PRECONDITIONING OF MEASUREMENT DATA FOR THE ELIMINATION OF PATIENT–SPECIFIC BEHAVIOR IN QUALITATIVE MODELING OF MEDICAL SYSTEMS

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ABSTRACT

A major problem in the biomedical domain is knowledge generalization. Is knowledge acquired from and about one patient at all applicable to another, and if so, to what extent? Can an inductive qualitative model acquired by analyzing data retrieved from one patient be used to predict the behavior of another? The purpose of this paper is to discuss these questions in the context of a qualitative modeling and simulation methodology entitled *fuzzy inductive reasoning.*

To this end, a technique based on combining knowledge obtained from different patients is presented in this paper that makes it possible to derive a single model characterizing a specific class of similar patients undergoing similar operations. Data streams stemming from different patients are grouped together, separated by segments of "missing data" in order to prevent the creation of fake causal relationships at the seam between neighboring data streams in the concatenated data set.

A medical application relating to the control of a specific anaesthetic agent administered to patients undergoing surgery is used to demonstrate the feasibility of this method. Two data streams stemming from two different patients undergoing different operations were used to obtain a single model identifying a similar patient/operation class.

It will be shown that the predictions obtained by this common model are not as good as those obtained from each patient alone using patient–specific models. This is reasonable and characteristic of all knowledge generalization schemes. However, the results obtained are still significant and useful for medical advice in the operating theater.

INTRODUCTION

Qualitative reasoning is currently an area of much interest in the research community. Different qualitative methodologies have been developed over the past two decades, including expert systems, inductive reasoning, neural networks, qualitative physics, discrete–event systems, and fuzzy systems.

An important area where these methodologies may play an essential role are the soft sciences, such as biomedicine, economy, and psychology. The underlying laws that govern the behavior of systems from such application areas are usually imprecisely known or totally unknown. Therefore, it is very difficult and in most cases even impossible to obtain a precise mathematical model identifying the dynamic behavior of such systems.

This is particularly true in many biomedical applications where the only knowledge of the system dynamics available is that learned by medical doctors through personal experience. However, this knowledge is difficult to communicate since it is not codified. It is therefore a worthwhile task to seek mathematical tools that promote the codification of qualitative medical knowledge for the purpose of better communication. Knowledge codified in this manner is commonly referred to as a qualitative model. The test by which the success of qualitative modeling is assessed is by measuring the predictive power of the model, ascertained by means of qualitative simulation.

One problem that researchers in biomedicine are often faced with is the large variability in individual patient behavior. Is knowledge acquired from and about one patient at all applicable to another, and if so, to what extent? Can an inductive qualitative model acquired by analyzing data retrieved from one patient be used to predict the behavior of another? It is this question that is at the heart of this paper.

This paper focuses on the preconditioning of biomedical data to eliminate patient–specific behavior. In most biomedical applications, such as, for instance, the control of depth of anaesthesia of a patient undergoing surgery, it is extremely useful to have available a model that identifies not only the behavior of one concrete patient on a specific day during a specific operation, but one that is able to capture the behavior of a class of similar patients undergoing similar operations. The definition of what makes different patients or operations similar is left to the medical experts.

It does not make practical sense, from a medical point of view, to first have to identify a model for a given patient during surgery to be able to predict his or her behavior at some later time. A reliable model must be ready for use before surgery begins. It is therefore important to be able to synthesize a generic model that is valid for a specific type of patient undergoing a given kind of surgery.

THE METHODOLOGY

For this porpose, a qualitative modeling methodology called *Fuzzy Inductive Reasoning* has been proposed. The inductive reasoning methodology had originally been developed by G. Klir (Klir 1985) as a tool for general system analysis to study the conceptual modes of behavior of systems. One implementation of this methodology is SAPS–II (Cellier and Yandell 1987). Fuzzy measures were introduced into the methodology independently by (Klir and Folger 1988; Klir 1989; Wang and Klir 1992) and by (Li and Cellier 1990). Even more recently, SAPS–II has been propagated as a tool for qualitatively studying the behavior of highly complex non–linear technical systems (Cellier et al. 1992; de Albornoz and Cellier 1993a, 1993b) as well as biomedical systems (Nebot et al. 1993).

In the fuzzy inductive reasoning approach, qualitative systems are represented (modeled) through finite state machines that are automatically derived by means of so–called *optimal masks*, and their episodical behavior is inferred (simulated) using a technique called *fuzzy forecasting*.

A mask denotes a structural relationship between different variables, and the optimal mask is the mask that maximizes the forecasting power of the inductive reasoning process. The optimal mask is selected from a set of candidate masks by a process of exhaustive search. The quality (forecasting power) of each mask is evaluated, and the one with the highest quality is returned as the optimal mask.

Once the optimal mask is found, it is possible to derive a state transition matrix from the optimal mask and the available data. The state transition matrix is a finite–state machine that lists, for each input state (i.e., each combination of input values), all possible output states together with an assessment of the likelihood of their occurrences. Once the state transition matrix has been found, a qualitative simulation can be performed by applying the *forecasting* function of the inductive reasoning methodology.

For a deeper insight into this methodology, the reader is referred to (Cellier 1991), (Cellier et al. 1992), (Cellier and Yandell 1987), and (Li and Cellier 1990).

In order to be able to combine two or more patient data sets, a new feature called *missing data option* has been used. Only complete data records are used in the computation of the state transition matrix, whereas contaminated data records are ignored. The missing data feature enables the researcher to work with sets of incomplete data (very common in biomedical systems), and extract as much information from them as they contain. The feature makes it possible to convert incomplete quantitative data sets to reduced qualitative data sets in order to derive the best possible qualitative model for prediction of future system behavior. The missing data option is described in detail in (Nebot and Cellier 1994).

This option is essential for combining data stemming from different patients for the purpose of desensitizing the derived qualitative model to patient–specific characteristics of the observed data streams. Since the research focuses on models of dynamic behavior, the advocated methodology searches for causal relationships between variables measured at different points in time. Therefore, if the data set stemming from one patient is placed immediately adjacent to the data set stemming from another patient, fake causal relationships are created at the seam on the two data streams. These fake relationships can cause a severe degradation of the forecasting power of the derived qualitative model. The solution is to add gaps of "missing data" between neighboring data streams stemming from different patients, thereby preventing the methodology from extracting from the combined data set contaminated data records containing mixed information from different data sources.

An important factor to take into account when different patients' data sets are combined is the normalization of the data. Usually, different patients will have different DC values for each variable. Therefore, if data stemming from such patients are to be combined, it is necessary to normalize the data. This process is called *prefiltering* of the data. Both linear and nonlinear prefiltering procedures are known, but only linear prefiltering should be applied in order to prevent a degradation of the relevant correlation functions (Nebot et al. 1994). In this paper, the mean value of each variable is subtracted from all elements of the corresponding trajectory. This simple normalization procedure is applied to the data of each patient separately, prior to concatenating the two data records.

In order to improve the quality of the prediction and reduce the risk of coming up with entirely incorrect forecast values, a *voting procedure* is adopted. Instead of working with a single optimal mask, as was done in earlier papers, the three best masks are evaluated, and three different state transition matrices are obtained. In the forecasting process, three separate forecasts are obtained using the three state transition matrices.

Let M_a, M_b, and M_c be the three best masks. Each of these masks leads to a different forecast. Let them be called F_a, F_b, and F_c. Three distance measures are computed in the following way:

$$D_a = abs(F_a - F_b) + abs(F_a - F_c) \qquad (1)$$
$$D_b = abs(F_b - F_a) + abs(F_b - F_c) \qquad (2)$$
$$D_c = abs(F_c - F_a) + abs(F_c - F_b) \qquad (3)$$

Once the distance measures have been computed, the predicted value with the largest distance measure is refused. The new forcast value will be the mean value of the two predicted points obtained with the two remaining masks. For instance, if $D_b > D_a$ and $D_b > D_c$, then forecast F_b is rejected, and the new forecast is computed as:

$$F = \frac{Fa + Fc}{2} \tag{4}$$

This technique offers a systematic way to compute predictions for all patients in the patient/operation class. In the next section, the technique is used in a biomedical application.

AN APPLICATION

The efficiency of the advocated technique is being demonstrated by means of an application from anaesthesiology. The techique is applied to a biomedical system for predicting the right value of an anaesthetic agent to be administered to patients during surgery. The control of depth of anaesthesia is a difficult undertaking. The use of anaesthetic agents can produce severe complications and side effects, which, under extreme conditions, may even cause the death of the patient. It is therefore essential that the dose of anaesthetic agents is limited to the minimum amount necessary for proper anaesthesia thereby reducing undesired side effects and minimizing the risk to the patient.

Two different data streams stemming from two different patients undergoing different types of surgery were analyzed. One data stream was obtained from a male patient 35 years of age weighing 50 kilograms undergoing a renal transplant operation. The other data set was obtained from another male patient 57 years of age weighing 75 kilograms undergoing abdominal–perineal resection surgery.

For both patients, the clinical variables comprising heart rate (HR), respiration rate (RR), and systolic arterial pressure (SAP) of the patient were selected as the key clinical indicator signals to be used for suggesting an anaesthetic dose ($Dose$), i.e., the control signal. The controller model is determined by the qualitative relationship between its three input variables: SAP, HR, and RR; and its single output variable: $Dose$.

SAP ——→
HR ——→ Controller Model ——→ Dose
RR ——→
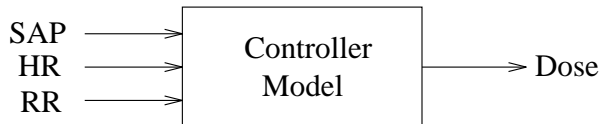
In a previous publication, (Nebot et al. 1993), separate qualitative models for the two patients had been obtained:

For the first patient, the model (optimal mask) obtained was the following:

$$
\begin{array}{c|cccc}
t\backslash^x & SAP & HR & RR & Dose \\
t-20\delta t & 0 & 0 & 0 & 0 \\
t-19\delta t & 0 & 0 & 0 & 0 \\
\vdots & \vdots & \vdots & \vdots & \vdots \\
t-11\delta t & 0 & 0 & 0 & 0 \\
t-10\delta t & 0 & 0 & 0 & -1 \\
t-9\delta t & 0 & 0 & 0 & 0 \\
\vdots & \vdots & \vdots & \vdots & \vdots \\
t-\delta t & 0 & 0 & 0 & 0 \\
t & -2 & 0 & 0 & +1
\end{array}
\tag{5}
$$

This mask denotes the relationship:

$$Dose(t) = \tilde{f}(Dose(t-10\delta t), SAP(t)) \tag{6}$$

For the second patient, the optimal mask obtained was:

$$
\begin{array}{c|cccc}
t\backslash^x & SAP & HR & RR & Dose \\
t-20\delta t & 0 & 0 & 0 & 0 \\
t-19\delta t & 0 & 0 & 0 & 0 \\
\vdots & \vdots & \vdots & \vdots & \vdots \\
t-11\delta t & 0 & 0 & 0 & 0 \\
t-10\delta t & -1 & 0 & 0 & -2 \\
t-9\delta t & 0 & 0 & 0 & 0 \\
\vdots & \vdots & \vdots & \vdots & \vdots \\
t-\delta t & 0 & 0 & 0 & 0 \\
t & 0 & -3 & 0 & +1
\end{array}
\tag{7}
$$

which denotes the relationship:

$$Dose(t) = \tilde{f}(SAP(t-10\delta t), Dose(t-10\delta t), HR(t)) \tag{8}$$

As can be seen, the obtained qualitative models were distinct, and it had not been possible at that time to apply either of the two qualitative models to the other patient and obtain meaningful predictions of that patient's future behavior.

Therefore, it was decided to combine the data from the two patients in order to extract a set of models that are able to offer acceptable predictions for both patients. The two individual data sets contain 325 and 369 records, respectively. A gap of 40 "missing values" were inserted connecting the two data sets. Consequently, a single data set of 734 values resulted to be used in identifying a set of three suboptimal masks.

```
      Patient A        Miss_data       Patient B
|------------------| |*********| |------------------|
1               325  1       40  1               369
```

As was to be expected, the DC values of the data sets from the two patients were different, thus, it was necessary to normalize the data in the manner previously described.

At this point, the data is ready to start the model identification process. To this end, it is required to recode the data into qualitative variables. It was decided to recode (discretize) the variables SAP, HR, and $Dose$ into three qualitative levels (classes), whereas RR was recoded into two qualitative levels only.

The first 291 rows of patient A combined with the gap of "missing values" together with the first 335 rows of patient B were used as past history data to compute the optimal mask.

```
Past history data:


     Patient A        Miss_data       Patient B
|------------------||**********||------------------|
1                291 1        40 1                334
```

Fuzzy forecasting is used to predict new qualitative class and fuzzy membership values for variable $Dose$ for the last 34 rows of each patient.

The optimal mask obtained for the combined data set was the following:

$$
\begin{array}{c}
t\backslash^x \\
t-20\delta t \\
t-19\delta t \\
\vdots \\
t-11\delta t \\
t-10\delta t \\
t-9\delta t \\
\vdots \\
t-\delta t \\
t
\end{array}
\begin{array}{cccc}
SAP & HR & RR & Dose \\
\left(\begin{array}{cccc}
0 & -1 & 0 & 0 \\
0 & 0 & 0 & 0 \\
\vdots & \vdots & \vdots & \vdots \\
0 & 0 & 0 & 0 \\
0 & 0 & 0 & -2 \\
0 & 0 & 0 & 0 \\
\vdots & \vdots & \vdots & \vdots \\
0 & 0 & 0 & 0 \\
-3 & 0 & 0 & +1
\end{array}\right)
\end{array}
\quad (9)
$$

This mask denotes the relationship:

$$
Dose(t) = \tilde{f}(HR(t-20\delta t), Dose(t-10\delta t), SAP(t)) \quad (10)
$$

It turns out that the prediction obtained using this optimal mask alone is not good enough, and therefore, the previously described voting method had to be used.

To this end, a set of three suboptimal masks needs to be defined. One of the three masks is the optimal mask obtained for the combined data set. The other two masks could be chosen as suboptimal masks from the mask history. However, a different approach was taken. The second mask was

obtained using "common sense." It has been shown that the two optimal masks obtained for the two patient data sets separately were different. Whereas one reaches the best forecast for patient A, the other does the same for patient B. However, neither of them gave acceptable results for the other patient. It makes sense to think that if the input patterns of the two masks are combined, a good forecast for both patients could be encountered. Following this reasoning, the second mask was constructed:

$$
\begin{array}{c}
t\backslash^x \\
t-20\delta t \\
t-19\delta t \\
\vdots \\
t-11\delta t \\
t-10\delta t \\
t-9\delta t \\
\vdots \\
t-\delta t \\
t
\end{array}
\begin{array}{cccc}
SAP & HR & RR & Dose \\
\left(\begin{array}{cccc}
0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 \\
\vdots & \vdots & \vdots & \vdots \\
0 & 0 & 0 & 0 \\
-1 & 0 & 0 & -2 \\
0 & 0 & 0 & 0 \\
\vdots & \vdots & \vdots & \vdots \\
0 & 0 & 0 & 0 \\
-3 & -4 & 0 & +1
\end{array}\right)
\end{array}
\quad (11)
$$

This mask denotes the relationship:

$$
Dose(t) = \tilde{f}(SAP(t-10\delta t), Dose(t-10\delta t), SAP(t), HR(t)) \quad (12)
$$

This mask, when used alone gives worse results than the previous one, but in concert with the other two voting masks, it may be acceptable.

Finally, the optimal mask obtained for the second patient when the two data sets were treated separately was chosen as the third mask in the voting set.

The forecasting results for the two data sets using the voting scheme are shown in Figure 1.
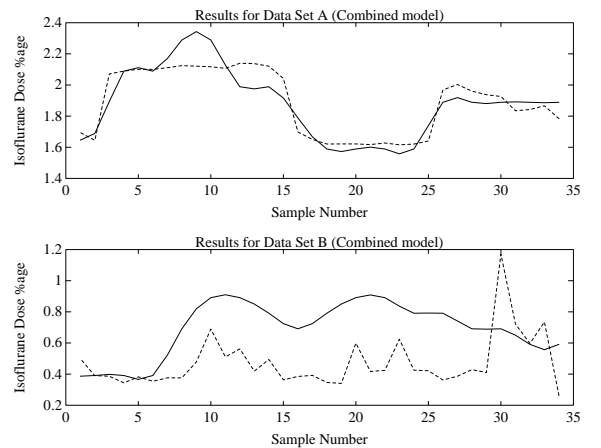

Figure 1: Prediction results using combined models

As can be seen, the prediction curve follows the real curve
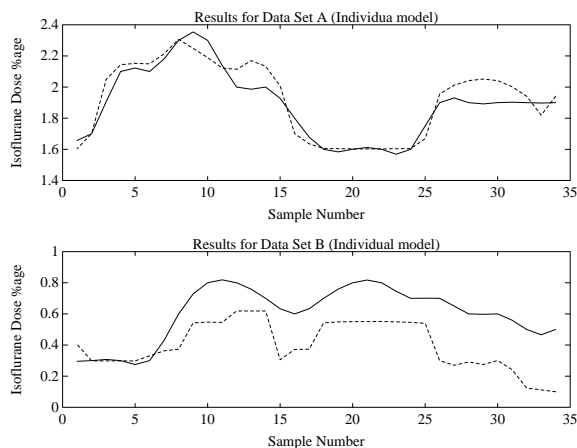
Figure 2: Prediction results using individual models

in an acceptable way. The predictions are not as good as those obtained from the individual models, shown in figure 2, but they are clinically meaningful.

Computing the least square error of the predictions for the two patients, the following results are obtained:

- The forecast *Dose* to be applied to patient A when the individual model is used has an error of 0.4886, whereas the error is 0.5449 when the combined model is used.

- The forecast *Dose* to be applied to patient B when the individual model is used has an error of 1.4156, whereas the error is of 1.8224 when the combined model is used.

Therefore, it is clear that the predictive power has decreased, but not to an unacceptably large extent.

CONCLUSIONS

This paper presents a systematic way for processing medical information obtained from different patients undergoing similar operations. The measured data streams stemming from different patients/operations are combined in such a way as to allow the synthesis of a common model that can be used for an entire class of similar patients undergoing similar types of surgery.

Using the fuzzy inductive reasoning methodology augmented by the missing data option, it has now become feasible to generate a single qualitative model that can be used to predict the future behavior of patients within an entire class of similar patient/operation pairs. The predictions are not as good as those obtained from individual models, but they are still clinically meaningful. Moreover, the new technique carries a potential for *knowledge generalization*, a desirable property lacking in the approach used earlier.

A quantification of the degradation of the predictive power of the combined model relative to the individual models was

also presented in this paper.

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