DESIGNING A MODEL TO ESTIMATE THE SEVOFLURANE DOSE FOR A PATIENT UNDER THE GENERAL ANAESTHESIA BY USING ADAPTIVE-NETWORK-BASED FUZZY INFERENCE SYSTEM

Umit TAS, PhD
Uskudar University/Istanbul, Turkey

Abstract

The field of Depth of Anaesthesia (DOA) is a very challenging area for neuro-fuzzy control since direct measurements are unavailable. During anaesthesia, the blood pressures (BP), the mean arterial blood pressure (MAP) and the heart rate (HR) are monitored to maintain hemodynamic stability and to assess the level of consciousness. The purpose of this study is to find the best input-output definitions in the Adaptive-Network-based Fuzzy Inference System (ANFIS) to control the Sevoflurane dose to patient under the general anaesthesia with the classical MAP and HR parameters. The best models have been found among many possible input combinations. This study helps to provide an alternate control for the dose of Sevoflurane which is widely used as an anaesthetic agent. The models have been trained and validated by clinical data. The results show that the patients can be modelled by ANFIS if sufficient HR and MAP data are provided. Furthermore, the model performance could be increased if the patients are grouped as adults and children. The performance (up to 0.99) in this study is comparable to recent works in similar subject which detect DOA by Electroencephalograms (EEG).

Keywords: ANFIS, sevoflurane, general anaesthesia, patient model, DOA

Introduction:

In an intensive care unit or a surgical arena, anaesthesiologists are responsible for maintaining all their patients' vital signs including mean arterial pressure (MAP), cardiac output (CO), carbon dioxide and oxygen levels, blood acidity, fluid levels, heart contractility and renal function. Many of these states do not have a direct measurement and must be inferred. These physiological states are maintained within acceptable ranges by infusing

drugs and/or intravenous fluids (Ramesh, 2003). In order to maintain these vital signs, some techniques were developed in the past by several research groups using hemodynamic variables, mean arterial pressure and cardiac outputs. In these types of the controllers:

1. The physician specifies a value or range for a vital sign along with drug infusion rate limits,
2. he/she decides what initial drug infusion rates should be used for a patient,
3. the controller takes that information and regulates the vital sign,
4. the physician monitors the control performance and has more time to evaluate the patient.

In the last decade, the modelling techniques including the fuzzy and neural approaches were applied to represent the dynamism of the various physiological systems such as Heart Disease Diagnosis (Adeli, 2010), building a gene interaction model that identifies triplets of activators, repressors and targets in gene expression data (Ressom, 2005), short-term prediction of heart rate variability in the neurological intensive care unit (McNamee, 2005), controlling of blood glucose in the critical diabetic patient (Dazzia, 2001), continuously modelling emotion using physiological data (Mandryk, 2007), Intelligent managing of wearable applications in rehabilitation (Wang, 2005).

The main idea of the AI based modelling is to develop a model by using human experience and available real data. The steps are:

1. deciding to the relevant inputs and outputs,
2. getting the past human experience and collecting the real system data,
3. training the model by using experiences and data,
4. testing and proving the model by using the real data.

In this context, ANFIS, since its being a class of adaptive network and its having got minimal restrictions on system modelling, it was employed directly in a wide variety of applications. Such an approach has been implemented in this study to develop a model in order to estimate the sevoflurane dose for a patient under the general anaesthesia.

In the past, deciding the depth of anaesthesia (DOA) under the general anaesthesia had been started by monitoring blood pressure (BP), heart-rate (HR), pupil diameter, sweating and so on. Linken DA describes the structure of a real-time measuring system based on fuzzy logic (Linkens, 2002). In his study, the system uses neuro-fuzzy and multiresolution wavelet analysis for monitoring the DOA based on AEP (Auditory Evoked Potentials). He claims that successful management of DOA has been achieved. Recently, some algorithms were developed by using EEG or Bispectral Index (BIS) (Tosun, 2012). Esmaeili and his team reports that

they successfully classified Depth of Anaesthesia using EEG features (Esmaeili, 2007).

We observe that EEG monitoring for DOA in the Operation Rooms (OR) is not as easy as BP and HR monitoring. EEG-based methods may be widely used for estimating the anaesthetic depth in the research areas, but still it doesn't have a common use in OR. The extra work load, the cost of disposable BIS electrodes and less knowledge about BIS signal decoding are some of the reasons for less usage. In the literature, still there are some suspicions for reliability of BIS that it may be affected by some muscle harmonics which are in the same frequency spectrum with some of the BIS signals (Dressler, 2004).

Here, the study steps are:

1. collect the real data from the patients,
2. classify data,
3. develop a neuro-fuzzy model by using these data.

I hope that this study makes a contribution to develop anaesthesia machines' providing an automation in order to help the anaesthesiologists and keep the patient's vital signs more easily.

A general model for a dynamic system is shown in Figure 1.

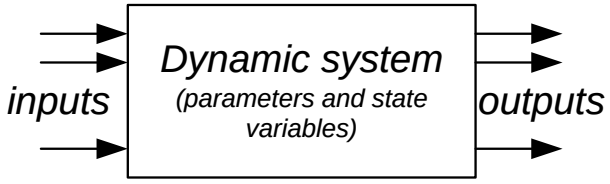


Figure 1. A general model of a dynamic system (Shearer, 1997)

The section named 'Materials and Methods' explains the Materials and Methods that are used in the modelling. The modelling method is divided into 2 sub-methods depending on whether the training and testing data are selected randomly from whole dataset or some of the patient's data are chosen as the training set while the other is the testing. The section named 'Conclusion' summarizes this study and gives the results.

I believe that by using traditional parameters such as BP and HR, we still have a good monitoring opportunity to estimate DOA and to decide the sevoflurane dose in order to keep the patient in desired situation.

Materials and Methods

Training and testing of the developed models have been performed by observed physiological system data obtained from different patients during anaesthetic conditions in the operation theatres of the hospital of the Faculty of Medicine of King Abdulaziz University in Jeddah- Saudi Arabia. The ethical committee permission has been obtained for all the patients.

American Society of Anaesthesiologists (ASA) grade is the most commonly used grading system for anaesthesia and surgery. Medical co-morbidity increases the risk associated with anaesthesia and surgery. ASA accurately predicts morbidity and mortality.

ASA Grade I: Normal healthy individual ASA Grade II: Mild systemic disease that does not limit activity.

46 patients, having ASA grade I and II. (Mostly Ear-Nose-Throat (E.N.T.) patients and few Bone and Stomach patients have been selected. Classifications are as below:

Female patients:
Age: 2y-11y; number of patient: 9
Age: 20y-73y; number of patient: 12
Female age mean: 23.05
Female age SD : 19.91
Male patients:
Age: 1y-13y; number of patient: 13
Age: 22y-72y; number of patient: 12
Male age mean: 24.5
Male age SD : 23.3

All the patients were premedicated with propofol, fentanyl(pain killer), muscle relaxants and steroids according to their weights and ages. Anaesthesia was maintained with an inhalation gas (Sevoflurane) for 28 patients out of 46. In this study, the purpose of propofol usage at the beginning is to provide quick unconsciousness and to remove the patient reactions during the face mask placing. Because, the induce time for propofol is few seconds but the induce-time for Sevoflurane is few minutes (3-6min).

Note that, the propofol and fentanyl have the effects on the BP and HR. It means, BP and HR measurements in certain steps, reflect the combined effects of Sevoflurane and propofol and fentanyl. Unfortunately, we were not able to track the time and dose information about other medications except anaesthetic agents during the operation. So, this study results should be considered under these constraints. However, by using data averaging, the short time reflections of these medications on BP and HR were eliminated or at least minimized.

In OR, the Drager-Zeus anesthesia machine was used. All the data were collected through the serial port. We developed a special software in MATLAB environment to read and decode the data from Zeus machine. A simplified connection diagram for ANFIS controller is shown in Figure 2.

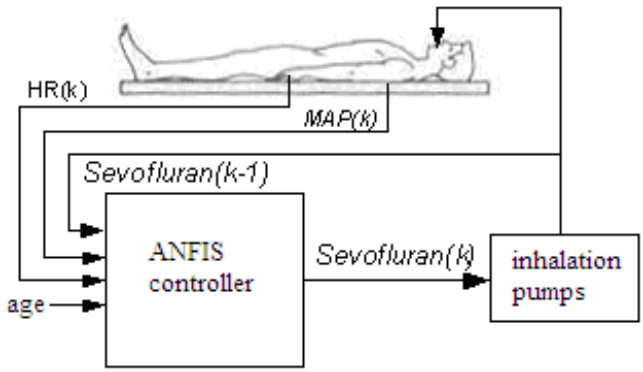


Figure 2. Connection diagram for ANFIS controller

One sample in every 3 sec. was collected (total 80.000 data rows for all the patients). In order to save the running time in some simulations, the sampling rate was reduced by (approx.) 15 times. Each row contains MAP (Mean Arterial Pressure), HR and Sevoflurane(%). By randomly grouping, these data were divided as 75% for the training set and 25% for the testing set as shown in Figures 3 and 4.

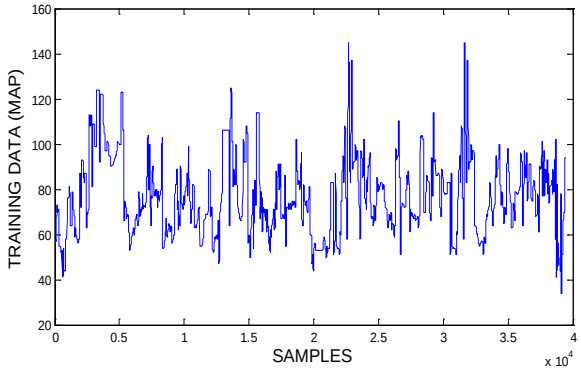


Figure 3. ANFIS training data (MAP only)

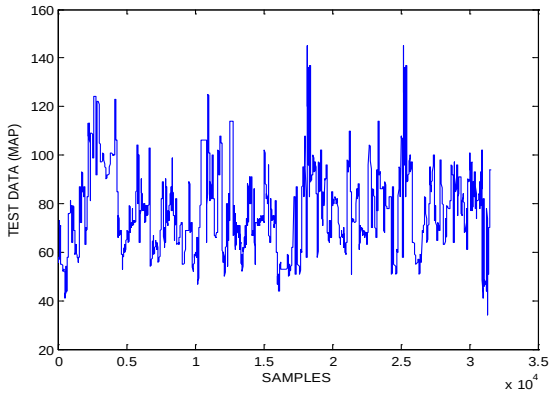


Figure 4. ANFIS test data (MAP only)

In order to provide a stable data reading, 'moving average' or 'locally-weighted polynomial regression' (lowess smoother) were used. Hence, the artefacts and worthless data were eliminated. For each method, the smoothing samples of a patient are shown in Figure 5.

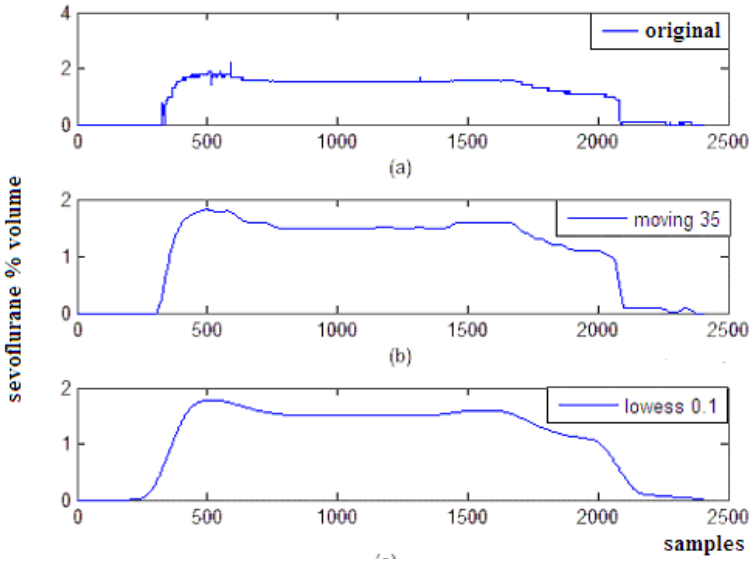
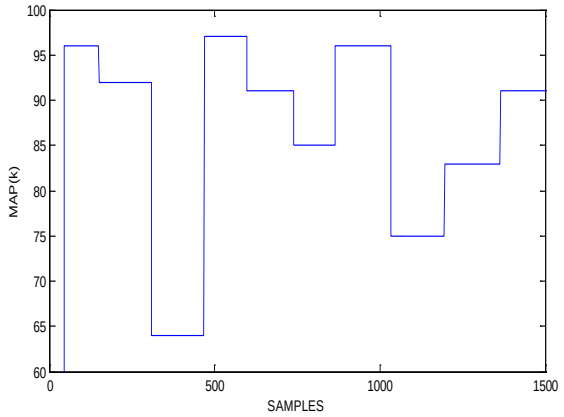
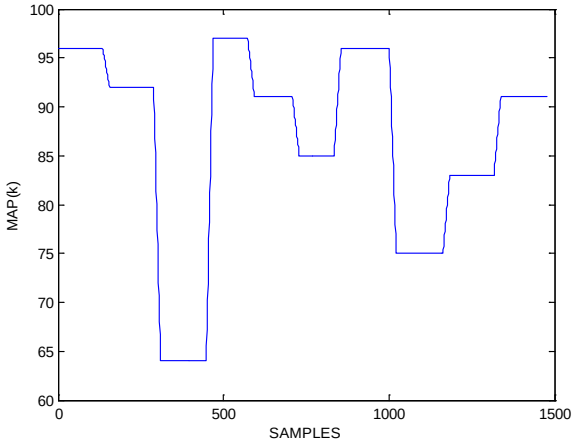


Figure 5. The smoothing samples for a patient data

The blood pressure values were measured every 5 minutes. In order to find the intermediate values (interpolating) for sequential readings, the smoothing method was applied for all measured parameters. Hence, it helps to find the unique values for other corresponding parameters at this range (for example Sevoflurane%), as in Figure 6. Otherwise, the same MAP values could be read for several sevoflurane values during 5 minutes. Of course, by increasing number of averaging points in the smoothing, causes increase the slope between sequential values.



(a)



(b)

Figure 6. The view of MAP (k) for a patient:
a) Before smoothing b) after smoothing

Design of ANFIS controller

The initial ANFIS model has these inputs: Mean Arterial Pressure (MAP), Heart Rate (Hr), Systolic Pressure (Sys), N2O, Sevoflurane and (k-1), (k-2), (k-3)th elements for all of these parameters and two other parameters: age and weight. (k-1), (k-2), (k-3)th elements are previous values of the corresponding parameters. For example Hr(k-2) stands for the value of Hr which is two steps before the current Hr. The model is shown in Figure 7.

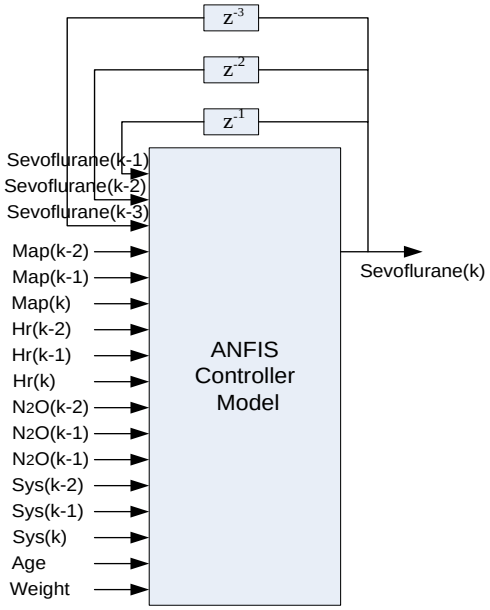


Figure 7. The general ANFIS controller model

The aim of this system is to search the best model for the obtained parameters. Around 30 combinations among inputs were used. For example, one of the configurations has the inputs sevoflurane(k-1), Map(k), Map (k-1), Map (k-2), Hr(k), N2O, the another one has the inputs Map(k), Map (k-1), Map (k-2), Hr(k), Hr(k-1), Hr(k-2), age, weight and so on. In this study, the membership functions and their positions in the work space decided by the subtractive clustering method and 500 epochs in the hybrid method were used (Chio, 1994; Jang, 1997).

ANFIS controller if the train and test data are selected randomly from whole dataset:

In first simulation, the model was trained with all data, and then each patient was tested by this model. The patients were grouped by two that all regression values in the first group were equal or bigger than 0.8 while the others were less than 0.8. Then, the train and test data were rearranged for each group. After a lot of simulation work, a best model was found as shown in Figure 8.

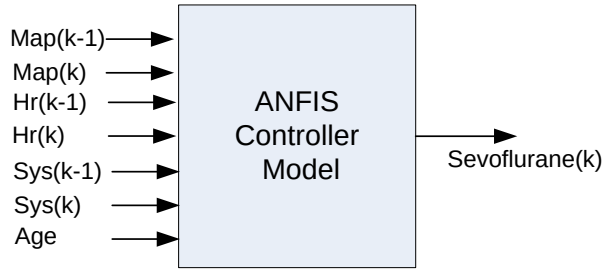


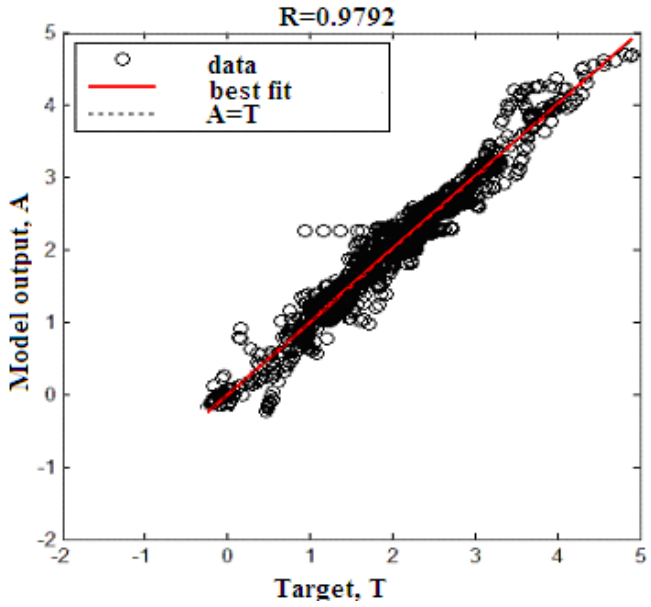
Figure 8. The best ANFIS controller model if the train & test data are selected randomly

The regressions summary for this model was given in Table 1:

Table 1: Regressions summary if the training and testing data are selected randomly

	Train	Test
1. Group	0.9807	0.9792
2. Group	0.9924	0.9909
All	0.8480	0.8707

The model's test simulation outputs for each group were given in Figure 9 and 10.



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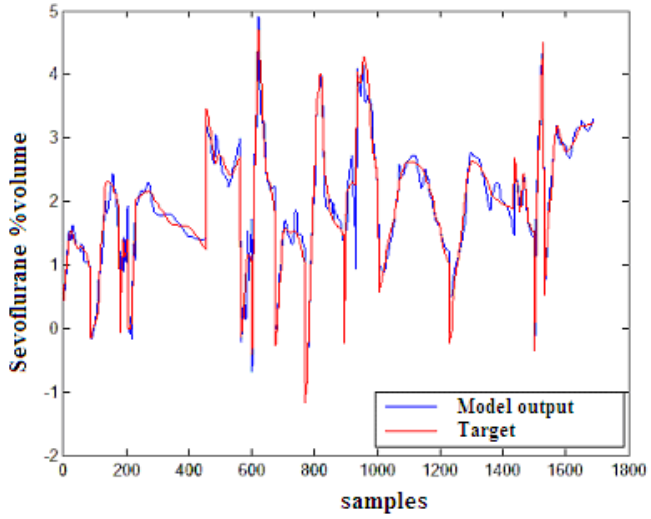

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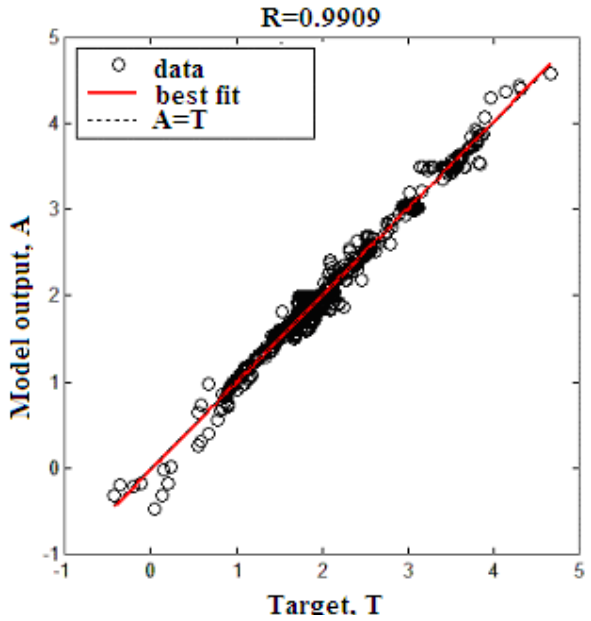
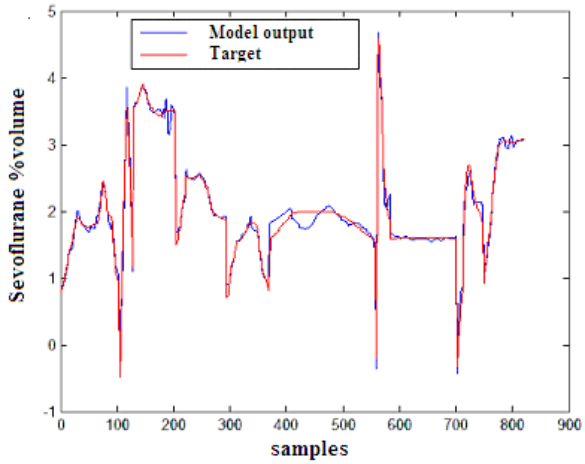
Figure 9. The first group test outputs: (a) Regression (b) Model's output for testing set



(a)



(b)

Figure 10. The second group test outputs: (a) Regression (b) Model's output for testing set

If the groups are rearranged based on ages (as adults and children), the regressions become as in Table 2.

Table 2: Regressions summary based on ages

	Train	Test
Adults	0.9988	0.9988
Children	0.9569	0.9571
All	0.8545	0.8429

In order to reflect these groups in the ANFIS model, a new model has two separated sub-models inside is suggested as in Figure 11. For each

patient, only one corresponding sub-model related to patient's age will be active. Each model's inputs are the same as in Figure 8 and were divided into 75% for the training set and 25% for the testing set. Both models were trained separately.

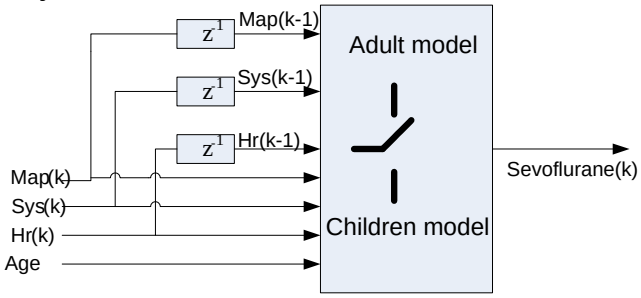


Figure 11. Age depended ANFIS controller

When all the patients were tested by this age-depended model separately, the regression for 6 patients (out of 28) are less than 0.85 while the others are more. If we are able to say that this is a critical point for the performance, then this model performance becomes:

$$\frac{28-6}{28} \times 100 = 78\%$$

An example study was conducted to test this model's performance for a patient whose results are the worst case among 22 patients:

Regression ….0.8595

RMSE…….0.1705

For this patient, the maximum deviation from target value is approx. 16% as seen on Figure 12. This can be considered as an allowable error since we observed the choice differences among anaesthesia teams in OR might be up to 20%.

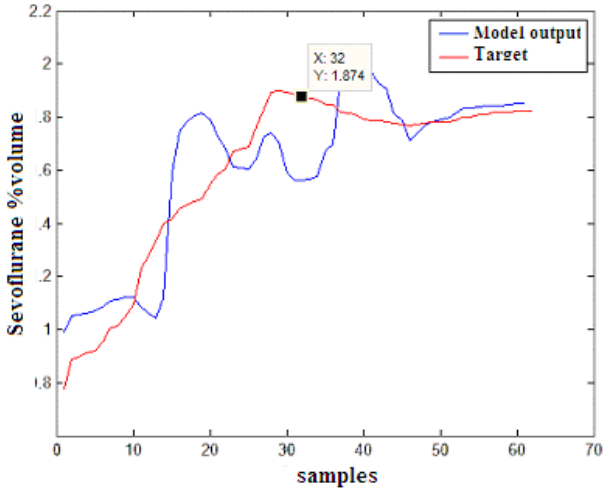


Figure 12. A test example for a worst case among 22 patients

ANFIS controller if the patients are selected randomly:

Some few abnormal examples of sevoflurane values versus MAP and HR are shown in Figure 13. It clearly shows that each of these trends are not similar to general trends. In some regions, the characteristics may become opposite of general trends. So, in order to construct a stabile model, these data should be removed if they were decided as abnormal data. All type of patient's data are supposed to be recognized by the ANFIS model. In the method of random data selection from whole dataset, the randomizing process is able to pick up the samples from most points in the workspace. But, if the patients are randomly selected and if the similar patient behaviours under operations are not presented in the training set, then the controller model may fail. In order to achieve a good model, a rich content in the training set is essential.

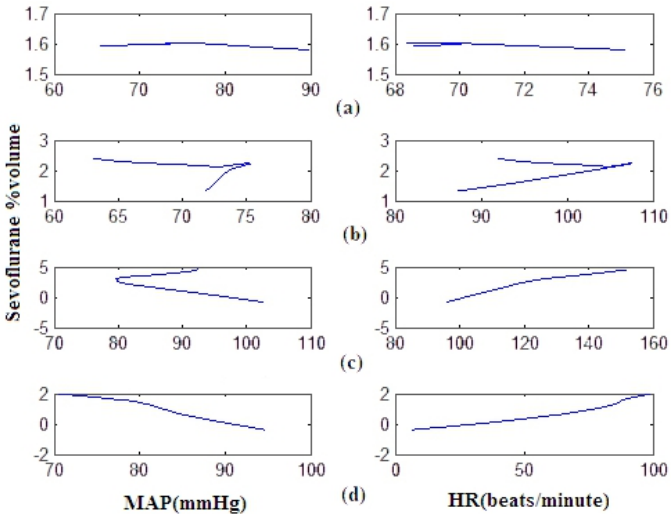


Figure 13. The abnormal sevolurane values vs MAP & HR for 4 patients (left column is MAP and right column is HR)

In this part of study, the data obtained from 9 patients (4 adult, 5 children) out of 28 were used as the testing set. The trial training phase was performed by using the adult and the children data as before: first separately, later all together. The best results were found among many input configurations shown in Figure 14. When all the patients (no age dependency) are in one group, all the regressions in the training phase are more than 0.8.

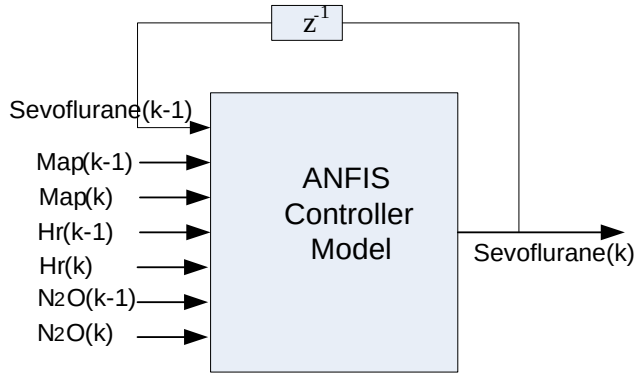


Figure 14. The best model when the patients were randomly divided as the train & test set

But, when this trained model was tested with the test patients, following were received:

The adult whose regression value > 0.85 is only 1 out of 4,

The children whose regression value > 0.85 is 3 out of 5.

The test performance for this model (respect to regression value > 0.8) becomes:

$$\frac{9-4}{9} \times 100 = 55.5\%$$

Conclusion

This case study is to prepare a model for a patient modelling under the general anaesthesia. The 'age' of the patient is observed as a useful input parameter which increases the model performance. Also, if the model consists of 2 sub-models as adult and children, the 'age' activates the corresponding sub-model. The performance of this switchable model is found as 78%.

When the training and testing data are selected randomly from whole dataset, the discovered models have good regressions from 0.87 up to 0.99 and the deviations from the target values are much less. This result is comparable to study [9] which the performance was reported in average accuracy of 94% of the cases. These models have good correlations with clinical assessments. On the other hand, on the separation of patients randomly as the training and testing patients, the performance decreases. In order to increase the performance in the random patient selection method, the data collection from many patients (as many as possible) are essential. Hence, the modelling can be done without other complex and costly measurements.

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