Labor Contraction Prediction via Demographic and Obstetrical Information Analysis

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***Abstract*—Designing an optimal dosing regimen for the systemic opioid remifentanil during labor necessitates the prediction of the pace of contractions, so that the drug can be given shortly before the pain of the contraction begins. The prediction and drug administration should be made early enough to allow for the administration of intravenous analgesia that will have maximal efficacy during contractions and little effect between contractions. Towards such a need, we propose a knowledge-assisted sequential pattern analysis framework to predict the changes in intrauterine pressure, which indicate the occurrence of labor contractions. In particular, a patient selection strategy is proposed to select a group of patients, from the stored record, who share similar demographic and obstetrical information with the current patient of interest. A sequential association rule mining approach is designed to learn the patterns of the contractions from the historical patient tracings, and to determine which demographic and obstetrical features have an impact on the contraction patterns. The promising experimental results show that the proposed framework is effective, robust, and efficient in predicting the labor contraction patterns.**

***Keywords*-predictive models; pattern analysis; labor contraction prediction; association rule mining.**

I. Introduction

Although neuraxial techniques, such as spinal and epidural, are still considered as the gold standard for labor analgesia, there are some parturients who cannot receive neuraxial analgesia because of pre-existing conditions, or who request analgesia other than epidural block. An alternative analgesia is remifentanil, which is a relatively new, very potent and short-acting opioid. It has been shown to be effective in the relief of labor pain, but the reports to date have failed to find the optimal dosing regimen [1]. A challenge to a systemic opioid is that it must match the unique time course of labor pain. A continuous infusion is not ideal, as the parturient experiences no pain between contractions. Moreover, a continuous infusion during times in which the patient does not experience pain may increase the risks of maternal respiratory depression, sedation and nausea. The continuous infusion also increases the amount of the drug to which the fetus is exposed.

The time to peak analgesic effect of a remifentanil bolus usually varies between 60 and 90 seconds [2], and a contraction generally lasts approximately 60 seconds. Thus a remifentanil bolus given at the beginning of a uterine contraction will not give the peak analgesic effect for the contraction for which it is administered. Therefore, if a remifentanil bolus is to be optimally administered, it is necessary to anticipate a forthcoming contraction. This, unfortunately, has been difficult. After a review of the physiology of labor contractions, we appreciate that a pacemaker for contractions has thus far not been found [3], and there is no such factor from the physiological point of view that is able to predict the uterine activities ahead of time. Therefore, an appropriate way for us to approach this problem is to analyze the intrauterine pressure time series, and then undertake the prediction of contractions based on some learned patterns.

The contraction pattern differs from woman to woman, from pregnancy to pregnancy, and also changes in different stages of a woman's labor, which makes it very challenging to accurately perform a prediction. To address the aforementioned challenges, a novel knowledge-assisted sequential pattern prediction framework is developed for predicting the intrauterine pressure multiple seconds ahead in real time. The flowchart of the framework is shown in Fig. 1. In the proposed framework, a group of historical patient tracings (HT) are selected from the stored records of patient information (HI) based on the current patient's demographic and obstetrical information. That is, the selected patients are those who share similar demographic and obstetrical information with the current patient of interest. A sequential association rule-based collaborative training dataset selection method is designed to dynamically select a training dataset from HT and the current patient's own most recent training time series for training the prediction models. A k-nearest neighbors (k-NN) based least squares support vector machine (LS-SVM) approach with heuristic parameter tuning is proposed to conduct long-term time series prediction. After that, a post-prediction process is applied to further enhance the prediction results. Please note that the focus of this paper is on patient selection

based on sequential association rule mining; while the k-NN based LS-SVM approach with heuristic parameter tuning component and the post-prediction process were presented in our previous publications [4] [5], and the details of the sequential association rule-based collaborative training dataset selection component were explained in another paper submission of ours.

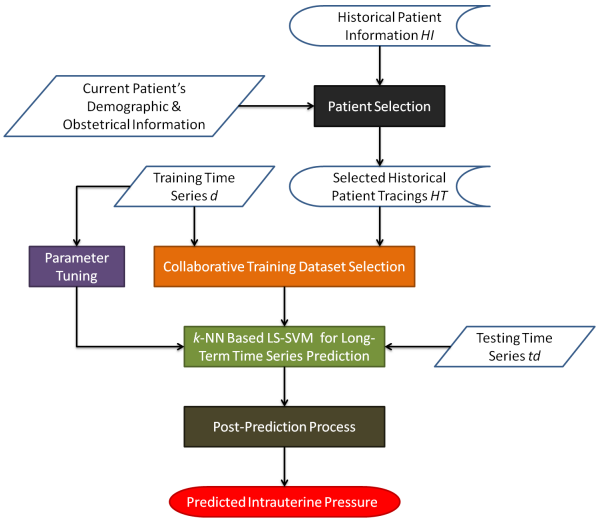

Figure 1. Flowchart of the Proposed Framework

The rest of the paper is organized as follows. Section II presents the sequential association rule mining algorithm. The patient selection component is given in Section III. Experimental results and discussions are shown in Section IV. Section V gives the conclusion of the paper.

II. Sequential Association Rule Mining Algorithm

A contraction can be described by the corresponding peak height and period in the intrauterine pressure tracing. The contraction pattern is determined by the combination of both the height and the period of a contraction. The aim of the proposed sequential association rule mining algorithm is to discover interesting sequential relationships between categorical variables in large databases. The features extracted for contractions are numerical. In order to discover the sequential association relationships among contractions, it is necessary to discretize the features. The equal-width discretization method is adopted here. Table I and Table II show the mapping tables used in the experiments, which are determined based on domain knowledge.

In our sequential association rule mining algorithm, an item is one contraction, and it contains two letters, representing its height and period, respectively. The sequential association rule mining algorithm takes the discretized contraction feature series derived from a group of historical patient tracings as the input, and returns a set of rules as the output.

Table I
Discretization Mapping Table for Height

Height (ht) range (mmHg)	Nominal marker
$ht < 40$	a
$40 \leq ht < 55$	b
$55 \leq ht < 70$	c
$70 \leq ht < 85$	d
$85 \leq ht < 100$	e
$ht \geq 100$	f

Table II
Discretization Mapping Table for Period

Period (pd) range (s)	Nominal marker
$pd < 25$	A
$25 \leq pd < 85$	B
$85 \leq pd < 145$	C
$145 \leq pd < 205$	D
$205 \leq pd < 265$	E
$265 \leq pd < 325$	F
$325 \leq pd < 385$	G
$pd \geq 385$	H

We first search for the frequent sequential itemsets for each individual patient separately, called local frequent sequential itemsets, and then generate the overall sequential itemsets, called global frequent sequential itemsets, based on the local frequent sequential itemsets. Three metrics are defined below to evaluate how interesting a sequential association rule is in the form of $wX \rightarrow yZ$, where w and y are discretized heights, X and Z are discretized periods.

Definition 1: $supL$: the local support. Let N_c be the total number of contractions in one patient's intrauterine pressure tracing. Let $\sigma(wX \cup yZ)$ be the occurrences of the local sequential itemset $wX \cup yZ$. $supL$ is defined in Equation (1).

$$supL(wX \rightarrow yZ) = \frac{\sigma(wX \cup yZ)}{N_c}. \quad (1)$$

Definition 2: $supG$: the global support. Let M be the total number of patients. Let N_p be the number of patients who have the sequential itemset as one of the local frequent itemsets. $supG$ is defined in Equation (2).

$$supG(wX \rightarrow yZ) = \frac{N_p}{M}. \quad (2)$$

Definition 3: PS: PS measure of a rule $wX \rightarrow yZ$, which is derived from a global frequent sequential itemset. Let $P(wX \cup yZ)$ be the probability of $wX \cup yZ$. Let $P(wX)$ and $P(yZ)$ be the probabilities of wX and yZ, respectively. PS is defined in Equation (3).

$$PS(wX \rightarrow yZ) = P(wX \cup yZ) - P(wX)P(yZ). \quad (3)$$

The PS metric was first introduced by [6]. PS is 0 if the variables, wX and yZ, are statistically independent. It is monotonically increasing if the variables occur more often together, and it is monotonically decreasing if one of the variables alone occurs more often. The PS metric is employed here to evaluate the strength of the sequential

association rule. Accordingly, three thresholds should be predefined, which are listed below.

Definition 4: $minSupL$: minimum support for deciding local frequent sequential itemsets. If the frequency of one itemset in one patient's discretized tracing, *i.e.*, $supL$, is no less than $minSupL$, the itemset is considered as a local frequent sequential itemset of the patient.

Definition 5: $minSupG$: minimum support for deciding global frequent sequential itemsets. If the percentage of patients who share one local frequent sequential itemset, *i.e.*, $supG$, is no less than $minSupG$, the itemset is considered as a global frequent sequential itemset of the patient.

Definition 6: $minPS$: minimum PS measure. If the PS measure of a sequential association rule derived from a global frequent sequential itemset is no less than $minPS$, the rule is considered as an interesting rule.

The proposed sequential association rule mining approach contains three steps. First, it generates local frequent sequential itemsets. Given the local support threshold, we first find the items that occur no less than $minSupL$ in each patient's tracing. The set of candidate m-itemsets is generated by connecting the frequent (m-1)-itemsets generated in the previous iteration. We bring in the principle of the Apriori algorithm to reduce the computation cost of the iterations, which is that if an itemset is frequent, all of its subsets must also be frequent. It significantly reduces the number of the generated candidate m-itemsets. If the local support of one candidate m-itemset is no less than $minSupL$, it is recognized as a frequent local m-itemset. For sequential association rule mining, the sequence of the occurrence is important. For example, the 2-itemset 'cAdB' is different from the 2-itemset 'dBcA'. 'cA' represents one contraction, where 'c' specifies the discretized height and 'A' specifies the discretized period. Similarly, 'dB' represents another contraction with height in range 'd' and period in range 'B'.

Second, it generates global frequent sequential itemsets. Combine the local frequent sequential itemsets derived from all the historical patient tracings, and generate candidate global frequent m-itemsets based on local frequent m-itemsets. If the global support of one candidate m-itemset is no less than $minSupG$, it is recognized as a frequent global m-itemset.

Third, it generates sequential association rules from the frequent global itemsets. In this algorithm, only one-item consequent sequential association rules are generated, *i.e.*, one contraction in the consequent part. This is because we are trying to predict the occurrence of the next coming contraction. If the PS measure of one derived rule is no less than $minPS$, it is recognized as an interesting sequential association rule.

The interesting sequential association rules of various lengths form the rule set R. The rules are sorted according to their PS values in the descending order. A larger PS value means that the rule is more interesting, *i.e.*, when the condition part of the rule occurs, the chance of the consequent part occurring as well is higher.

III. Patient Selection

To the best of our knowledge, there are no prior studies that try to analyze how to link demographic or obstetrical features with the uterine contraction pattern in labor. Even though obstetricians have some empirical observations on how the demographic and obstetrical features impact the uterine contraction pattern, a systemic and theoretical study is challenging due to the difficulties in formulating the problem. A sequential pattern analysis on intrauterine pressure tracings provides a way to characterize the pattern of contractions. This enables the analysis on whether and how the demographic and obstetrical features impact the sequential uterine contraction pattern.

Based on domain knowledge, we summarize some demographic and obstetrical features that might have some impacts on the uterine contraction pattern in labor. The features include maternal age, body mass index (BMI), gestational age, number of pregnancies, living children pregnancy history, labor anesthesia, and indication of oxytocin.

- The maternal age is a numerical value, and it is stored as an integer. The maternal age determines the contractility of the muscles, so it might influence the uterine contraction pattern.
- The BMI is a heuristic proxy for human body fat based on an individual's weight and height. The BMI is a numerical value as well.
- The gestational age is defined as the time elapsed since 14 days prior to fertilization, and it is recorded in terms of the number of weeks.
- The number of pregnancies means the number of babies that the parturient is carrying.
- The living children pregnancy history indicates if the woman has ever given birth before. We differentiate the multiparous from the primiparous.
- For labor anesthesia, most of the women in the study have chosen epidural, and some other chose anesthesia other than epidural, for example, intravenous sedation or no anesthesia.
- Oxytocin can be used for induction or labor augmentation. The amount of oxytocin for induction is much larger than it is for augmentation. Oxytocin promotes and accelerates uterine contraction.

We divide the patients into several groups with different ranges of values for one feature, and then analyze the sequential uterine contraction pattern of each group. If the sequential uterine contraction patterns of these groups are different, it means that this feature has a strong impact or determines the sequential uterine contraction pattern. Thus the feature is kept for grouping the patients for later analysis;

otherwise, the feature is discarded. This process is repeated for each of the considered features.

Based on the analysis on 611 patients' records, we observe that maternal age, gestational age, labor anesthesia, and indication of oxytocin have an impact on the sequential uterine contraction pattern, and the impact is more significant than the rest of the features. We use three of the chosen features to construct a tree (as shown in Fig. 2) to classify the patients in historical patient information HI into 7 groups. The three chosen features are gestational age, labor anesthesia, and indication of oxytocin.

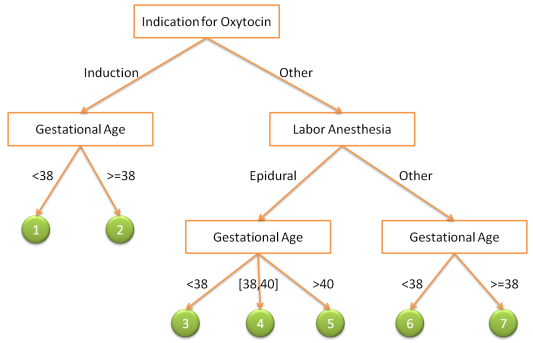

Figure 2. A Tree for Patient Selection

A large amount of oxytocin alters how frequently the uterus contracts. The retrieved sequential uterine contraction patterns are significantly different. Therefore, we choose indication for oxytocin as the root node to separate the patients who had induction from the patients who gave natural birth. For patients who did not experience induction, labor anesthesia is used to differentiate the patients who had epidural from the patients who had analgesic other than epidural. For induced labor, it usually takes a longer time. All the patients who had induced labor chose to have epidural. Therefore, we omit the labor anesthesia node in the left branch. We further divide the groups by gestational age to differentiate pre-term labor (gestational age < 38) from term and post-term labor (gestational age ≥ 38). For patients who gave natural birth and had epidural (majority of patients are in this case), we also separate term labor ($38 \leq$ gestational age ≤ 40) from post-term labor (gestational age > 40). Accordingly, we can divide the patients into 7 groups based on this built tree.

The inputs of the patient selection component are historical patient information HI and the current patient's demographic and obstetrical information. HI includes multiple past patients' preprocessed intrauterine pressure time series and their demographic and obstetrical information. The patients in HI are divided into 7 groups using the tree shown in Fig. 2. The output is the selected historical patient tracings HT. The purpose of patient selection is to select those patients who share similar demographic and obstetrical features with the current patient of interest. Based on our analysis, the chosen demographic and obstetrical features have a strong impact on the sequential contraction patterns.

First, we determine which group the current patient should belong to according to her gestational age, labor anesthesia, and indication of oxytocin using the tree in Fig. 2. Let the current patient belong to group i, where $1 \leq i \leq 7$. Second, select $nPatient$ patients from group i whose age are closest to the current patient's age. Thus, four features in total are used in this selection, which are maternal age, gestational age, labor anesthesia, and indication of oxytocin. The selected patients' intrauterine tracings are the output of this component, and are passed to collaborative training dataset selection component as one of its inputs to form a training dataset for building the prediction models.

IV. Experimental Results

To demonstrate the merits of the proposed framework, we present the experimental results on multiple de-identified labor tracings. We compare with four existing methods, namely LL-MIMO [7], LS-SVM [8] [9], AR [10], and autoregressive moving average (ARMA) [11]. We employ $RMSE$ (defined in Section IV-B) to evaluate the performance of the algorithms. In addition, the purpose of the proposed framework is to predict the starting points of the coming contractions, so as to give the signal for analgesia injection ahead of time to relieve the labor pain. Therefore, a criterion is proposed in Section IV-B to evaluate the prediction accuracy of the starting point.

A. Dataset

We received de-identified pressure data files of 8460 women who gave birth between April 2010 and September 2011. Each patient's tracing is stored in a single file. In each file, there is a matrix with interleaved rows representing intrauterine pressure data and baby's heart rate. The first cell of each row contains the day and time information. The second cell specifies if the row contains 'UA' (uterine activity) or 'HR2' (heart rate) data. The third cell specifies the type/method/status of the measurement, such as 'IUP' for intrauterine pressure and 'TOCO' for external uterine pressure. The remainder of the row, a total of 240 cells, contains the numerical data corresponding to one-minute record.

The uterine pressure signal collected externally is usually contaminated by lots of noise. In contrast, the 'IUP' signal is collected internally, which has a much clearer contraction pattern as compared to the 'TOCO' signal. Therefore, we only consider 'IUP' signals at this stage. The intrauterine pressure measure is an invasive measurement, and it can be applied only after rupture of the membranes. Most of the files we received do not contain 'IUP' signals, because those data were collected externally using a tocodynamometer. Out of the 8460 files, 2422 files contain 'IUP' signals, but some of them are shorter than 30 minutes, which are too short for

the useful analysis. We select 611 women's 'IUP' tracings, together with their demographic and obstetrical information, to form the historical patient information HI. We randomly select 11 patients' records for testing. The selected tracings, either for training or for testing, contain a sequence of recognizable peaks.

B. Framework Evaluation Criteria

We employ an error measurement, root mean squared error ($RMSE$), to evaluate the performance of the prediction models,. Let X be the real time series, and $\overline{X}$ be the predicted time series obtained at prediction horizon n. The length of both X and $\overline{X}$ is m. $RMSE$ is the square root of the variance, which is defined in Equation (4). $RMSE$ is closely related to the value range of the time series data.

$$RMSE = \sqrt{\frac{\sum_{t=1}^{m} (x_t - \overline{x}_t)^2}{m}}. \quad (4)$$

We also conducted comparison experiments to evaluate the abilities of the prediction models in predicting the starting points of the contractions. Each of the testing time series contains more than one contraction. The prediction for each contraction is assigned an accuracy weight based on the distance between the predicted starting point and the true starting point of the contraction, and then the average of the weights for all the contractions in a testing time series is calculated as the accuracy measure. Table III shows the weights for different distance ranges, which are defined based on domain knowledge and empirical studies.

Table III
WEIGHT DISTANCE MAPPING TABLE

Distance (de) (s)	Weight
$0 \leq de < 10$	1
$10 \leq de < 20$	0.8
$20 \leq de < 30$	0.6
$30 \leq de < 40$	0.4
$40 \leq de < 50$	0.2
$de \geq 50$	0

For the error measurement ($RMSE$), when the values are smaller, the prediction models perform better. Contrarily, for the accuracy measurement, when the values are larger, the prediction models perform better.

C. Experiment and Results

An intrauterine time series is subsampled once every second during the data-preprocessing step. The onset of the remifentanil's effect is approximately 30 seconds, so the prediction should be made approximately 30 seconds ahead of the next contraction to accurately match the effect of analgesia. Accordingly, we set the prediction horizon to 30. In addition, we set $minSupL$, $minSupG$, and $minPS$ to 0.03, 0.1, and 0.01, respectively for the sequential association rule mining process. These thresholds can be adjusted if we get more patient tracings or a different set of patient tracings in the selected historical patient tracings HT.

Table IV
EXPERIMENTAL RESULTS IN TERMS OF ROOT MEAN SQUARED ERROR

Patient ID	LL-MIMO	LS-SVM	AR	ARMA	Proposed Framework
1	16.61	10.28	16.60	13.36	**8.11**
2	16.98	11.12	21.81	10.72	**10.27**
3	15.99	12.16	20.36	18.03	**9.83**
4	10.87	6.78	14.12	8.41	**5.79**
5	15.66	11.43	19.03	18.49	**9.98**
6	15.67	11.04	19.07	15.76	**8.45**
7	21.98	15.76	26.57	22.05	**13.74**
8	20.24	16.07	28.28	15.64	**15.17**
9	15.99	10.46	22.78	11.37	**9.21**
10	25.82	19.28	33.19	20.98	**16.08**
11	12.67	8.69	14.93	14.37	**8.17**

The comparison results are shown in Table IV in terms of $RMSE$. As we can see from the results, the proposed approach achieves the lowest prediction error in terms of $RMSE$. The experimental results show that the proposed framework is superior to the compared four methods, on average 64.2%, 15.9%, 106.2%, and 51.3% better in terms of $RMSE$ than LL-MIMO, LS-SVM, AR, and ARMA, respectively. The intrauterine pressure time series are rather dynamic and complex, thus we do not expect the prediction error to be 0.

Not every model that works for short-term time series prediction would work well for long-term prediction. The long-term time series prediction is a much more challenging task due to the ever-changing labor contraction pattern. LL-MIMO is a simple and low computational cost algorithm. It predicts the future values by calculating the average of the training instances. LL-MIMO does not train a model to describe the inherent relationship between inputs and outputs, and its prediction ability is very limited as analyzed above.

The LS-SVM method gives fair prediction results, but it is computationally expensive due to using a large training dataset and complex computing. On average, it takes 20.4 seconds to perform a single 30 seconds-ahead prediction using LS-SVM, while it only takes 1.0 second for the proposed framework, which is about 19 times faster than LS-SVM. Therefore, LS-SVM is not applicable for real-time prediction, even though it gives better prediction than LL-MIMO.

The autoregressive model is a linear prediction method that attempts to predict the next value based on the previous observations. Because of its linear nature, it is not able to achieve good prediction precision if the time series contains non-linear components. In the case of long-term time series prediction, the mapping function is usually non-linear. Therefore, the autoregressive model is not preferable. The

prediction errors of AR are usually the highest among the compared algorithms. Comparing to AR, ARMA includes a moving average part, which incorporates the prediction error to build the prediction model. This makes ARMA more capable and faster in following a time series trend. It can be also observed from Table IV that ARMA always outperforms AR.

We include some plots of the predicted intrauterine pressure time series together with the original tracings in Fig. 3 and Fig. 4 to demonstrate the prediction performance of the complete proposed framework. The accuracy for each tracing is included in the title of the plot. Due to the space limit, we are not able to show the results for all the testing cases. It can be observed that the prediction is able to anticipate and preserve the trend of the intrauterine pressure. High accuracies demonstrate that the proposed framework is capable of predicting the start of the upcoming contractions consistently.

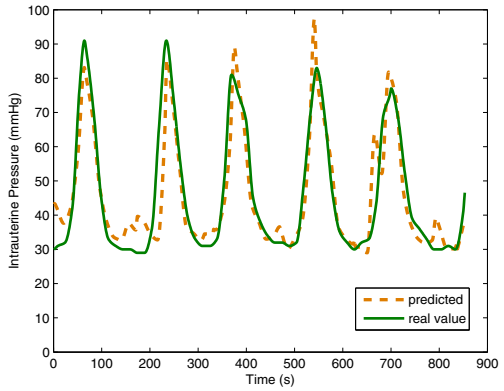

Figure 3. Prediction Results for Patient 1 (Accuracy = 0.92)

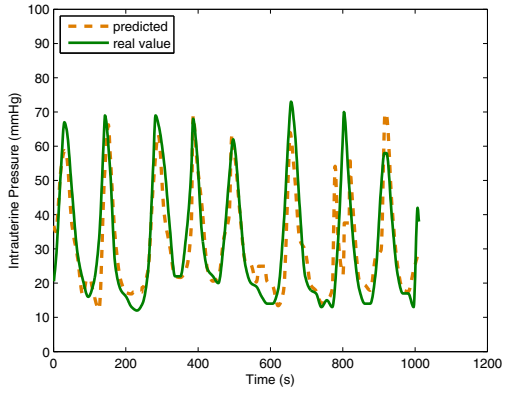

Figure 4. Prediction Results for Patient 2 (Accuracy = 0.91)

V. Conclusion

In this paper, we propose a solution to tackle the difficult task of predicting the timing of the upcoming labor contractions. The framework reveals interesting sequential patterns in the intrauterine pressure sequences, which we employ to assist contraction prediction by selecting patients to train the prediction model via demographic and obstetrical information analysis. The prediction accuracy is essential in order to maximize the effect and minimize the side effect profile of remifentanil. The experimental results have shown that the proposed framework outperforms some existing methods in both $RMSE$ and prediction accuracy.

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