Chapter 6
Exploiting Expert Systems in Cardiology: A Comparative Study

George-Peter K. Economou, Efrosini Sourla, Konstantina-Maria Stamatopoulou, Vasileios Syrimpeis, Spyros Sioutas, Athanasios Tsakalidis, and Giannis Tzimas

Abstract An improved Adaptive Neuro-Fuzzy Inference System (ANFIS) in the field of critical cardiovascular diseases is presented. The system stems from an earlier application based only on a Sugeno-type Fuzzy Expert System (FES) with the addition of an Artificial Neural Network (ANN) computational structure. Thus, inherent characteristics of ANNs, along with the human-like knowledge representation of fuzzy systems are integrated. The ANFIS has been utilized into building five different sub-systems, distinctly covering Coronary Disease, Hypertension, Atrial Fibrillation, Heart Failure, and Diabetes, hence aiding doctors of medicine (MDs), guide trainees, and encourage medical experts in their diagnoses centering a wide range of Cardiology. The Fuzzy Rules have been trimmed down and the ANNs have been optimized in order to focus into each particular disease and produce results ready-to-be applied to real-world patients.

Keywords Artificial intelligence • Decision making • Cardiovascular diseases

G.-P.K. Economou (✉)
Department of Computer Science, Hellenic Open University, 26335 Patras, Greece
e-mail: econom@upatras.gr

E. Sourla • Konstantina-Maria Stamatopoulou • A. Tsakalidis
Computer Engineering & Informatics Department, University of Patras, 26500 Patras, Greece
e-mail: sourla@ceid.upatras.gr; stamatok@ceid.upatras.gr; tsak@ceid.upatras.gr

V. Syrimpeis
3 General Hospital of Patras Agios Andreas, 26335 Patras, Greece
e-mail: siva@upatras.gr

S. Sioutas
Department of Informatics, Ionian University, 49100 Corfu, Greece
e-mail: sioutas@ionio.gr

G. Tzimas
Computer & Informatics Engineering Department, Technological Educational Institute of Western Greece, 26334 Patras, Greece
e-mail: tzimas@teimes.gr

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6.1 Introduction

Single analysis techniques [7] for many years have been the bases with which engineers worldwide tried to equip Medical Doctors (MDs) with computational means inasmuch has to improve their performance. Yet, those techniques only enhanced Medical Data provided by various examinations and methods; they could not support MDs with their diagnoses. On the other hand, Artificial Intelligence (AI) methodologies have proven to be crucial in utilizing the knowledge of specialized experts in various fields of human activities [10].

Artificial Neural Networks (ANNs), in particular, have been employed so that to process medical information and classify symptoms into diseases and proper treatment, hence reaching correct diagnoses. The general and flexible structure of a Medical Decision Making System (MDMS), composed of ANNs, is capable of being adjusted to different areas of either medical interest or where human knowledge and reasoning prevails simply by providing applicable learning data [10]. Similarly, Fuzzy Logic is considered to be one of the most suitable approximations of decision making, since it deals with reasoning that is approximate rather than fixed and exact, thus closer to human reasoning [2]. Therefore, both AI domains are capable of modeling complex phenomena [8, 12].

In this work, an Adaptive Neuro-Fuzzy Inference System (ANFIS) was developed for the MDMS to be trained, tested, and applied in the field of Cardiovascular Diseases (CDs). The team of MDs also decided that five different and medically critical CDs were to be the focus of the project and five distinctive sub-systems, one for each particular disease, were to be developed. The CDs, namely Coronary Disease, Hypertension, Atrial Fibrillation, Heart Failure, and Diabetes, were chosen due to the number of real-world clinical data that could be analyzed.

Thus, for the MDMS presented in this paper, medical data from real clinical cases were used to model both learning patterns for its ANNs and its fuzzy rules. Medical data, the inputs of the five sub-systems, were converted to the different members of the associated membership functions based on their value, so as to be fuzzy-fied and hence be exploited by the Stage 1 of the MDMS. Stage 2 exploits the necessary fuzzy rules, a direct mapping of MDs expertise, to treat the inputs of the previous stage. Each rule provides for a (fuzzy) output. Stage 3 combines all partial (fuzzy) outputs and Stage 4 de-fuzzy-fies the output into a more medical response. All stages have been implemented by ANNs.

The rest of the paper is organized as follows: Related work to the proposed project is presented in Sect. 6.2. Section 6.3 approaches the implemented ANFIS via a thorough description, followed by the system evaluation and comparison data in Sect. 6.4. Finally, Sect. 6.5 hosts conclusions and future work.

6.2 Related Work

A large number of joined MDs and engineers teams' research projects nowadays reflect the manifold integration of artificial intelligence in medicine. MDMSs combined with genome information and biomarkers [10]; cancer biomarker discovery and multiplexed nanoparticle probes for cancer biomarker profiling [14]; molecular diagnosis and individualized therapy of human diseases [9]; identification of potential responders to a certain medication therapy using random forests algorithms [13]; classification of electroencephalogram signals through feature extraction, using the wavelet transform [7].

Most of the abovementioned MDMSs concentrate on MDs requirements for educational reasons or to serve plain advisory roles. More vigorous efforts have also been proposed [4] upon which ANNs play dominant roles, as well as technology evolution and "smart" devices features and potential [3]. As far as it concerns MDMSs in CDs, there are also a number of research projects. One treating hypertension [15] recommends two separate ANNs propagating medical data regarding healthy and possible patients' symptoms and extrapolating the diagnosis by comparing their outputs. Another one employs a multi-layered perceptron neural network and support vector machine, determining Coronary Artery Disease by being fed exercise stress testing data [1]. In [16], ANNs are used as most suitable to outcome prediction trends in post-operative cardiac patients.

Guidi et al. [6] operated a system to assist non-specialists in the analysis of heart failure patients' data. ANNs compete with a support vector machine, a decision tree, and a fuzzy expert system whose rules are produced by a Genetic Algorithm, all AI-techniques contributing to the final outcome. ANNs achieved the best performance with an accuracy of 86 %. Health care systems are proposed in [5] that allow patients to self-record Electrocardiograms (ECGs) with "smart" portable devices that analyze the signal inputs and through a set of rules and risk factors can estimate the severity and the condition of life threatening heart episodes. These projects needed extra hardware in order to produce the ECGs and export the final results.

6.3 Description of the MDMS

In this section, the proposed MDMS is described. First though, we present an introduction to Fuzzy Logic and ANNs.

6.3.1 Introduction to Fuzzy Logic

All computational machines can process crisp data such as either (logical) "0" or "1." In order to enable them to handle vague language input, the crisp input and output must be converted to linguistic variables, thus forming fuzzy components. A crisp input will be converted to the different members of the associated membership functions based on its value. From this point of view, the output of a fuzzy logic controller is based on its memberships of the different membership functions, which can be considered as a range of inputs [2].

Generally, fuzzy-fication involves two processes: derive the membership functions for input and output variables and represent them with linguistic variables. In practice, membership functions can have multiple different types, such as the triangular waveform, trapezoidal waveform, Gaussian waveform, etc. [2]. In the proposed ANFIS triangular membership functions are used, since significant dynamic variation in a short period of time is needed.

Then, for the Fuzzy Inference Process to begin, fuzzy inputs, and membership functions utilization along with the control rules are combined to derive the fuzzy output. The control rules are the core of the fuzzy inference process and are directly related to a human being's intuition or expertise [2]. MDs were asked to assess the severity of every rule, according to their experience and knowledge. To make the fuzzy output available to real applications, a de-fuzzy-fication process is needed. A fuzzy output is still a linguistic variable, hence it needs to be converted to the crisp variable via the de-fuzzy-fication process. All proposed CDs sub-systems function on the weighted average de-fuzzy-fication method [2]. Figure 6.1 shows an example of a stored membership function.

6.3.2 Introduction to ANNs

ANNs consist of a large number of Artificial Neurons (ANs), similar or not to each other, that form networks by the way they are combined. ANs vary in structure and function and, because of their connections (called *Synapses*), exhibit different characteristics. Figure 6.2a shows a typical AN [4, 11]. Its inputs and outputs generally obey the equation:

$$\psi = \phi(\Sigma_{i=1}^{n}\beta_i \cdot \chi_i) \tag{6.1}$$

An AN can accept large number of (digital or analogue) inputs ($\chi_1, \chi_2, \ldots, \chi_n$), multiply them by the factors $\beta_1, \beta_2, \ldots, \beta_n$ (called *weights*), and extract an output that can feed similar, or not, neurons. The outputs can be made discrete or analogue and when they have a non-zero value the neuron is said to have *fired*. The weighted inputs sum up and are expressed in a non-linear function $\phi(\cdot)$. The non-linear

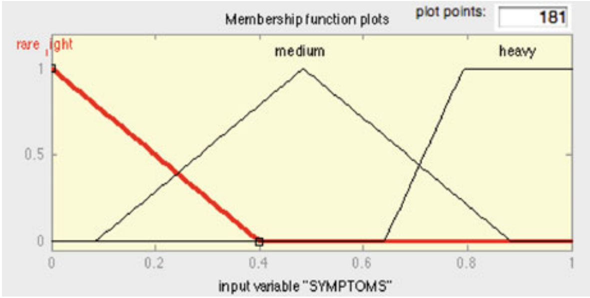

Fig. 6.1 Membership function

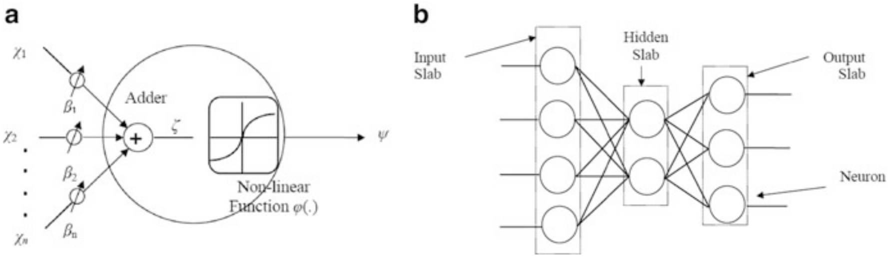

Fig. 6.2 (**a**) Typical AN and (**b**) ANNs Feed forward architecture

function $\phi(\cdot)$ corresponds to biological models' performance and is called *Sigmoid* due to its shape (similar to the Hellenic capital letter Σ). Figure 6.2a shows a usual AN, whereas Fig. 6.2b a typical ANNs architecture (feed forward—fANNs).

In a fANN, the connections are only allowed between ANs belonging to adjacent architecture levels ("Slabs"). Between input and output Slabs and depending on the application, a number of hidden Slabs of ANs intervene in which input vectors do not have access and they do not contribute directly to the output ones.

The number of hidden Slabs/ANs defines the fANNs performance and effectiveness. ANNs can be taught by feeding typical data to their inputs and forcing their outputs to appropriate ones by means of learning algorithms that calculate their weights' values [11]. Those Input/Output vectors are referred to as learning patterns and each time all ANNs weights are calculated anew denotes an epoch.

6.3.3 The ANFIS

Systems integrating the parallel computation and learning capabilities of ANNs with the human-like knowledge representation of fuzzy systems form neuro-fuzzy systems. Those have far better explanation abilities supporting their outputs (and in the case of CDs, medical diagnoses) than either separate AI methodologies. As a result, neural networks mode of operation becomes more understandable and additionally fuzzy systems become adroit of adaptation and of learning.

A neuro-fuzzy system (ANFIS) basically is an ANN which is functionally equivalent to a fuzzy inference model. Moreover, as already stated, it can adapt to virtually every area of human expertise provided with the necessary training patterns (representative pairs of vectors of inputs/outputs used in their learning phase). Thus, an ANFIS can be trained to develop IF-THEN fuzzy rules and determine membership functions for input and output variables of a particular area. Therefore, building the fuzzy inference engine is avoided, which not only entails a substantial computational burden but also depends on experts' subjectivity and knowledge-extraction methodology (see also Sect. 6.4).

The structure of an ANFIS is similar to a multi-layer ANN (Fig. 6.2b): it has input and output slabs; the number of each slab's ANs is dictated by the expert. Also, it is generally provided with three hidden slabs that represent membership functions and fuzzy rules. Each slab in an ANFIS is associated with a particular step in the fuzzy inference process. The first slab is the input layer (or Stage 1 of the MDMS). Each of its ANs is input data that have been through a fuzzy-fication procedure. The second slab (Stage 2) determines the degree to which this input vector belongs to the ANs fuzzy set; the appropriate AN, then fires and its output propagates to the ANs of the next hidden layer, up to the output slab (Stage 3). ANs of that Stage are also especially aggregated (always under an expert's guide when building this whole infrastructure) to produce the closing vector of fuzzy outputs. Lastly, the final AN slab (Stage 4) operates as the de-fuzzy-fication operand, being set to "transform" the MDMS data into an actual diagnosis.

6.3.3.1 The MDMSs

- The **Coronary Disease** MDMS sub-system (cMDMS) has five vectors of inputs, namely *Family History, Risk Factors, Myocarditis Probability, Other Reasons for the disease*, and *(older) Clinical Examinations Results (CEx)*. Its outputs are *No Further Evaluation, Re-Evaluation after 3 Months, Perform a Computerized Tomography (CT), Perform a Magnetic Tomography (MRI)*, and *Perform Surgery -percutaneous coronary intervention (PCI)*, all set by experts.

  The severity of the above factors is fuzzy-fied into three membership functions *min, med*, and *max* (as shown in Fig. 6.1). The rules constructed for the cMDMS are close to 300 and are established similarly to the following one:

  IF *Family History* IS *min* AND *Risk Factors* IS *med* AND *Myocarditis Probability* IS *min* AND *Other Reasons for the disease* IS *min* AND *CEx* IS *med* THEN *Outcome* IS *MRI*.
- The **Hypertension** MDMS sub-system (hMDMS) has three vectors of inputs, namely *Risk Factors, Performed Echocardiogram (Echo)*, and *Other (older) Clinical Examinations Results (CEx)*. Its outputs are *No Further Evaluation, Re-Evaluation after 3 Months, Re-Evaluation after 12 Months, Two Consecutive Weeks Evaluation*, and *Therapy*, all set by experts.

The severity of the above factors is fuzzy-fied into three membership functions *min, med*, and *max*. The rules constructed for the hMDMS are close to 30 and are established similarly to the one of the cMDMS.

- The **Atrial Fibrillation** MDMS sub-system (afMDMS) has five vectors of inputs, namely *Family History, Risk Factors, CHA2DS2VASC Score Results, (various) Symptoms Assessment (SA)*, and *Documentation of Arrhythmia*. Its outputs are *Regular Assessment of Performed Electrocardiography (ECG), Holter Use, Perform Echocardiogram (Echo), Perform Cardioversion-Ablation, Treatment Underlying Disease, Rhythm Control, Rate Control, Aspirin Use*, and *Oral Anticoagulant Use*, all set by experts.

  The severity of the above factors is fuzzy-fied into three membership functions *min, med*, and *max* (as shown in Fig. 6.1). The rules constructed for the afMDMS are close to 200 and are established similarly to the one of the cMDMS.
- The **Heart Failure** MDMS sub-system (hfMDMS) has four vectors of inputs, namely *Family History, Risk Factors, Symptoms Assessment (SA)*, and *Performed Echocardiogram (Echo)*. Its outputs are *No Heart Failure, Heart Failure (HF) Class I (NYHA), HF Class II (NYHA), HF Class III (NYHA)*, and *HF Class IV (NYHA)*, all set by experts.

  The severity of the above factors is fuzzy-fied into three membership functions *min, med*, and *max* (as shown in Fig. 6.1). The rules constructed for the hfMDMS are close to 80 and are established similarly to the one of the cMDMS.
- The **Diabetes** MDMS sub-system (dMDMS) has four vectors of inputs, namely *Family History, Risk Factors, (older) Clinical Examinations results (CEx)*, and *(existing) Cardiovascular Problem*. Its outputs are *No Further Evaluation, Periodical Fasting Glucose, Fasting Glucose and 2 Hours Postprandial Glucose Every 2 Years, Fasting Glucose and 2 Hours Postprandial Glucose Every Year* and *HgbA1C*, all set by experts.

  The severity of the above factors is fuzzy-fied into three membership functions *min, med*, and *max* (as shown in Fig. 6.1). The rules constructed for the dMDMS are close to 80 and are established similarly to the one of the cMDMS.

6.3.4 Choosing the Proper Fuzzy Method

There are two types of fuzzy methods widely accepted for capturing expert knowledge: Mamdani and Sugeno. Mamdani method allows for the description of expertise in more intuitive, human-like manner, but it entails a substantial computational burden. On the other hand, Sugeno method is computationally efficient and works well with optimization and adaptive techniques, which makes it very attractive in control problems, particularly for dynamic non-linear systems. These adaptive techniques can be used to customize the membership functions [12].

6.4 Evaluation and Comparison Data

6.4.1 ANFIS vs. Previous Work

In [17] previous work on building a working MDMS in the field of CDs was presented. Its performance was evaluated by three different teams of experts, specifically Group A (expert MDs that did not participate the design of the MDMS), Group B (general MDs), and Group C (medical students). All groups were asked to grade the system on its Medical Reliability, Assistance in Work, and Usability.

The former MDMS received good/very good grades regarding Medical Reliability and medium/good rating on Assistance in both Work and Usability. The newly proposed MDMS strives to overcome the difficulties and reservations users may have towards handling the system, mostly by the design of a new MDs-to-machine interface and by the application of ANNs to add to its adaptation capabilities and decision support aspects of an expert system designed for MDs.

Since MATLAB [12] was the tool used for developing the former MDMS, it was kept to also design the proposed one. Typical comparison data and diagrams showing divergences between the two systems follow in Table 6.1.

The reader promptly realizes that the performance of the ANFIS is somewhat "worse" of the former one, at least comparing the two systems' numerical data. Yet, one should carefully contemplate the typical diagrams in Fig. 6.3a, b.

It is clear that no ANFIS was left to generalize its learning inputs into the outputs. The various MDMSs have some epochs left in order to reach their minima. Still, it was decided their number to be kept similar to the previous ones.

6.4.2 Fuzzy Rules Reduction

The numbers of fuzzy rules that were employed for the previous MDMS, as already stated (Sect. 6.3), were 300 for the cMDMS; 30 for the hMDMS; 200 for the afMDMS; 80 for the hfMDMS; and 80 for the dMDMS. The engineer team reduced those numbers by first sorting the rules out with respect to their outputs; then, they eliminated the redundant ones that only differed in one of their vector inputs preserving the other vectors, i.e.:

Rule 1	IF *a1* IS *min* AND *a2* IS *med* AND . . . THEN *Outcome* IS *d11*.
Rule 2	IF *a1* IS *med* AND *a2* IS *med* AND . . . THEN *Outcome* IS *d11*.
Rule 3	IF *a1* IS *max* AND *a2* IS *med* AND . . . THEN *Outcome* IS *d11*.
Winning Rule	IF *a2* IS *med* AND . . . THEN *Outcome* IS *d11*.

Table 6.1 Typical comparison data of former/ANFIS MDMSs

	Hypertension		Heart failure		Diabetes	
	Former	ANFIS	Former	ANFIS	Former	ANFIS
Max error	0.3010	0.3458	0.0514	0.0540	0.0382	0.0446
Min error	-0.3462	-0.7775	-0.0582	-0.0631	-0.0545	-0.0557
Standard deviation	0.0031	0.0039	1.9145e-04	1.9145e-04	8.2153e-05	1.0326e-05

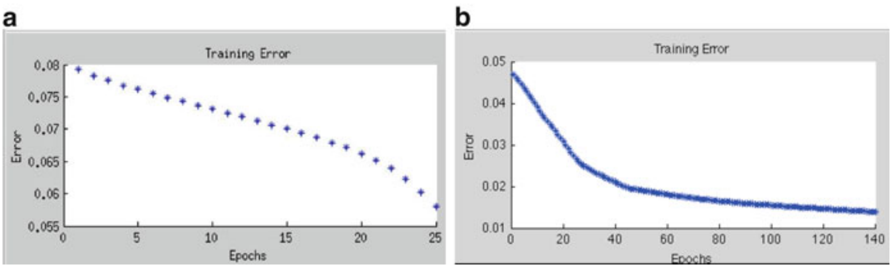

Fig. 6.3 (**a**) hMDMS's learning and (**b**) hfMDMS's learning

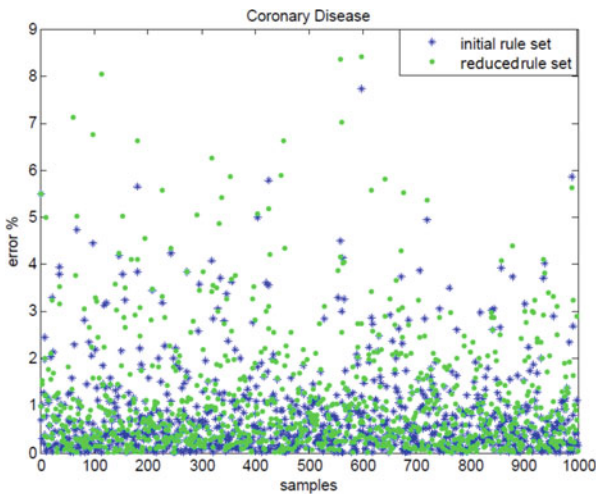

Fig. 6.4 cMDMSs' generalization errors

The input that got all the range of possible values, though the other inputs retained theirs, was eliminated. Figure 6.4 shows the differences between the two cMDMSs when left to generalise un-trained (testing) input patterns into the appropriate output ones.

Conclusions and Future Work
A new MDMS is proposed in the field of Cardiovascular Diseases. The new system is an improvement of a former one, both in potential and in less computing requirements, whereas its performance is comparable to it. In its next phase, its evaluation by MDs is scheduled, over some period of time, and several aspects of its design architecture are going to be optimized: MDs-to-machine interface, training data, number and quality of fuzzy rules, programming code portability, and porting to "smart" devices using the Android Operating System, thus ensuring its acceptance by MDs on an everyday working basis.

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