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Ledys Izquierdo M.D., Luis Fernando Niño, Jhon Sebastian Rojas, "Modeling the vital sign space to detect the deterioration of patients in a pediatric intensive care unit," Proc. SPIE 11583, 16th International Symposium on Medical Information Processing and Analysis, 115830Q (3 November 2020); doi: 10.1117/12.2579629

SPIE.

Event: The 16th International Symposium on Medical Information Processing and Analysis, 2020, Lima, Peru

# Modeling the vital sign space to detect the deterioration of patients in a pediatric intensive care unit

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## ABSTRACT

In the field of continuous vital-sign monitoring in critical care settings, it has been observed that the "early-warning signs" of impending physiological deterioration can fail to be detected timely and sometimes by resource-constrained clinical staff. This effect may be escalated by the "data deluge" caused by acquisition of more complex patient data during routine care. The objective of this study is to develop a probabilistic model for predicting the future clinical episodes of a patient using observed vital sign values prior to a clinical event. Vital signs (e.g. heart rate, blood pressure) are used to monitor a patient's physiological functions and their simultaneous changes indicate transitions between patient's health states. If such changes are abnormal then it may lead to serious physiological deterioration. The CRISP-DM (CRoss-Industry Standard Process for Data Mining) methodology was used as a data mining process and then we used Markov chains to identify the clinical states through which the patient passes. Then, a Hidden Markov model (HMM) based approach was applied for classification and prediction of patient's deterioration by computing the probability of future clinical states. Both learning models were trained and evaluated using six vital signs data from 94,678 records from 90 patient, collected from the database of real patients who were in the Pediatric Intensive Care Unit of the Central Military Hospital in the city of Bogotá, Colombia. The proposed technique based on monitoring multiple physiological variables showed promising results in early identifying the deterioration of critically ill patients

**Keywords:** Vital signs, Hidden Markov model, Clinical event, pediatric critical care

## 1. INTRODUCTION

The importance of monitoring vital signs in clinical practice is undisputed, but it is still unclear how best to monitor and interpret them and the frequency with which they should be measured [1] Thus, this motivated us to search the literature for studies that explicitly attempt to determine and quantify the increase or decrease in risk associated with changes in vital signs, measured intermittently or continuously [2].

Since around 2000 there has been a growing interest in retrieving data and extracting knowledge from large volumes of data, through the efficient application of data analysis techniques and different models to try to assess the behavior of vital signs in both the hospitalized and in the patients outside the hospital, i.e, at home. It can be seen that the greatest efforts so far have been in trying to look for normal patterns in the vital signs of healthy patients [3][4], patients with chronic pathologies [5] and very few in critically ill patients [6][7]. It can also be seen that the studies to date have been carried out with patients to a greater extent in out-of-hospital settings [8], rather than in-hospital settings [9][10]. The in-hospital setting studies have been developed in the areas of emergency, hospitalization and intensive care [11][6][7]. Among these, the vast majority have been performed on adult patients [11] and very few in pediatric patients [12][13].

Today the admission of patients to the Pediatric Intensive Care Unit (PICU) is due to increasingly complex pathologies and nurses must not only know how to measure vital signs accurately, they must also know how to interpret and act on them [2][14]. Previous studies have also attempted to relate the variables of vital signs to search for predictors of patient deterioration. But, so far they have typically only related two variables.

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16th International Symposium on Medical Information Processing and Analysis, edited by Eduardo Romero Natasha Lepore, Jorge Brieva, Marius Linguraru, Proc. of SPIE Vol. SIP220, SIP22000
 · doi: 10.1117/12.2579629

Models have been designed in patients with chronic diseases and patients at home, very few studies[14][15] have interrelated more than two variables of vital signs in order to predict a pattern of abnormality in chronic diseases. Additionally, there are very few studies even in acutely ill patients such as PICU patients [16].

Considering all of the above, it is necessary to transform the vital sign space during patient monitoring, through a model that helps to simplify the work of health professionals, presenting them early alerts in a more understandable way, and reducing false alarms. The main contribution of this study is to use a predictive model for clinical abnormality detection using pervasive computing technology that uses several machine learning techniques, particularly, K-means clustering, Markov chains and Hidden Markov Models (HMMs). The proposed method uses clustering of vital sign patient data to recognize hidden information in clinical states using past observations, in an attempt to early identify the deterioration of critically ill patients.

## 2. METHODS

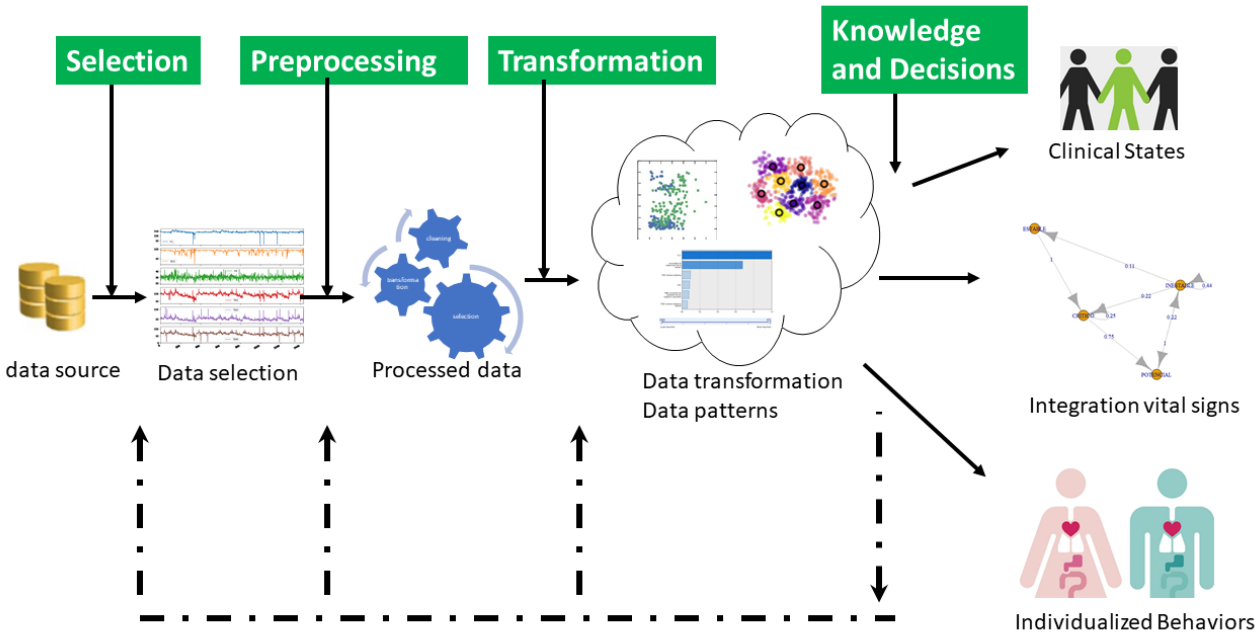



Figure 1: Machine learning based process to classify patients' clinical events

Figure 1 depicts the general learning process to generate several Hidden Markov Models from a data set coming from monitoring the vital signs of pediatric patients in an Intensive Care Unit.

### 2.1 Data set

This exploratory analysis was conducted on a data set of patients who were in the pediatric intensive care unit of the Central Military Hospital in the city of Bogotá, Colombia. The data set included a representative number of samples: 94.678 records from 90 patients, obtained under the appropriate approval of a certificated ethical committee. Children under 18 years of age were included. Epidemiological and demographic data such as: age in months, weight in kilograms (Kg), height in centimeters (cm), admission diagnosis, complications during the monitoring period and mortality were also included. With this information, patients will be classified by age categories because the values of vital signs are specific to the patient and their normality, and the range varies according to age, sex, and medical condition

Each patient record contains the second-by-second observation of six vital signs for upto 24 hours. For each patient record, we performed a search to identify the clinical events with a duration of 3 seconds or more. The six vital bio-signals collected for abnormality detection were SBP (Systolic Blood Pressure), DBP (Diastolic Blood Pressure), MBP (Mean Blood Pressure), HR (Heart Rate), RR (Respiratory Rate) and SaO2 (arterial oxygen saturation). In this work, the general normal ranges of vital signs determined by the literature [17] and the experience of the clinician were used to define normality according to the individual clinical situation of each patient. Thus, this information will be used to determine clinical events when vital signs are above or below normal ranges, as shown in Table 1. (consult database critically ill pediatric patients in PICU.csv. " Kaggle, doi: 10.34740 / KAGGLE / DSV / 1518232)

| **Biosignal** | Acronym | Normal range |
|---|---|---|
| *Heart rate* | HR | according to the age of each patient |
| *Systolic blood pressure* | SBP | according to the age of each patient |
| *Diastolic blood pressure* | DBP | according to the age of each patient |
| *Mean blood pressure* | MBP | according to the age of each patient |
| *Respiratory rate* | RR | according to the age of each patient |
| *Blood oxygen saturation* | SPO2 | according to the age of each patient |

Table 1: The vital signs and their generalized normal value

## 2.2 Data Processing and Classification

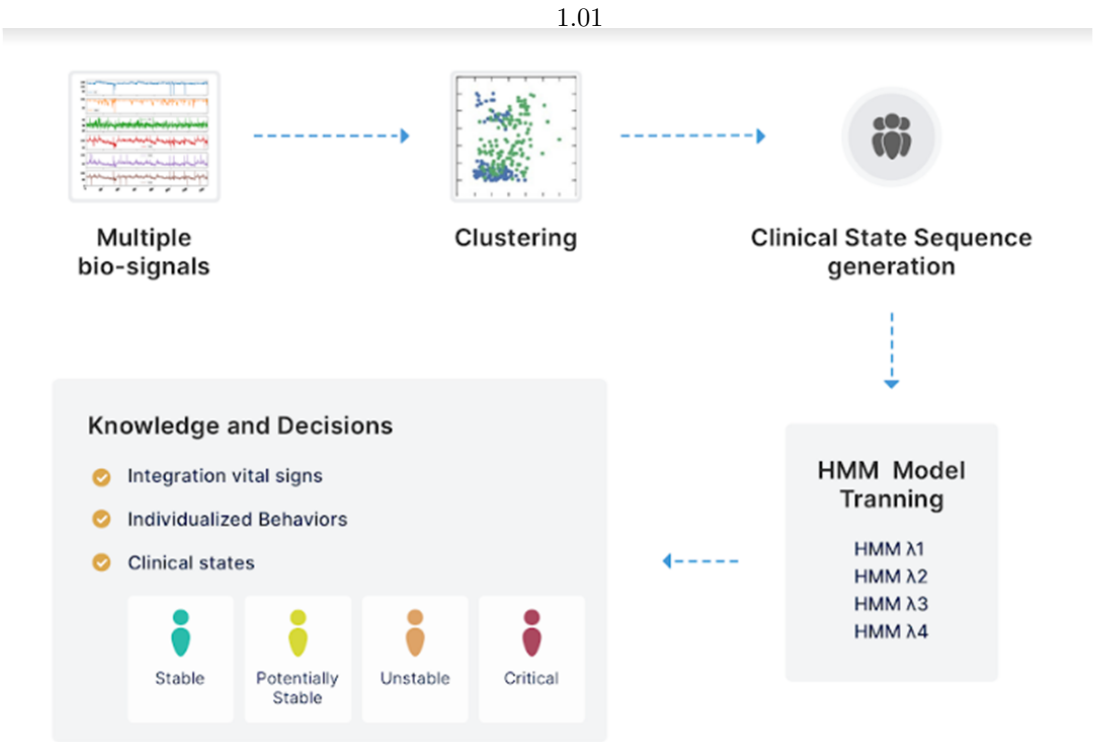



Figure 2: Stages of the learning process

Figure 2 shows the stages of the learning process using multiple vital sign data from a set of patients with different clinical conditions. The learning process produces several HMMs which are used to try to predict future clinical events of the patients

2.2.1.Cluster Analysis

We explored three clustering approaches: hierarchical cluster analysis, k-means clustering analysis (which is non-hierarchical) and, finally, two-stage clustering. The best results were obtained by k-means cluster analysis. K-means is an unsupervised learning algorithm that iteratively finds a fixed number (k) of clusters in a set of data. It groups together data points based on similarities in their features. Particularly, k-means was executed several times for different values of k, and computing the value of inertia for each k. Thus, the resulting graph is a descending curve (the greater the number of groups, the less the inertia). This graph is used to look for the best value of k. This type of graph is usually known as an elbow graph, then the point of inflection on the curve (the "elbow") is the best value of k [18][19].

2.2.2.Analysis using Temporal Models:

Analysis using Markov chains

A Markov chain is a mathematical model (system) that undergoes transitions from one state to another according to a given set of probabilistic rules. Markov chains are stochastic processes, but differ in that they lack "memory". That is, the probability of the next system state depends only on the current state (or recent states) of the system and not on other previous states [20]

In this analysis, sequences of observations from the clinical states of the patients are used to generate some Markov chains that describe the probabilistic transitions of the patient through different clinical states.

## 2.3 Training the HMMs

The main goal is to use the proposed method in real time patient monitoring to classify the streaming data of multiple vital signs of unknown patients. Thus, during recognition, a sequence of observations of multiple vital sign data (O) from an unknown patient are extracted and then presented to L HMMs. The probability of each i-th model $P(O|\lambda_i)$ for a given observation vector O is calculated by means of the forward (backward) procedure [20]. The model with maximum log likelihood probability, $logP(O|\lambda_i)$ is recognized as the most likely clinical case for observation O. Indeed, this process can be used for real-time monitoring. Accordingly, continuous maximum probabilities are computed and predictions are obtained over time based on probabilistic match.

The training process of the L HMMs was carried out by splitting the data set using two-thirds of the samples as the training set and the rest was used for validation in a 3-fold cross validation process. Given a training set, the parameters of the HMM models were estimated using such training data. The Baum–Welch algorithm, an efficient algorithm, was used for estimating the model parameters $(A, B, \Pi)$ [20]. Specifically, the algorithm starts with a random initial guess $\lambda_0 = (A_0, B_0, \Pi_0)$ and follows an iterative process which converges to the final model $\lambda$ that yields the maximum output probability. However, to make the initial guess, the number of hidden states N need to be specified. Accordingly, to estimate an appropriate number of hidden states, we train each HMM model from 2 to 10 hidden states using the same training data and computing the maximum likelihood probability. Thus, the value of N is determined experimentally, using the maximum likelihood probability. It is worth mentioning that the complexity of Baum–Welch algorithm increases exponentially with the number of states.

## 2.4 Validation, classification and probabilistic prediction

The performance of the classifier is evaluated using the validation set and by computing maximum likelihood probability for a given observation. Here, the developed HMM-based classifier serves multiple purposes. First, it can tell which one of the possible L clinical events a patient will be in prediction window TP, using T seconds of

observed data immediately before such clinical event may occur.This process also helps to estimate future states for possible observations and, thus, to detect future abnormalities. Second, it can be used in real-time patient monitoring by estimating the probability of each one of the L clinical events At time $t$, the observed sequence is generated from the data in $(t-T)$ continuously and $logP(O|\lambda)$ is computed for each one of the L models, which outputs L probability estimations. Hence, at time $t$ we get the maximum $logP(O|\lambda)$ and continuously classify patients' condition into one of L possible clinical events [20].

### 2.5 Statistical analysis

Preprocessing: a description of the demographic and clinical variables was made using the most appropriate measures of central tendency and location according to the nature of the variable and its distribution. The variables that were significant in the bivariate analysis were entered into a prediction model modeling The most relevant variables, whether categorical or continuous, were modeled on the data, using Dimensional Reduction techniques, grouping analysis, analysis of time series, classification analysis, choosing the model with the best performance. The models that had better performance especially when evaluated by physicians experts and they had clinical significance were used to design a new space for vital signs.

## 3. RESULTS

To evaluate the performance of the proposed prediction model, we conducted some experiments using a data set of patients from the pediatric intensive care unit of the Central Military Hospital in the city of Bogotá, Colombia. This dataset contains different vital sign data of various types of critically ill patients. For this experiment we only considered the records that contained of six bio-signals as discussed above. All the samples are converted to per seconds sampling. Data with consecutive missing values over a long time period were filtered out and noisy data were eliminated using median-pass and nearest-neighbor filter. Finally, a large number of samples from 94,678 patient records, distributed in 90 patients remained for our evaluations.

K-means

It is an unsupervised-non-hierarchical model, through which the size of the clusters was calculated, ant then the centroids of the clusters were determined, the centroids of the clusters were drawn and then iteration of k-means for different values of k was performed to determine the number of k. The model was validated observing that the best clusters were those that had proper values of inertia and the highest silhouette coefficient (sc) values, Within cluster sum of squared errors, this could be applied later in all patients. When performing k-means, each cluster was associated to the clinical meaning, based on the limits of normality of the six biosignals, for the particular age of a patient, according to the literature. Accordingly, it was observed that the clusters corresponded to four clinical states that were called: stable, potentially stable, unstable and critical. This classification of clinical events could be reproduced in all the patients (see Table No. 2)

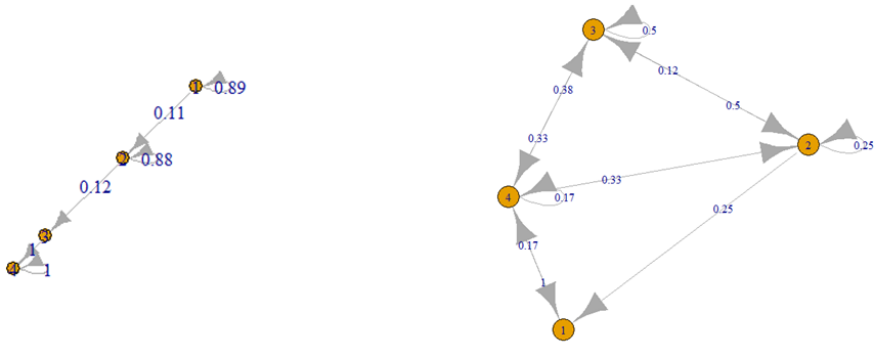
| **Clinical event** | Acronym | Code |
|---|---|---|
| *All six bio-signals are in normal range* | stable | 1 |
| *1-2 six bio-signals are abnormal range* | potentially stable | 2 |
| *3-4 six bio-signals are abnormal range* | unstable | 3 |
| *All six bio-signals are abnormal range* | critical | 4 |

Table 2: The occurrence of our targeted clinical events for evaluation, their acronym and class labels

Markov chains

A matrix was created where we had information about the clinical states, and where we could calculate the probability of transition and of being absorbed by a particular state. Thus, the Markov chain package performs a useful function called verify Markov Property [20]. that tests whether a given sequence of events follows the Markov property by performing Chi-square tests on a series of derived contingency tables of the sequence of

events, p-values (higher 0.05) indicate that the null hypothesis of a sequence that follows the Markov property should not be rejected. When applied to the entire data series, specifying the clinical states, with continuous or categorical variables, all had a p-value greater than 0.05, thus meeting the Markov property. It was observed in the evaluated data series that the Markov chains with the following features: non-recurrent, or null recurrent, with absorbable state, reducible and aperiodic are found in patients who died in contrast with those who did not.




A. Markov Chain

B. Markov Chain

Figure 3 shows two examples of Markov chains obtained for two particular patients. Markov Chain A represents non-recurring states, null, with absorptive, reducible and aperiodic states. This characteristic was more frequent in patients who died. On the other hand, Markov Chain B represents the vast majority of data behavior, where recurring, accessible, irreducible, transitory and periodic states are observed.

HMM based clinical event classification

Four clinical events are used for anomaly detection using six biosignals. The threshold values described in Table 3 are used to define the range of normality and different clinical types. The four clinical events are used to define the sequence of patient clinical events after applying k-means clustering. Such sequences of observations are then used to build the four HMM models.

We also tested the performance of the classifier in real-time abnormality prediction. Specifically, 6 patients data are randomly picked for the experiment having a combination of normal and abnormal clinical events. The objective here is to convert the observation window to observation sequence in every seconds, feed it to the HMM classification engine, and get continuous classification results for the next 3 seconds prediction window. Accordingly, in continuous data classification, the four probability values $P(O|\lambda_i)$ for the four HMMs are obtained and the decision is made by taking the maximum likelihood probability value.

The anomalies occurred at different times for each patient, observing that critical states were the least frequent in most of the data, this being a limitation for the model to be able to predict the less frequent states. For this, a single database with all the records was necessary to separate the training set and the validation. The best performance was obtained with 10 cross validation.

Then, several classification measures were computed to evaluate the performance of the classifiers Namely, the confusion matrix, Accuracy, Recovery Index (Recall) and the F1 score. The F1 score was considered as the most relevant measure since it accounts for the class imbalance in the dataset. Table 3 shows the results of the four HMMs for the experiments applying 10-fold cross validation on all the patient data.

| **States** | Accuracy | Recall | F1 | Sensitivity |
|---|---|---|---|---|
| *Stable* | 0.81 | 0.9 | 0.7 | 0.9 |
| *Potencially stable* | 0.8 | 0.7 | 0.7 | 0.7 |
| *Unstable* | 0.6 | 0.93 | 0.7 | 0.93 |
| *Critical* | 0.5 | 0.6 | 0.5 | 0.6 |
| *Total* | 0.7 | 0.75 | 0.65 | 0.75 |

Table 3: 10-fold cross validation average performance measures for each clinical event using HMM classifiers.

## 4. DISCUSSION

In the implementation of the model for monitoring and supporting the medical diagnosis of the clinical situation of the ICU patients satisfactory results were obtained, The use of Dimensional Reduction techniques, grouping analysis, classification analysis in medical applications can be very useful if considered as a very significant support tool for health professionals.

It was found that integration of grouping analysis with techniques k-means and two-step clustering provide interesting results for the classification of four clinical states (i.e., 1-stable, 2-potentially unstable, 3-unstable; 4-critical) predicted by the model.

Although there are differences in the way of experimental setup for our model, the dataset, and the particular area of application we have targeted, in comparison with other similar models, it is still possible to draw some performance and feature-wise comparisons. Therefore, we compared our model with other three previous works. The work in [21][22] presented a hospital-focused probabilistic model using a Gaussian mixture model (GMM) and one-class support vector machine (SVM) to identify patient deterioration using four vital signs (HR, SBP, RR, SPO2) that we also used in this study. Other studies have used fewer biosignals for predictions. The results of this work are promising in an attempt to predict the next clinical state. Thus, it provides valuable information to the clinician so they can take proper early management of the patients.

## 5. CONCLUSIONS

In this work, we have presented an HMM-based probabilistic estimator of abnormal clinical episodes using vital sign data from pediatric patients in an ICU. We have shown how different clinical events can be effectively separated using k-means (non-hierarchical) cluster analysis. Also, how such clustering can be used to identify clinical states, which can then be used to define sequences of clinical events that can be used to generate the Markov processes can help the doctor to understand the clinical response that the patient has to the different clinical states individually. HMMs are utilized for learning and classification and We have showed how it can serve multiple purposes in case of abnormality prediction.

This model could be deployed in a hospital monitoring system and can be capable of handling vital sign data from patients with several pathologies.The proposed approach is a valuable contribution to the healthcare industries as they are struggling to meet the demand of increasing population and acute illness.

As a part of ongoing work, we are interested in utilizing this model to predict clinical episodes in big data from vital signs of a large number of patients.

Finally, from this study numerous possibilities for future work arise, such as: more experiments with a larger data set including other pathologies. Also, a validation of the model in a real clinical scenario and environment, confronting the real-time alarm generation and reception of messages being evaluated by the patient's physician, an increase of vital signs in the model, inclusion of specific alarms for each patient.

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