semi-supervised learning approaches have been proposed in recent years, such as e.g., [8]. Although there have been semi-supervised algorithms proposed in the literature, to the best of our knowledge, there has been no attempt so far to systematically investigate the power of semi-supervised algorithms in the bipolar disorder domain, which is highly characterized by the presence of both labeled and unlabeled data of uncertain nature. This gap will be addressed by the BIPOLAR project. **BIPOLAR’s ambition is to provide an analytical software package that facilitates timely and contextual mental health monitoring aiming to set the foundations to further innovate in the intelligent sensor-based prediction of bipolar disorder episodes.**

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To sum up, smartphones have tremendous potential to improve the early detection and monitoring of episodes of mental illnesses, but they are still underutilized in the area of supporting mental diseases. Furthermore, there is still need for common standards and clear guidelines about machine learning algorithms and metrics to be applied when reporting the results [17]. Finally, there is still an unmet clinical need to explain relations between attributes, symptoms, and states for this particular applied context [32].

### 3. Future work

The discussed methodological aspects will be further investigated in the other tasks of the project under WP2, 3 and 4. In particular, none of the works above discussed the additive combination and its explainability. We will examine this aspect and prepare a manuscript to be submitted for a journal. Another aspect that will be investigated is the modeling uncertainty in the semi-supervised learning. Furthermore, a survey related to “Machine learning for mental health monitoring using speech” will be prepared following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

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