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# Automated knowledge-based fuzzy models generation for weaning of patients receiving Ventricular Assist Device (VAD) therapy

Markos G. Tsipouras, Evaggelos C. Karvounis, Alexandros T. Tzallas *Member, IEEE,* Yorgos Goletsis, *Member, IEEE*, Dimitrios I. Fotiadis, *Senior Member, IEEE*, Stamatis Adamopoulos and Maria G. Trivella

***Abstract*—The SensorART project focus on the management of heart failure (HF) patients which are treated with implantable ventricular assist devices (VADs). This work presents the way that crisp models are transformed into fuzzy in the weaning module, which is one of the core modules of the specialist's decision support system (DSS) in SensorART. The weaning module is a DSS that supports the medical expert on the weaning and remove VAD from the patient decision. Weaning module has been developed following a "mixture of experts" philosophy, with the experts being fuzzy knowledge-based models, automatically generated from initial crisp knowledge-based set of rules and criteria for weaning.**

## I. Introduction

Heart failure (HF) is one of the basic public health problems in western countries [1]. The treatment of HF is mainly based on Ventricular Assist Devices (VADs), which provide circulatory support to patients. For a growing number of patients with HF, VAD therapy has demonstrated the potential to extend life, and even lead to cardiac recovery [2]. Only few clinical decision support systems (DSSs) have been reported in the literature for weaning [3,4]. Dandel *et al* [3] used a set of expert rules and criteria to analyze data related to cardiac function/morphology and duration of HF before VAD implantation, echocardiographic parameters recorded during 'off-pump' trials, and recovery stability before and after VAD removal. Santelices *et al* [4] developed a clinical DSS based on a Bayesian Belief Network created using expert knowledge and multivariate statistical analysis, to support decisions for weaning or not weaning.

Fuzzy logic is the multivariate extension of the binary (crisp) logic, thus presenting high similarity to the human logic and being more able to deal with problems originated from real world domains of application [5]. Fuzzy models present several advantages over the crisp ones, mainly having flexible decision boundaries and thus presenting higher ability to cope with imprecise and noisy data. A fuzzy model can be generated by fuzzyfication of an initial crisp model; several issues must be defined in this procedure for the model to be generated. The creation of knowledge–based fuzzy models has been addressed in several papers presented in the literature. The main idea is to define an initial fuzzy model and then apply an optimization technique in order to optimize it. In this context presented approaches include fuzzy rules with modified controlled random search [6], simulated annealing [7] or genetic algorithms [8], and multicriteria decision analysis with genetic algorithms [9].

In this paper, the knowledge-based fuzzy approach of the weaning module of the SensorART project is presented. SensorART project emphases on the controlling and remote treatment of HF patients that have a VAD installed. The project includes a specialist's DSS, which comprises from several sub-modules, mainly focusing to: (i) identify VAD patients who can be weaned (weaning module), (ii) detect suction events of the rotary blood pumps (suction module), and (iii) determine an optimal VAD pump speed (speed optimization module). The weaning module is a web-based tool that allows the experts to easily create and modify knowledge-based weaning models, based on a set of comprehensive and personalized crisp rules. The rules are created using the disjunctive normal form (DNF) formulation, i.e. the model is a disjunction of rules (rules connected with the OR binary operator) and each rule is a disjunction of literals (literals connected with AND binary operator). Then crisp model is automatically transformed into its fuzzy equivalent [10]. The main idea is to include in the SensorART weaning module several available models presented in the literature and, along with the models that will be included from the project's experts, to achieve a "mixture of experts" approach, i.e. to be able to examine a patient's health status and weaning possibility against several different experts.

## II. Methodology

### A. Initial Crisp Models

The initial knowledge is originated from expert cardio-surgeons and it is imported from the clinical knowledge editor tool (a snapshot is presented in Fig. 1). The clinical knowledge editor is constructed to accept the input model as a set of crisp rules formulated in DNF. The number of literals per rule and number of rules per model is unlimited. Each model is saved in XML format. Using this tool all available models are imported and stored in the weaning module, while additional models can be included at any time.

Each crisp classification rule $r_i^c(x,\theta_i^c)$ is expressed as: $r_i^c(x,\theta_i^c)$: $d_i^c(x,\theta_i^c) \rightarrow y_i$, where $r_i^c$ is the $i^{th}$ crisp rule, $x$ is a feature vector comprised from a number of features $a_j$, $\theta_i^c$ is a vector of thresholds, $d_i^c$ is the precondition of the crisp

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M. G. Tsipouras, E. C. Karvounis, A. T. Tzallas, Y. Goletsis and D.I. Fotiadis are with the Biomedical Research Institute-FORTH, GR 45110, Ioannina, Greece (e-mail: markos@cs.uoi.gr, ekarvuni@cc.uoi.gr, atzallas@cc.uoi.gr, goletsis@cc.uoi.gr, fotiadis@cs.uoi.gr). Dr. S. Adamopoulos is with 2nd Department of Cardiology, Onassis Cardiac Surgery Center, Athens, Greece (e-mail: sadamo@bigfoot.com). Dr. M.G. Trivella is with the Istituto di Fisiologia Clinica-CNR, Pisa, Italy (e-mail: trivella@ifc.cnr.it).

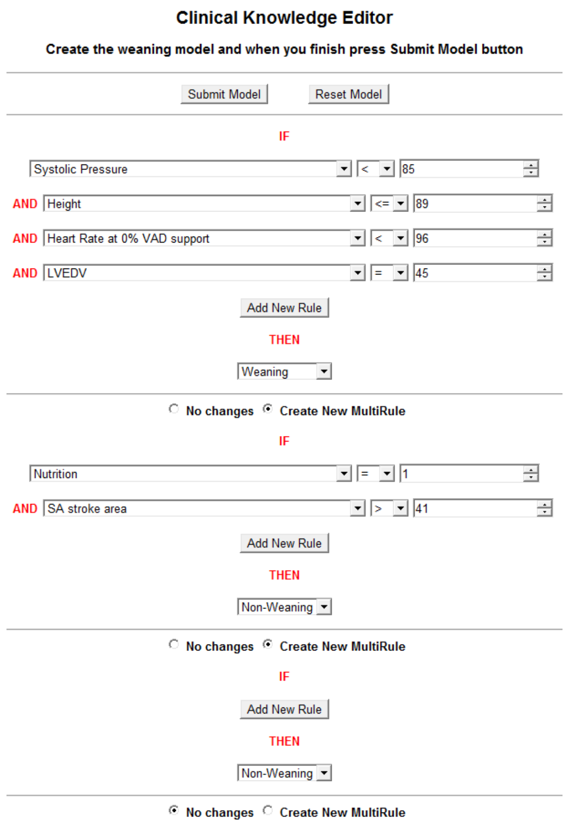


Figure 1. Clinical knowledge editor for weaning model creation.

rules (conjunction of feature tests), and $y_i$ is the predicted class. Precondition is defined as: $d_i^c = g^c_{op_1}(a_1, \theta_1^c) \wedge \ldots \wedge g^c_{op_j}(a_j, \theta_j^c)$, where $g^c_{op_j}$ is the crisp membership function, with:

$$g^c_{op}(a_j, \theta_j^c) = \begin{cases} 1, & a_j \; op \; \theta_j^c \\ 0, & else \end{cases}, \qquad (1)$$

and $op_j = \{=, \neq, <, >, \leq, \geq\}$. The symbol $\wedge$ denotes the binary AND operator. All crisp rules from the medical rule set that result in the same class are combined into a single class rule, defined as:

$$R_k^c(x, \theta_k^c) : r_1^c(x, \theta_1^c) \vee \ldots \vee r_k^c(x, \theta_k^c) \rightarrow y_k. \qquad (2)$$

The symbol $\vee$ denotes the binary OR operator. Thus, a crisp model can be defined as:

$$M^c(x, \Theta^c) = \Phi^c(R_1^c, R_2^c, \ldots, R_N^c), \qquad (3)$$

where $M^c$ is the crisp model, $\Theta^c$ is the threshold vector containing all values used in the model, $\Phi^c$ is a decision function and $N$ is the number of classes in the problem, and thus the number of class rules $R^c$ .

## B. Fuzzy Models Generation

An equivalent fuzzy model $(M^f)$ is generated from the crisp one $(M^c)$ as follows: (i) the crisp membership function $g^c$ is replaced by a fuzzy one $g^f$, (ii) the binary AND and OR operators are replaced by $T_{norm}$ and $S_{norm}$ functions, respectively, and (iii) the decision function $\Phi^c$ is replaced by a defuzzyfication function $\Phi^f$. Based on these changes, the fuzzy model is defined as:

$$M^f(x, \Theta^f) = \Phi^f(R_1^f, R_2^f, \ldots, R_N^f), \qquad (4)$$

where, $\Theta^f$ is the parameter vector containing all parameters used in the fuzzy model and $R_k^f$ is the fuzzy class rules, defined as:

$$R_k^f(x, \theta_k^f) = T_{norm}\left(r_1^f(x, \theta_1^f), \ldots, r_k^f(x, \theta_k^f)\right), \qquad (5)$$

where $r_i^f$ is the fuzzy rule defined as:

$$r_i^f(x, \theta_i^f) = S_{norm}\left(g^f(a_1, \theta_1^f), \ldots, g^f(a_j, \theta_j^f)\right). \qquad (6)$$

The obtained fuzzy model $M^f$ is optimized with respect to $\Theta^f$ parameters. For this purpose an objective function must be defined using a training dataset (such as the square error function), and then minimized with respect to a $\Theta^f$ using a local or global optimization technique. Local optimization methods begin from an initial starting point and try to locate the respective local minimum while global optimization techniques attempt to find all local minima of the objective function inside a bounded set and then locate the global minimum. The described methodology for fuzzy expert systems creation is based on the fuzzyfication of an initial (crisp) medical rule set, thus, the final fuzzy expert system is based on the initial crisp rule set, with more "flexible" boundaries.

# III. Application

The SensorART weaning module is based on a "mixture of experts" approach, thus several (and possible all) available models presented in the literature will be included. Thus, the above described methodology has been applied to known models and set of criteria for weaning presented in the literature. The models presented from Dandel *et al* [3] and Santelices *et al* [4] have been used as initial crisp knowledge-based models in order to produce fuzzy knowledge-based weaning models.

## A. Fuzzy model based on Dande set of weaning criteria

In Dante *et al* [3] pre-implantation data were used to evaluate their potential usefulness for weaning decisions by the assessment of their predictive value for post-weaning stability of unloading-induced cardiac improvement. For this reason, Dandel *et al* compared the pre-implantation data of weaned patients with and without long-term post-weaning cardiac stability. Pre-implantation data were collected from their database before VAD removal and did not interfere with weaning decisions. In addition to diagnosis and NYHA class, the duration of heart disease, ECG, and echocardiographic data, as well as data provided by preimplantation right- and left-heart catheterization (including coronary angiography) were collected for evaluation. Histological data on myocardial hypertrophy and interstitial fibrosis obtained in all evaluated patients from apical cores removed at VAD implantation were also collected for further evaluation. The variables presented in Table I are used in the weaning criteria of [3].

The variables can be formulated in a vector $x = (HR_{100}, HR_0, BAP, LVEDD, LVEF, MAVR, RVOT, SLAR, TPVR, CI, PAWP, RAP)$. From the logic chart, the crisp rule is extracted:

$$if \begin{pmatrix} HR_{100} < 90,\ HR_0 < 112.5, \\ BAP \geq 65, LVEDD \ \leq 55, \\ LVEF \geq 45, MAVR \leq 2, \\ RVOT < 35, SLAR < 0.6, \\ TPVR \leq 2, CI > 2.6, \\ PAWP < 13, RAP < 10 \end{pmatrix} \ then \begin{pmatrix} wean\ and \\ remove \\ VAD \end{pmatrix}, \quad (6)$$

which preconditions are:

$$d_1^c(x, \theta_1^c) = \wedge \begin{pmatrix} g_<^c(x_1, 90), g_<^c(x_2, 112.5), \\ g_\geq^c(x_3, 65) \\ g_\leq^c(x_4, 55), g_\geq^c(x_5, 45), g_\leq^c(x_6, 2), \\ g_<^c(x_7, 35), g_<^c(x_8, 0.6), g_\leq^c(x_9, 2), \\ g_>^c(x_{10}, 2.6), g_<^c(x_{11}, 13), g_<^c(x_{12}, 10) \end{pmatrix}, \quad (7)$$

and $\theta_1^c = (90,112.5,65,55,45,2,35,0.6,2,2.6,13,10)$, is the vector of parameters. Based on the above, the crisp rule is formulated as: $r_1^c(x, \theta_1^c): d_1^c(x, \theta_1^c) \rightarrow y_1$, where $y_1 = wean\ andremove\ VAD$. The second class of the problem is $y_2 = no\ wean$; the second class is resulted if the rule is false. The class rule for the first class is defined as: $R_1^c: r_1^c(x, \theta_1^c)$, and, the crisp model can be defined as: $M^c\ (x, \Theta^c\ ) = \Phi^c(R_1^c)$, where $\Theta^c\ = \theta_1^c$ and the decision function is defined as:

$$\Phi^c = \begin{cases} y_1, & if\ R_1^c\ is\ true \\ y_2, & else \end{cases}. \quad (4)$$

TABLE I. VARIABLES USED IN WEANING CRITERIA [3]

| Variable name | Type | Label |
|---|---|---|
| HR at 100% VAD support | Integer | HR100 |
| HR at 0% VAD support | Integer | HR0 |
| Brachial Artery Pressure (mean) | Real | BAP |
| Left Ventricular End-Diastolic Diameters | Real | LVEDD |
| Left Ventricular Ejection Fraction | % | LVEF |
| No or maximum grade II mitral and/or aortic valve regurgitation | Integer | MAVR |
| RVOT diameter | Real | RVOT |
| Short-/long-axis ration | Real | SLAR |
| No or maximum grade II tricuspid or palmonary valve | Integer | TPVR |
| Cardiac Index | Real | CI |
| Pulmonary Artery Wedge Pressure (mean) | Real | PAWP |
| Right Atrial Pressure (mean) | Real | RAP |

The crisp model $M^c$ can be transformed into an equivalent fuzzy model $M^f$ , using a fuzzy membership function instead of the crisp, $T_{norm}$ and $S_{norm}$ functions instead of the binary AND and OR operators and a defuzzyfication function instead of the decision function. The selection of these functions (fuzzy membership function, $T_{norm}$, $S_{norm}$, defuzzyfication function) is not obligatory: several different definitions of appropriate mathematical functions has been presented in the literature for each one of them. However, based on these selections, different fuzzy models can be defined which will have different characteristics. An important issue is the optimization step that will follow the fuzzy model definition: if an optimization technique that will require the calculation of the first derivatives is going to be employed, then the fuzzy model must be differentiable and thus known functions (such as min/max functions for $T_{norm}/S_{norm}$) cannot be involved.

For the fuzzy model formation, the sigmoid function is used as the fuzzy membership function, defined as: $g_{inc}^f(a, \theta_1, \theta_2) = \frac{1}{1+e^{\theta_1(a-\theta_2)}}$, when it is increasing and $g_{dec}^f(a, \theta_1, \theta_2) = \frac{1}{1+e^{\theta_1(\theta_2-a)}}$, when it is decreasing. Also, based on these definitions, the equality and inequality functions are defined as: $g_{eq}^f(a, \theta_1, \theta_2) = 4g_{inc}^f(a, \theta_1, \theta_2)g_{dec}^f(a, \theta_1, \theta_2)$, and $g_{ineq}^f(a, \theta_1, \theta_2) = 1 - g_{eq}^f(a, \theta_1, \theta_2)$.

Product and probabilistic OR are employed as $T_{norm}$ and $S_{norm}$: $T_{norm}(a, b) = ab$ , $S_{norm}(a, b) = a + b - ab$. Based on these function selections, the fuzzy rule function is defined as:

$$r_1^f(x, \theta_1^f) = \prod_{i=3,5,10} \left(1 + e^{\theta_{i,a}^f(x_i - \theta_{i,b}^f)}\right)^{-1}$$

$$\prod_{i=1,2,3,6,7,8,9,11,12} \left(1 + e^{\theta_{i,a}^f(\theta_{i,b}^f - x_i)}\right)^{-1}, \quad (8)$$

while, $R_1^f = r_1^f(x, \theta_1^f)$. Thus, the fuzzy model is defined as: $M^f(x, \Theta^f) = \Phi^f\left(R_1^f(x, \Theta^f)\right)$, where, the defuzzification function is defined as: $\Phi^f = \left[R_1^f(x, \Theta^f) \quad c\right]$, and $\Theta^f$ is the set of parameters of the fuzzy model, while $c$ is a constant value (threshold). The train dataset is formulated as: $D_{train} = \{X, T\}$, where $X$ being an 12x$N$ matrix and $T$ being an 2x$N$ matrix. The optimization function is based on the sum of square errors function:

$$F(D_{train}, \Theta^f) = \sum_{i=1}^N \left\| M^f(X^i, \Theta^f) - T^i \right\|^2. \quad (9)$$

Local optimization has been involved, starting from an appropriate initial point: $\theta_{i,b}^f = \theta_i^c$ and $\theta_{i,a}^f \gg 1$. Also, upper and lower bounds for each one of the optimization parameters ($\Theta^f$) have been set in order to and limit the optimization procedure inside this search area. The rational of this approach for fuzzy model definition (i.e. with first derivatives) and local optimization procedure strategy is addressed in the discussion section.

## B. *Fuzzy model based on Sentelices flowchart*

In Santelices *et al* [4], medical knowledge was derived from interviews of 11 experts and this was supplemented by retrospective clinical data from the 19 VAD patients considered for weaning between 1996 and 2004. A data-driven modeling with 250 numeric variables from 6 categories: demographics, complications, laboratory tests, exercise tests, right heart catheterization, and echocardiographic tests: were analyzed using ANN to identify the most predictive variables and their associated thresholds. The variables were reduced using the prune algorithm to eliminate those that were weakly correlated with weaning. To avoid overtraining, only 50% of the datasets were analyzed at a time. Additional analysis was performed on the written shift notes recorded by the clinical staff responsible for routine monitoring of these patients. Language patterns within the textual data contained in the shift notes were identified by natural language processing (NLP). Finally, an expert-data hybrid model was used where the relationships between variables extracted from data-driven model and expert interviews were modeled. From the knowledge-derived flowchart presented in Fig. 1 of [4] five rules are extracted, based on 18 variables. The classes of the crisp model are defined as: $y_1 = wean\ andremove\ VAD\ from\ patient$, and $y_2 = wait\ 2-4\ weeks\ and\ repeat\ ECHO$. All rules in the crisp rule set are resulting the first class; the second class is resulted if all rules are false. The crisp model is fuzzyfied following the same procedure described for the fuzzy model based on Dande *et al* set of weaning criteria.

# IV. VALIDATION

The fuzzy models have been validated using a simulated dataset that has been medically validated, i.e. the simulated data have been validated from an expert cardio surgeon in order to be consistent with real life data. This is mainly a technical validation, in order to demonstrate the accurate function of all parts of the weaning module (import of the model using the clinical knowledge editor, crisp model definition, fuzzyfication of the crisp model and fuzzy model definition, optimization of the fuzzy model). The data were created as 3-5 recordings from 10 subjects, with half of them presenting a graduate improvement (and thus annotated as wean cases) and the other half presenting a steady or declining heart condition. Validation results from crisp models and initial fuzzy models (i.e. fuzzy models before the optimization) indicated that the above described methodology produces knowledge-based fuzzy models accurately. Optimization of the fuzzy models was performed only for the technical validation of the described optimization strategy.

# V. DISCUSSION AND CONCLUSIONS

In this work, the fuzzy approach of the SensorART project weaning module is presented. The weaning module is based on a “mixture of experts” approach with the experts being fuzzy knowledge-based systems. The rational of this approach is to resemble the real life situation, where a patient in critical condition will seek the medical opinion of more than one medical experts. Knowledge-based crisp models have been selected as the initial expression of the experts’ knowledge since it is more comprehensive for the medical experts to formulate their knowledge and expertise. However, fuzzy models have been developed since the definition and parameter set of the fuzzy model allows it to be extremely more flexible and thus being able to cope with the complexity of the respective medical decision. However, this flexibility can become a disadvantage since it can allow the fuzzy model to result to a set of parameter values that do not reflect any real medical knowledge. To avoid this situation, a local optimization technique is involved along with the definition of an appropriate initial starting point ($\Theta^f_{initial}$). The employment of local optimization techniques imposes the definition of a differential fuzzy model, and thus known functions (such as min/max functions for $\mathrm{T_{norm}}/\mathrm{S_{norm}}$) cannot be involved. For the definition of the initial point (to start the local optimization) the main idea is to set the initial values of the fuzzy model’s parameters so as the fuzzy model to approximate the initial crisp model (set of rules), i.e. setting: $\theta^f_{i,b} = \theta^c_i$ and $\theta^f_{i,a} \gg 1$, it is: $M^f(x, \Theta^f) \rightarrow M^c(x, \Theta^c)$. Initiating the local optimization technique from this point, the final local minima ($\Theta^{f*}$) will be a set of parameter values that will allow to the fuzzy model to be more flexible than the initial set of rules, however laying in a relatively close distance from the initial point ($\|\Theta^f_{initial} - \Theta^{f*}\| < \varepsilon$), thus maintaining the properties of the initial medical rule set. Nevertheless, this may not be enough, since during the local optimization procedure the search may drift far away from the starting point. Thus, an additional measure is to define an upper and lower bound for each one of the optimization parameters ($\Theta^f$) and limit the optimization procedure inside this search area.

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