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Neural, Fuzzy, and Neurofuzzy Systems for Medical Applications

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CONTENTS

4.1 Introduction

An immense quantity of information is available in all sectors of human activity, especially in the healthcare and medical sector. The processing of that information is a challenge to the human user—the medical doctor. The challenge is to develop tools (systems, procedures, and methods), to support clinicians, which are more exact, cost-effective, and friendly to use. Information of several kinds is available.

- Numeric analytic from known cause–effect relations that can be formalized through a mathematical (in the classical sense) relation.
- Numeric empirical, issued from experimentation and practical work but to which there is no known cause–effect relation.
- Linguistic (qualitative), expressed in an approximate way by the user, with several levels of granularity (detail). Granularity may be connected to the words of common language (big, small, strong, weak, etc.) or to intervals whose limits are not clearly defined.

In most cases the available information is empirical or linguistic, issued from complex and imprecisely known relations in complex systems, such as those with which the clinicians work. To process all these kinds of information, several approaches have been developed, each one more appropriate for a certain context:

- The integral–differential approach, purely numeric, aiming at the determination of a set of mathematical equations building a model of the process (in the classical sense). This model assumes usually the form of integral or differential equations, and is seldom applicable in a medical context.
- The empirical-data approach, using some basic tools for nonlinear function approximations. The aim is to obtain a compact tool able to predict behaviors of systems (in the more general sense), after the tool has been trained with past known data. Because most real systems (such as the human biologic systems) are nonlinear, nowadays the most-used tool to synthesize relations between sets of data is the artificial neural network (ANN) formalism, giving space to the so-called neurocomputing body of knowledge.
- The linguistic approach where tools enabling computers to compute with words are used. These tools enable computers to process the language of the clinician and to make inferences and deductions. Fuzzy logic is the most-used framework for that purpose. Because of the type of information, computing with fuzzy logic is sometimes called granular computing.
- Finally, because in real situations the available information is a mix of these three types, combinations of these tools are used to build flexible systems capable of working in a diversity of situations with an acceptable degree of efficiency.

Many situations require searching for the "best" solution or, at least, a "good" solution. To search for better solutions with a computer, one must have some mathematical way of expressing what is good or not good, and an analytical formalism to search iteratively from a solution to another, improving its quality.

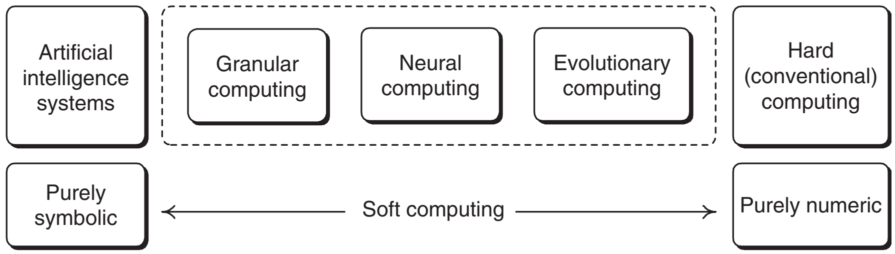

FIGURE 4.1
The place of soft computing.

Unfortunately, the body of knowledge of traditional mathematical optimization requires formal constraints and the possibility to write a mathematical criterion for comparison between solutions. In real life this classical framework is of limited applicability, because most of the real problems are ill-conditioned in the sense that they cannot be mathematically formalized in a proper way.

Soft computing techniques are a family of tools to "exploit the tolerance for imprecision, uncertainty and partial truth to achieve tractability, robustness and low solution cost" [1]. Besides neurocomputing and fuzzy computing, it also includes genetic (evolutionary) computing and other techniques able to deal with incomplete knowledge. Figure 4.1 represents the soft computing family of techniques among the computing discipline at present times (adapted from Ref. 218 and according to Ref. 217). Numeric computation deals with numbers, whereas symbolic computation deals with symbols (for example, letters) and its mathematical manipulation [2]. **AQ1**

A brief introduction to these techniques will be presented in the following section. Section 4.3 discusses some medical application involving these techniques, covering the following domains: modelling and biosignal processing and interpretation, biological system control and prognosis, and image-processing and decision-supporting system.

4.2 Soft Computing Techniques

4.2.1 The Data Paradigm: Artificial Neural Networks

This representational/computational tool derives its name from its similarities with the natural neuron (Figure 4.2). The basic element of an ANN is a single neuron, shown in Figure 4.3. It is inspired by the natural neuron and its first use in the academic community was in 1944, more or less at the same time as the birth of the digital computer. For a brief history of ANNs, see Ref. 3. **AQ2**

The natural neuron receives electrical impulses from its neighbors through dendrites, these impulses being combined in the cell body that attains a certain

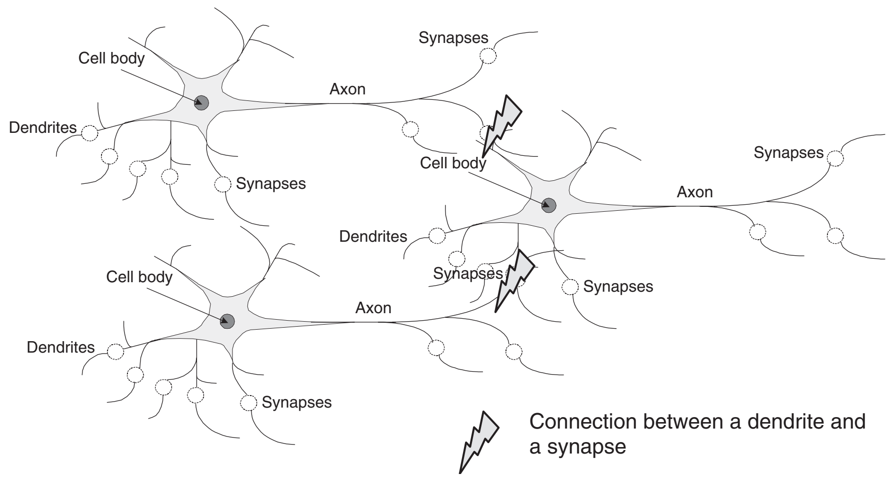

FIGURE 4.2
The biological neuron and its connections. One neuron is composed of dendrites, cell body, and synapses. A synapse transmits a signal to another neuron by contacting one dendrite.

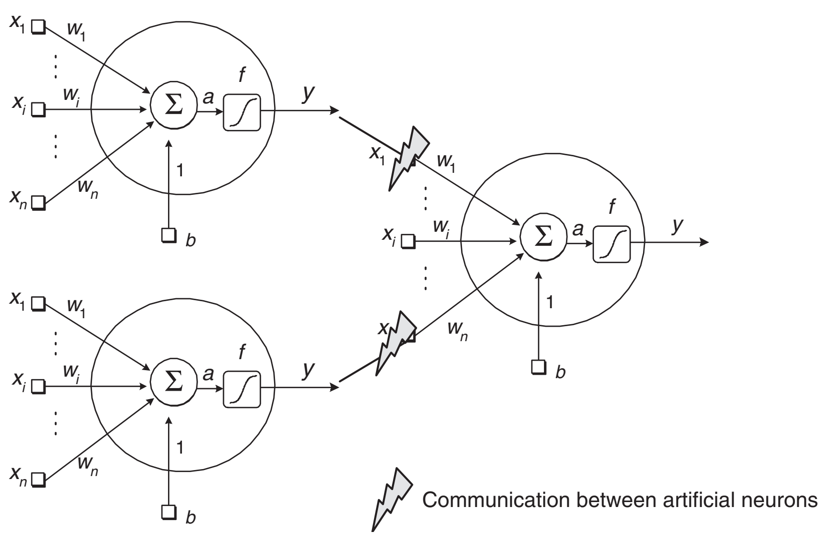

FIGURE 4.3
Artificial neuron and its connections.

activation degree and an electrical impulse is then transmitted through the axon to a synapse of the following neuron. In the artificial neuron, signals represented by numeric values are presented to the input, weighted by the artificial synapses (called weights for this reason), are combined (usually summed), and the resulting signal is the argument of a certain function—the activation function—that produces a transformed signal as output [4].

Figure 4.3 shows the usual representation of an artificial neuron. A single artificial neuron is a simple and powerful computational tool. The weighted sum a of several inputs is passed through an activation function f to produce the output y of the neuron; Equation 4.1.

$$a = w_1x_1 + w_2x_2 + \cdots + w_nx_n + b \Leftrightarrow a = w^Tx + b \tag{4.1}$$
$$y = f(w^Tx + b)$$

An alternative architecture is the radial basis neuron measuring a radial distance between the input presented to it and an interior center (the radbas function is illustrated in Figure 4.4d).

$$y = radbas(a) = radbas(\|w - x\|b) \tag{4.2}$$

$$y = radbas\left(\sqrt{(w_1 - x_1)^2 + (w_2 - x_2)^2 + \cdots + (w_n - x_n)^2}\right)$$

The special input of constant value 1 is called the bias of the neuron, allowing a nonzero output for a zero input. One neuron has the following degrees of freedom: the number of inputs, the value of the weights, the type and parameters of the activation function f, and the value of the bias weight b. It is possible to use a multiplicity of activation functions. Figure 4.4 shows some of them [5].

A neuron can be combined (networked) in an arbitrary way in series and in parallel, giving place to structures that can model any nonlinear relations between a set of inputs and a set of outputs, with or without feedback. One of the most used structures is shown in Figure 4.5, the multilayer feedforward neural network (MLFNN), also known as perceptron [6].

Other well-known structures are radial basis function neural network (RBFNN), having only a radial hidden layer, and recurrent neural networks (RNN), which involve dynamic elements and have feedback connections. Each structure has its own potentialities and is more adequate for certain types of applications. In general terms, ANN is used to find relations between two sets of data: an input set is presented to the network, that is, the network is trained to reproduce at its output the other set, the target set, or to classify the input set among a finite number of classes. Training means to use its degrees of freedom to find the configuration that best fits the situation (best according to some criteria). Figure 4.6 illustrates how this is done in the case of modelling biological systems. The same input set is given to the

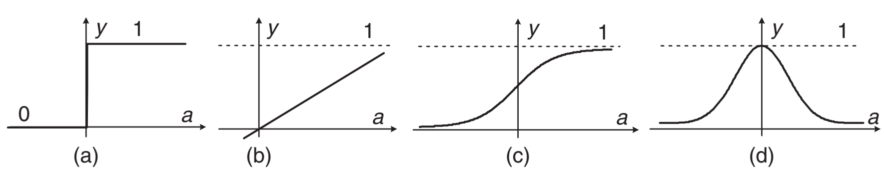

FIGURE 4.4
Some types of activation functions. (a) Binary; (b) linear; (c) logistic; (d) radial based.

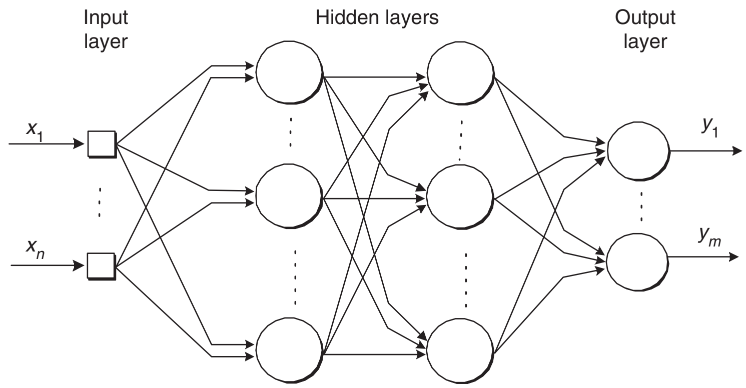

FIGURE 4.5
Multilayer feedforward neural network (in this case with two hidden layers).

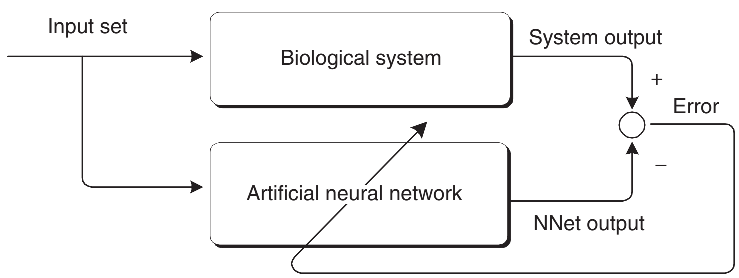

FIGURE 4.6
Training the artificial neural network to model biological systems.

system to be modelled and to the network. The output of the network is compared with the system output (the output set) and an error information is fed back to the network, where a training algorithm changes its degrees of freedom (usually the weights) until the error is minimized.

The MLFNN and RBFNN are appropriate for function approximation such as in modelling biological systems. There is one weight for each input for each neuron, resulting in a high number of weights even for small networks. For a particular problem, the training of the network is just the procedure to find the best set of values of these weights such that the network is able to mimic the response to a certain history of inputs. After the training phase, the network is able to predict the future behavior, or give answers to new inputs (data generalization). Of course the generalization capability of the network depends on many factors, namely the quantity and quality of inputs and the particular architectures. Similarly, because of the complexity and variety of the human body, doctors make decisions that are not based on a single symptom [4]; a doctor with more experience is more likely to make correct decisions than a newcomer because of his learnings from past mistakes

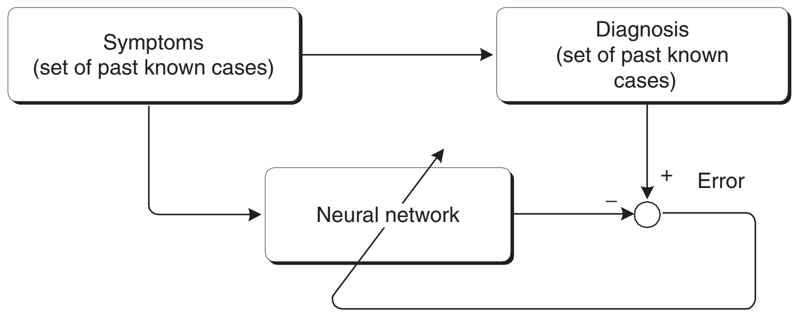

FIGURE 4.7
Training the artificial neural network for diagnosis tasks.

and successes (he has more training data). To have a good set of examples is decisive for the "experience" of the neural network.

For pattern recognition, some kinds of single-layer networks (Hebb, Widrow–Hoff, etc. [6]) can also be adequate. In medical decision problems, the medical symptoms such as "stabbing pain in head," are presented to the inputs (after being codified by a numerical value) as training examples. For a set of past data, containing symptoms for which the correct diagnosis is known, the weights of the network are varied in a systematic way such that the output of the network produces the correct diagnosis (also codified by a numeric value)—"brain tumor," "stress," etc. The hidden layers are just used for the computation of the mapping between the inputs and the outputs (Figure 4.7).

Therefore, the network is trained just like a doctor, being presented with a large number of known cases (training set) with known outcome. The most used algorithm for training the multilayer network, that is, the adjustment of its weights, is the backpropagation algorithm [7], using the backward propagation of the information. Basically it is a computational procedure that varies the weights to progressively reduce the distance between the correct answer and the network answer. The information is sent backward because only at the end of the network (its output) this distance can be computed and the changes of the weights in the beginning of the network depend on that information. If properly trained, the network can give answers to new unknown cases with some reliability. If the training is made constantly, as new cases happen, the network becomes adaptive and with improved capabilities. For a good review see Ref. 8.

The simple structure of a neural network has a high number of degrees of freedom: type of activation function, number of layers, and number of neurons per layer. Moreover there are two fundamental learning approaches: supervised learning and unsupervised learning. In supervised training a desired behavior of the network output is previously specified, as in Figure 4.6. In unsupervised learning no such behavior is provided; unsupervised learning can be used for analyzing (clustering, for example) the input data and to find features embedded in the data expressing properties of the system in study. Self-organizing maps (SOM), introduced by Kohonen [9] in

1982, are originated from learning vector quantization (LVQ) that was also introduced by Kohonen [10]. If systems continue to remain adaptive, care must be taken such that previously learned information is not lost. Grossberg [11] has coined the term stability–plasticity dilemma for this problem introducing adaptive resonance theory (ART). Regarding the flow of information, basically, neural networks can be classified as static (feedforward) and dynamic (recurrent). RNN were first introduced by Hopfield [12], and then developed by some other authors. Unlike the neurons in MLNN, the Hopfield network consists of only one layer whose neurons are fully connected with one another. Owing to their intrinsic abilities to incorporate time, they have some advantages with respect to static neural networks (feedforward multilayer perceptrons), particularly for modelling dynamic processes. AQ4

Additionally, other properties justify their application in the medical domain, [13–17]: noise is quite well managed by neural networks, their prediction capabilities are well-suited for regressive models, the on-line learning capabilities allows to face the possibilities of automatic analysis and diagnosis with updated knowledge. On-line learning means that data are processed

TABLE 4.1

Publications in Pub Med with "Artificial AND Neural AND Networks"

Year	Number of Papers
1996	168
1997	209
1998	233
1999	229
2000	252
2001	298
2002	311
2003	321
2004	498
2005	428

TABLE 4.2

Publications in Pub Med with "Neural AND Networks"

Year	Number of Papers
1996	632
1997	641
1998	728
1999	809
2000	895
2001	998
2002	996
2003	1185
2004	1542
2005	1548

iteratively as it is obtained, as opposed to off-line learning where complete data are firstly obtained and then the learning process is launched with all data simultaneously considered.

The total number (on June 20, 2006) of references in Pub Med under "artificial AND neural AND networks" was 2617 ([18], in all fields). For the past 10 years, the number is indicated in Table 4.1. Under "neural AND networks," the total number was 11293 (most of these are related with artificial networks) and for the past 10 years the number of publications is shown in Table 4.2.

The main drawback of ANNs is that they are "black boxes," that is, they do not give any understandable explanation for the relation between its inputs and outputs. They just give numbers that cannot be interpreted in terms of a natural language. If the model would become transparent, explaining the reasons for the diagnosis, then it would increase its importance and usability. Fuzzy systems allow making this evolution of the machine because fuzzy logic is a way to compute with words.

4.2.2 The Linguistic Paradigm: Fuzzy Logic and Fuzzy Systems

Fuzzy logic was born in 1965 by the pioneer work of Lofti Zadeh [1], at MIT, United States, as a mathematical tool for dealing with uncertainty. In fuzzy logic, statements are not "true" or "false" (as in the Aristotelian bivalued logic), but they may have several degrees of truth and several degrees of false. Fuzzy sets do not have a well-defined frontier, but an imprecise (fuzzy) one. It is not only black and white but it has many levels of gray in between. Consider, for example, the classification of teeth development in preeruption, emerging, and posteruption. Is there a well-defined frontier between these phases? If a tooth has a state of eruption 0.2, what is its state? It is still emerging, but has it already emerged! How can we represent this in the classical binary Aristotelic logic (true or false, 0 or 1, black or white)? Fuzzy sets are very convenient to represent the situation (see Figure 4.8)[19].

The membership functions (*mf*), representing the membership degree may have several shapes (see Figure 4.9).

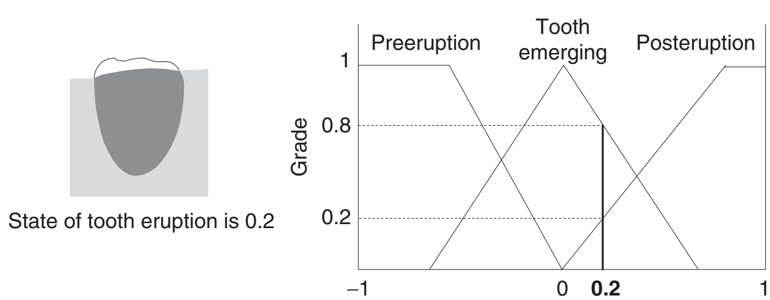

FIGURE 4.8
Membership functions (b) of teeth development phases.

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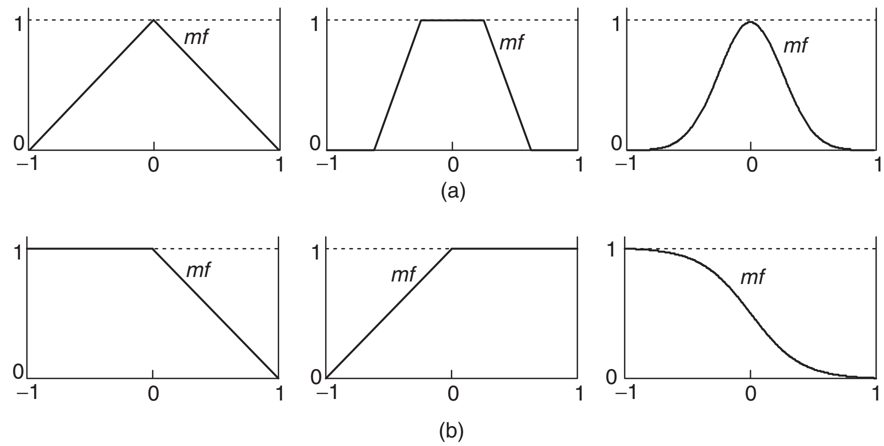


FIGURE 4.9
Membership functions: (a) symmetrical (triangular, trapezoidal, Gaussian); (b) nonsymmetrical.

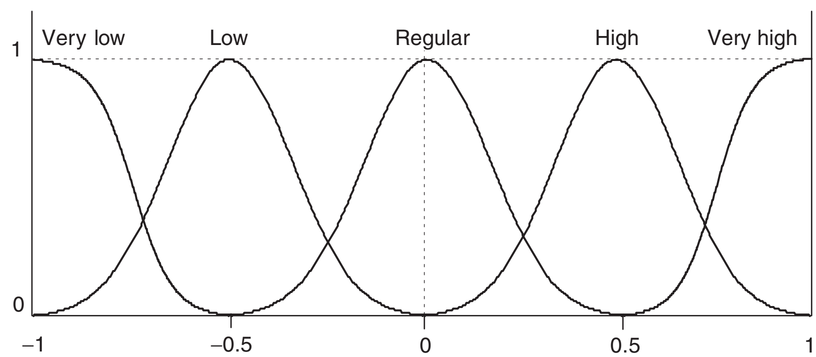


FIGURE 4.10
A universe of discourse (one variable) divided into five fuzzy sets. The first and last ones are nonsymmetrical.

For any variable (for example, temperature) its universe of discourse is divided into several labels, each one corresponding to a fuzzy set (e.g., "very low," "low," "regular," "high," and "very high").

The fuzzy sets must overlap and they must cover completely the universe of discourse (all the intervals of possible temperatures, in the example, and as illustrated by Figure 4.10). Usually they must overlap in such a way that the sum of the membership degrees for any point is 1, and at most two sets are valid for that point. Fuzzy logic is the logic of fuzzy sets. In fuzzy logic there are many levels of truth and of false, in the real interval [0,1]. A value in the universe of discourse belongs simultaneously to several fuzzy sets, eventually with different membership values.

There are some characteristics of our perception systems that can be seen as fuzzy sets. For example, according to Sir Thomas Young's (1802) theory

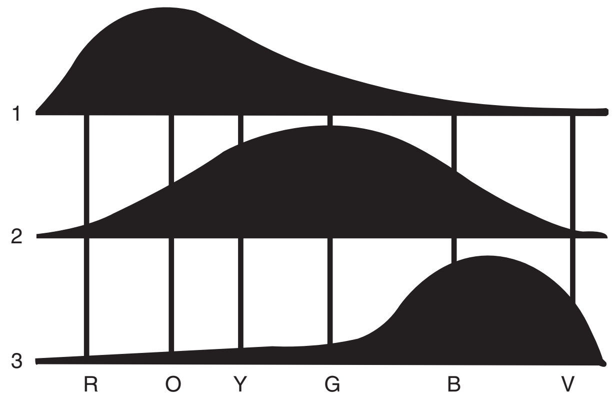


FIGURE 4.11
Illustration of the theory of Young. The curves show the amount of activity of each of the three visual receptors types by each wavelength (of the several colors). Maximum excitation in each is produced by one wavelength, and adjacent wavelengths produce progressively less activity. (From Erikson, R., Chelaru, M., and Buhusi, C., *Fuzzy and Neurofuzzy Systems in Medicine,* CRC Press, Boca Raton, FL, 1999.) AQ34

[20] for color perception, there are three principal colors—red, green, and blue—and three types of visual receptors.

The way these visual receptors vibrate with the colors' wavelengths is illustrated in Figure 4.11. Maximum excitation in each is produced by one wavelength; adjacent wavelengths produce progressively less activity in the particular receptor.

This seems to be the case of all sensorial systems: although we have many neurons, there are not enough such that each neuron has a specific function (e.g., to encode red apples) distinct and disjoint from that of every other neuron. There is too much information to be encoded. The sensitivity functions of all individual neurons in all sensory systems are bell-shaped at a first approximation and have been referred to as neural response functions (NRF) [18]. There are few neural resources to represent many stimuli. So the few neurons available must have fuzzy sets (NRF) that can as broadly as possible cover all stimuli (Figure 4.12). AQ5 AQ6

Fuzzy systems work in a similar way. Using fuzzy sets and fuzzy logic, fuzzy inference systems may be built enabling to compute a decision based on a set of rules. Fuzzy rule–based systems perform a sequence of fuzzy logical operations: fuzzification, conjunction, inference, and defuzzification [21].

A fuzzy system consists of three stages: the fuzzification, the deffuzification, and the inference procedure (Figure 4.13). The fuzzification stage determines the membership degrees of the input values in the antecedent fuzzy sets, converting numerical values of patient data (symptoms that mainly define the patient's state of health) into linguistic variables. The inference mechanism combines input information with the knowledge stored in the fuzzy rules and determines the output of the rule-based system. The knowledge base consists into the diagnosis scheme, expressing associations between symptoms and AQ7

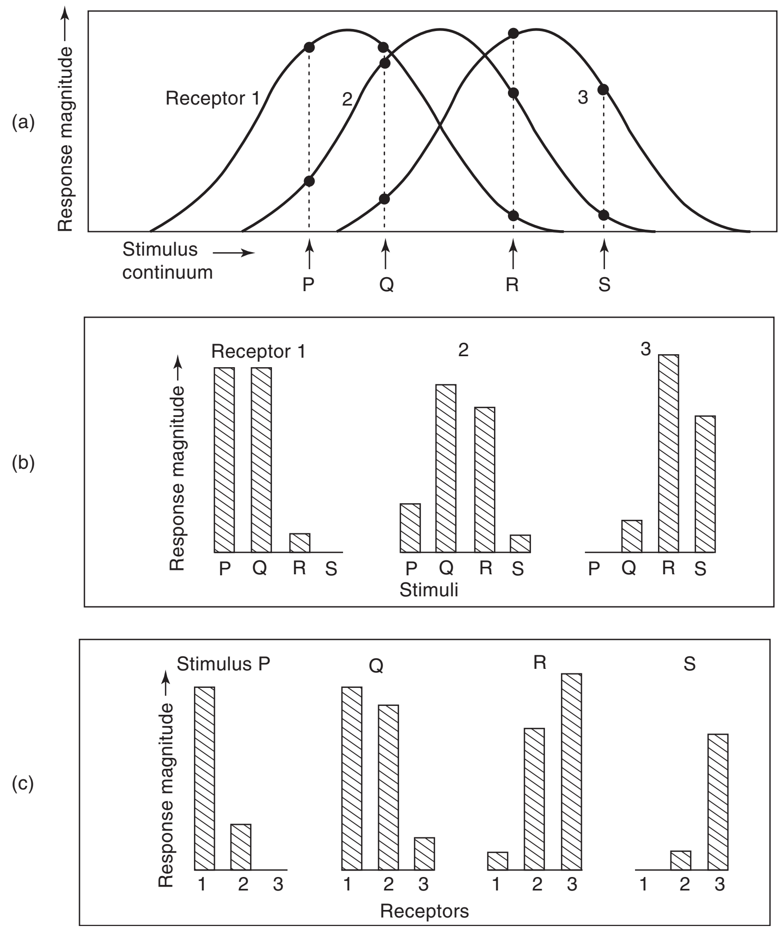


FIGURE 4.12
Fuzzy sets and neural codes according to Young's theory. (a) Three idealized receptor types (1, 2, 3) and four stimulus (P, Q, R, S); (b) the magnitude of the response of each receptor to each stimulus; (c) the neural codes for P, Q, R, S. The brain interprets these codes. (From Erikson, R., Chelaru, M., and Buhusi, C., *Fuzzy and Neurofuzzy Systems in Medicine,* CRC Press, Boca Raton, FL, 2000.)

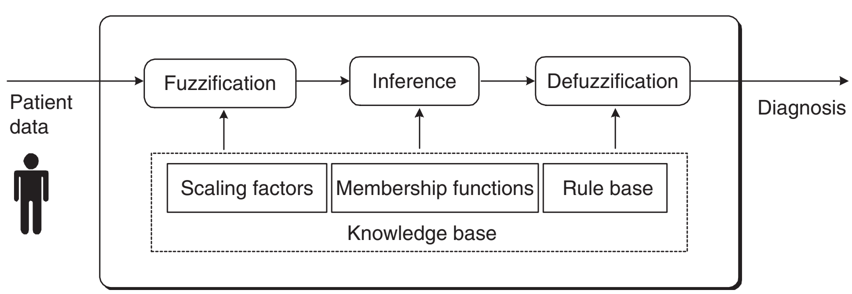


FIGURE 4.13
Different modules of a fuzzy system.

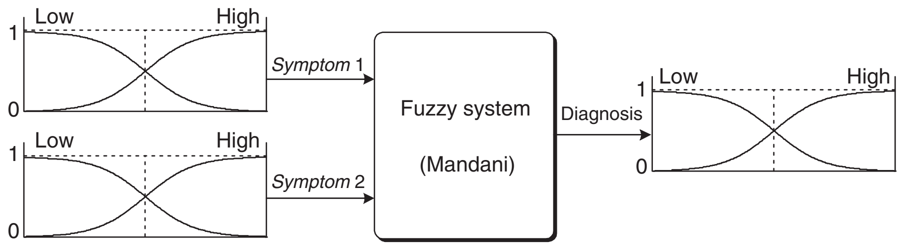


FIGURE 4.14
The fuzzy system and membership functions.

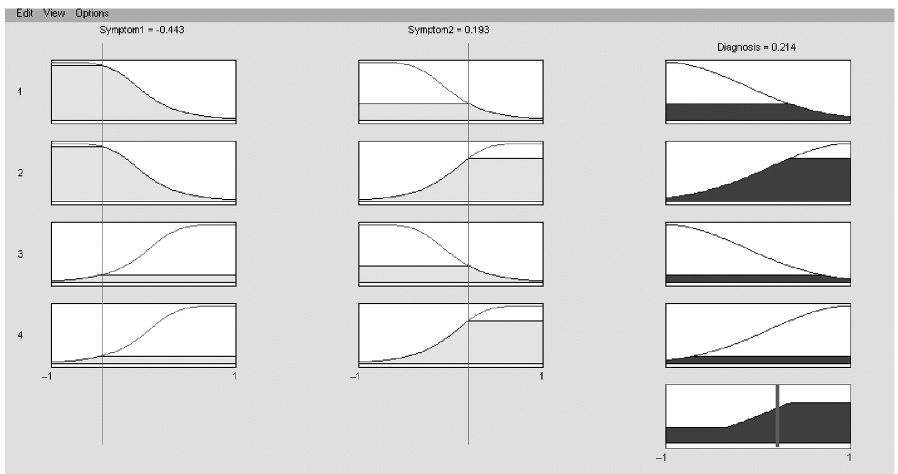


FIGURE 4.15
Firing the rule base: fuzzification, conjunction, inference, defuzzification (obtained with the Fuzzy Logic Toolbox, the Mathworks, Inc).

diseases by means of fuzzy rules. The diagnosis is obtained by the defuzzification part, which chooses among rules that have been fired simultaneously.

Let us consider a fuzzy system with four rules in the form depicted in Figure 4.14.

Rule 1: If Symptom1 is LOW and Symptom2 is LOW then Diagnosis is LOW.
Rule 2: If Symptom1 is LOW and Symptom2 is HIGH then Diagnosis is HIGH.
Rule 3: If Symptom1 is HIGH and Symptom2 is LOW then Diagnosis is LOW.
Rule 4: If Symptom1 is HIGH and Symptom2 is HIGH then Diagnosis is HIGH.

Fuzzification is the operation of transforming a numeric value, issued from a measurement, into a membership degree of a fuzzy set. Figure 4.15 shows 2 measurements: Symptom1 = -0.443 and Symptom2 = 0.193. All four rules have some degree of truth and some degree of false. All rules must be fired. To compute the firing intensity of one rule, one may consider the weakest case in the antecedents, corresponding to the application of the minimum operator. Now we transport these values to the consequents. This is done by cutting the fuzzy set of the consequent at the height equal to the firing intensity of the antecedent. The graph shows that (on the right-hand side) rule 3 is quite truth, rule 1 is about 0.3 truth, rules 2 and 4 are about 0.2 truth.

The final decision is the result of the balanced contribution of the four rules. Defuzzification is this balancing to obtain a numerical value to be assigned to the decision. If the four figures (of the consequents) are superposed, in geometrical terms the point of equilibrium is the center of mass. This is the most used defuzzification method and it is applied in the example. The graphical construction is quite intuitive. Formally, there are some properties and operations of fuzzy logic supporting it. For example, the cutting of the membership function on the consequent is made by a minimum operator:

$$DiagnosisOut = min(sympotom1, symptom2)$$

The operator maximum performs the aggregation of outputs:

$$OutputFinal = max(diagnosis1, diagnosis2, diagnosis3, diagnosis4)$$

Takagi-Sugeno-Kang (TSK) fuzzy systems are based on rules that have a nonfuzzy consequent. For a zero order TSK system, each consequent is simply a constant: they are in the form (for a similar example, and with constants 0 and 1 in the consequents).

Rule 1: IF Symptom1 is LOW	*and Symptom2 is LOW*	*then Diagnosis is 0.*
Rule 2: IF Symptom1 is LOW	*and Symptom2 is HIGH*	*then Diagnosis is 1.*
Rule 3: IF Symptom1 is HIGH	*and Symptom2 is LOW*	*then Diagnosis is 1.*

Figure 4.16 illustrates how it works. Now for the same measurement values, it proceeds as follows:

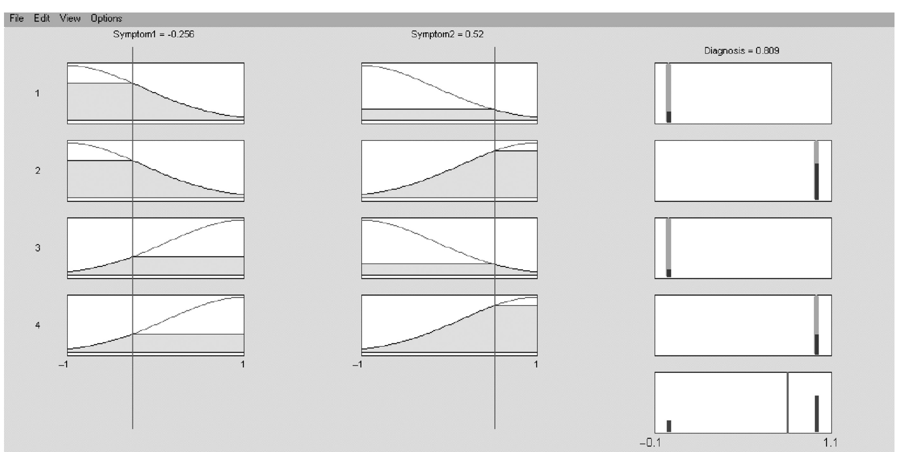


FIGURE 4.16
Firing the rule base in TSK model: fuzzification, conjunction, inference, defuzzification (obtained with the Fuzzy Logic Toolbox, the Mathworks, Inc).

Rule 1: firing strength: 0.15 output1 = 0
Rule 2: firing strength: 0.75 output2 = 1
Rule 3: firing strength: 0.15 output3 = 0
Rule 4: firing strength: 0.4 output4 = 1

The overall output is the sum of the individual outputs weighted by their degrees of truth, that is, the firing strength of the respective rule, giving 0.8, shown on the right-hand side of Figure 4.16.

TSK fuzzy systems are simpler to compute than the previous ones called Mamdani fuzzy systems. They are particularly important in neurofuzzy systems. A fuzzy system is a set of fuzzy rules describing what is known about some problem. The development of the fuzzy system is basically the writing of the rules. However, how are these rules obtained? Several approaches may be applied:

- Expert interviews (actual medical knowledge)
- Simulation using models of the processes (seldom possible)
- Rule extraction from data (data mining)

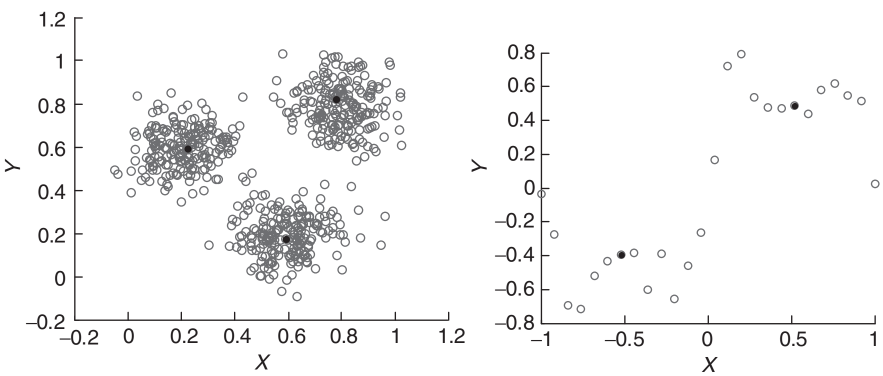
The latter is becoming the most important approach, where the machine (computer) learns from data. Two aspects must be analyzed: the determination of an initial set of rules (the initial structure of the system) and the update and optimization of the rules as new data and knowledge become available. For the determination of the initial set of rules, the most important technique is clustering. The second operation, the optimization of the fuzzy structure (i.e., the number of rules, the parameters of the membership function, etc.) is actually carried out in the context of neurofuzzy systems. The first application of fuzzy logic to the medical field dates back to 1969, when Zadeh published a paper on the possibility of applying fuzzy sets in biology [22].

The medical field has inheritably several sources of inaccuracy [23]: information about the patient consists of a number of categories, all of which have uncertainties; medical history of patients is most of the times subjective and may include nonunderstandable symptoms (supplied by the patient); and lack of knowledge of previous diseases that usually leads to doubts about the patients' medical history. Additionally, although results of laboratory tests are objective data, they are however dependent on the accuracy of the measurements and on the possible inadequate behavior of the patient during the examination. Fundamentally, fuzzy systems allow transparency in knowledge representation and in the formulation of decision rules that mimic human thinking, justifying its medical application in the representation of narratives and clinical guidelines in decision-support systems [24,25].

The number of papers published on fuzzy logic in medicine during the past 10 years are given in Table 4.3. (Pub Med [18] under "fuzzy" on June 20, 2006, all fields).

TABLE 4.3
Publications in Pub Med with "Fuzzy" (All Fields)

Year	Number of Papers
1996	98
1997	128
1998	135
1999	135
2000	152
2001	218
2002	191
2003	201
2004	304
2005	278



(a) (b)

FIGURE 4.17
Clustering is a classification of multidimensional points into classes. The black points represent the centers of (a) FCM used; (b) the classes obtained by subtractive clustering (obtained with the Clustering Interface, the Mathworks, Inc.).

The first applications were related to assessing of symptoms and the modelling of medical reasoning. For a more detailed historical perspective of the early stage, see Ref.26. For the similarity between fuzzy reasoning and the physiology of the nervous system, see Ref. 20, where the dynamic model of sensory systems by the neural response functions, for example, for taste neurons, is made by a TSK fuzzy system.

4.2.3 Clustering and NeuroFuzzy Systems

Clustering is basically the detection of similar points in an input–output space data set. Figure 4.17 illustrates the case of a bidimensional data space for a system with two variables (e.g., input x and output y).

A region where there is a concentration of data forms a cluster. A cluster then represents a repetition of facts resulting from some property such as input–ouput relation. Computational clustering techniques form a large body of knowledge. In soft computing, the most used are the Fuzzy C-means (FCM), the mountain, and the subtractive clustering [27–29].

Clustering is an operation that requires high-computational resources and currently, the main research direction is to obtain recursively implementable clustering techniques such that the clusters are continuously updated with new data. This is particularly important for systems that operate in changing environments needing permanent adaptation and learning.

A cluster identifies a working region, so it defines a relation between the variables; this relation may be translated into a fuzzy rule. One of the main important applications of clustering is precisely in the development of rules from data, leading to the neurofuzzy systems. Once the clusters have been identified, fuzzy rules can be built based on the identified centers $c_i = (x_i, y_i)$, of the form:

$$\textit{IF Input is } X_i \textit{ THEN Output is } Y_i$$

where X_i and Y_i are the fuzzy sets centered on x_i and y_i, respectively.

Fuzzy systems are designed to work with knowledge in the form of linguistic rules; neural networks to deal with data. The optimization of rules with respect to a set of data or to new data needs an efficient computational tool able to process a nonlinear mapping (a rule is in general a nonlinear mapping). Neural networks enter here in a natural manner. A hybrid technique is defined as any effective combination of different techniques that performs superior or, in a competitive way, over simple standard techniques [15,30]. Neurofuzzy systems are possibly the most promising hybrid soft computing technique, combining the capabilities of neural networks with fuzzy systems, that is, enabling to acquire knowledge (fuzzy rules) from experimental data. Because of the accuracy and the interpretability that they may allow to achieve, neurofuzzy systems have shown a high potential of success when applied in complex domains of application such as in the medical field [23].

The artificial neural fuzzy inference system (ANFIS) [31,32], depicted in Figure 4.18 is probably used the most. It is based on TSK fuzzy rules and have the structure of an MLFNN neural network with five layers.

Each layer computes a fuzzy operation:

- Layer 1—the fuzzification layer (A_i, B_i): each numerical input is presented to each neuron. The neuron output is the membership value of the input. For each input variable there are as many neurons as fuzzy sets in its space.
- Layer 2—the conjunction layer (T): each neuron computes the conjunction of the antecedents of each rule. Usually the conjunction operator is the algebraic product of the antecedent membership values. The output of the neuron is the absolute firing strength of the rule. There are as many neurons as rules.

- Layer 3—the normalization layer (*N*): each neuron computes the relative firing strength of the rule with respect to the sum of all strengths of all fired rules.
- Layer 4—the inference layer: computes the consequent value for each rule weighting the consequent function by the relative firing strength of the rule.
- Layer 5—the defuzzification layer: computes the overall output of all the rules by summing the individual consequents from the previous layer.

The operations of the network are the same as we saw in the graphical inference method (Figure 4.17). The advantage is that we now have a neural network that can adjust its weights to a set of data in a way such that the output of the network approaches optimally the experimental output. We have here simultaneously the advantages of fuzzy logic and the advantages of the neural networks. Neurofuzzy systems have this nice property. AQ8

The research of new architectures for neurofuzzy systems is very active. Several developments from ANFIS architecture can be found: DENFIS [33], GENFIS, [34] and others [35]. AQ9

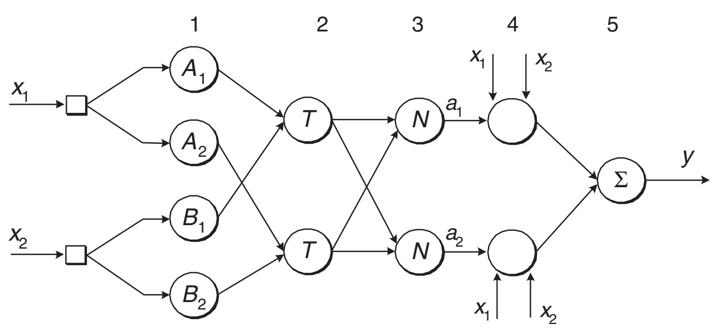


FIGURE 4.18
The ANFIS neurofuzzy system is composed of five layers.

TABLE 4.4
Publications in Pub Med with "Neurofuzzy"

Year	Number of Papers
1996	1
1997	1
1998	0
1999	6
2000	4
2001	10
2002	10
2003	9
2004	10
2005	12

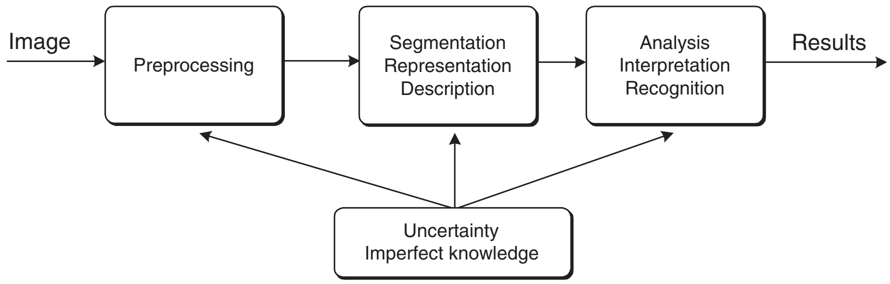


FIGURE 4.19
Imperfect knowledge in image processing. (Adapted from Tizhoosh, H., *Fuzzy Image Processing: Introduction in Theory and Practice*, Springer-Verlag, Heidelberg, 1997.)

Under "neurofuzzy," all fields, the number of publications in Pub Med on June 20, 2006, was as indicated in Table 4.4.

4.2.4 Fuzzy Medical Image Processing

Medical images convey uncertainty due to the intrinsic nature of modalities that originate noise, blurring, background variations, partial volume effects (this effect is induced by low-resolution sensors, which induce borders strictly not defined between tissues), low contrast, and certain modality-specific effects. This uncertainty is not always due to randomness but due to ambiguity and vagueness and may propagate to the entire image-processing chain, that is, from the low- to the high-level image-processing stages (see Figure 4.19). According to Refs. 37 and 38, besides randomness three other sources of imperfection can be distinguished in images in general: (1) grayness ambiguity, (2) geometrical fuzziness, and (3) vague (complex/ill-defined) knowledge.

These uncertainties are difficult to overcome using the traditional image-processing approaches such as probabilistic and physics-based image interpretations. Under these circumstances, expert knowledge can provide a valuable source of information to deal with uncertainty.

Following Tizhoosh's [36,37] definition, fuzzy image processing comprises the collection of all approaches that understand, represent, and process the images, their segments, and features as fuzzy sets. The representation and processing depend on the selected fuzzy technique and on the problem to be solved. From this definition it becomes clear that to integrate the fuzzy framework into image processing, a new image definition has to be applied, that is, images and their components have to be fuzzified, whereas relationships between image parts have to be extended into fuzzy sets. During the processing stage, appropriate fuzzy techniques modify the membership values. These can be fuzzy clustering, fuzzy rule-based approaches, fuzzy-integration approaches, or others. As one would expect, a defuzzification stage has to be performed to obtain crisp results. This general procedure is illustrated in Figure 4.20

Typical fuzzifiers depend on the task at hand. For instance, to perform global image-processing tasks, that is, point operations, each pixel should

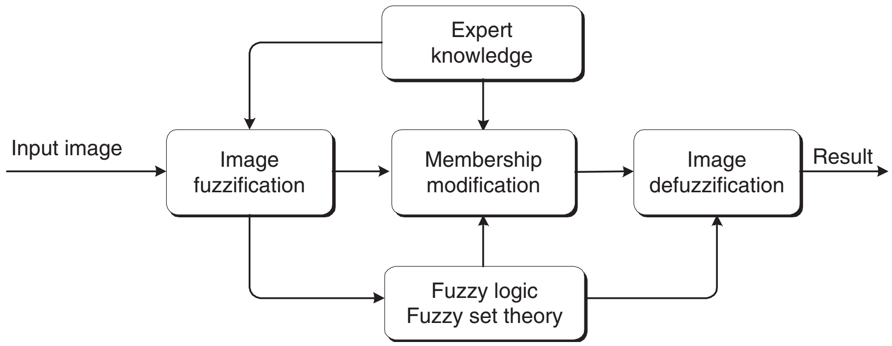


FIGURE 4.20
The general structure of fuzzy image processing.

be assigned one or more membership values. This is known as histogram-based gray-level fuzzification that can easily be extended for color image point processing. For typical neighborhood-based pixel operations, such as in filtering (e.g., noise filtering and edge detection) and local contrast enhancement, image fuzzification usually takes into account the same neighborhood applied during the processing step. For intermediate- and high-level image-processing tasks, fuzzification of the extracted image features is required (e.g., shape descriptors, corners, curvature, texture, and motion). Again the fuzzifier is application dependent and should be set up based on expert knowledge, and eventually combined with a learning strategy [36–38].

Fuzzy processing is performed by modifying the membership values of pixels or features by means of a suitable fuzzy approach. The most common modification principles are [37] (1) aggregation using, for instance, fuzzy integrals, (2) membership value transformation (this is usually the case for contrast enhancement), (3) classification by means of fuzzy classifiers such as fuzzy clustering or syntactic approaches, and (4) inference by means of if–then rules. Low- and intermediate-level image-processing operations usually require crisp outputs; these may be computed during a defuzzification stage. For image processing two general groups of defuzzifiers exist: (1) conventional defuzzifiers such as center of area and mean of maximum and (2) inverse mapping for point-based operations.

For further reading on fuzzy image-processing principles and theory refer to Refs. 36,37,39,40].

4.3 A Brief Review of Applications in the Medical Field

Regarding medical domain applications, handled with soft computing schemes, numerous approaches have been presented in literature. Significant medical applications that make use of neural networks, fuzzy systems, and both involve the following among others:

Medical Application	Reference
Bacteriology	41
Cardiology	39,40,42–44
Dentistry	45
Drug and anesthesia delivery	24,46
Gastroenterology	47
Genetics	48,49
Intensive care	50,51
Neurology	52,53
Nuclear medicine	54
Obstetrics and gynecology	55
Oncology	56–59
Ophthalmology	60,61
Otology-rhinology-laryngology	62
Pathology	63,64
Radiology	65–68
Sleep research	69
Urology	70,71

The review presented in this work is structured on medical application domains, covering the following areas: modelling and biosignal processing and interpretation, biological system control and prognosis, and image-processing and decision-supporting system [42].

4.3.1 Modelling and Biosignal Processing and Interpretation

Our understanding of biological systems is incomplete. There are features and information hidden in the physiological signals that are not clear, and effects between the different subsystems that are not evident. Moreover, biological signals are characterized by significant variability, caused by impulsive internal mechanisms or external stimulus and, most of the times, are corrupted by noise.

There are two main, recognized advantages of using neural networks for modelling and biosignal processing [72]: one is their capacity to perform any nonlinear mapping between input and output patterns (providing an adequate number, type, and association of neurons). This capacity offers an universal approximation property of unknown systems based on sparse sets of noisy data, such as biological systems. Another advantage is the adaptive learning capacity of neural networks, enabling them to adapt to new input patterns. Unfortunately, it is almost impossible to come to a reasonable and human understandable (transparency) interpretation of the overall structure of these networks. Furthermore, the existence of previous knowledge, for instance, the explanation of clinical rules, is not easily incorporated into the neural model. In the context of modelling and biosignal processing, fuzzy systems provide tolerance and partial correctness; thus a suitable way to represent qualitative linguist information. Independently or combined, neural network and fuzzy systems can assist the modelling of their relationships

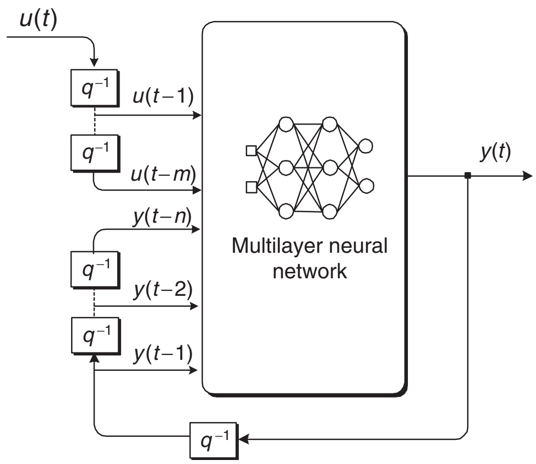


FIGURE 4.21
Multilayer neural network with external recurrence.

containing uncertainty and nonlinearity characteristics, extract parameters and features, identifying and removing biosignal artifacts.

Multilayer perceptrons with external recurrence have been extensively applied in biological systems domain. Using this structure, the nonlinear mapping between output and past information is implemented by a neural network, the output being $y(t)$ function of the m past inputs, $u(t-1), \ldots, u(t-m)$ and the n past outputs, $y(t-1), \ldots, y(t-n)$, as described in Equation 4.1 and depicted in Figure 4.21 (q^{-1} represents the unitary delay operator). AQ10

$$y(t) = NN\,\{y(t-1), y(t-2), \ldots, y(t-n), u(t-1), u(t-2), \ldots, u(t-m)\} \qquad (4.3)$$

In the field of biosignal processing (mainly for cardiology), soft computing techniques have been widely used in clinical practice for automatic electrocardiographic (ECG) analysis. There have been several attempts to use neural networks to improve the ECG diagnostic accuracy and achieve more faultless operation, even in the presence of complicating factors. In this context, Lee et al. [73] have studied and compared multilayer RNN with conventional algorithms for recognizing fetal heart rate abnormality, revealing the exceptional performance of neural networks. Multilayer neural networks were also used to model heart rate regulation [74,75], although Ortiz et al. [76] have applied them to examine heart failure. Assessment of long-term ECG recordings (Holter-monitor) is a time-consuming and exhausting procedure (nearly 90.000 ECG-complexes a day). Neural networks have shown capabilities to recognize disorder events automatically, which occur infrequently with up to 99.99% sensitivity [77]. For long-duration ECG recordings, Papaloukas et al. [78] have presented a method that employs neural networks for the automated detection of ischemic episodes.

Silipo and Marchesi [79] have demonstrated the capabilities of neural networks to deal with the ambiguous nature of ECG signals. In their work they have used static and RNN architectures and explored ECG analysis for arrhythmia detection, myocardial ischemia recognition, and chronic alterations. Janet et al. [44] discuss a neural network that has been trained to detect AQ11 acute myocardial infarction. They have used ECG measurements from more than 1,000 patients who had suffered a heart attack, and more than 10,000 healthy persons, with no history of heart attack. They have concluded that neural networks were 15.5% more sensitive than an interpretation program and 10.5% more sensitive than experienced cardiologists in diagnosing any abnormalities. However, the cardiologist was slightly better at recognizing ECGs with very clear-cut acute myocardial infarction changes.

Waltrous and Towell [80] reported the use of a neural network, synthe- AQ12 sized from a rule-based classifier, applied to an ECG patient monitoring task. Serum enzyme–level analysis forms the basis of acute myocardial infarction diagnostics. The neural network has been trained based on the analysis of these heart enzyme levels, showing a diagnostic accuracy of 100% with an 8% false-positive rate. The neural beat classifier was integrated into a four-stage procedure for the diagnosis of ischemic episodes.

When conditions are such that an RBFNN can act as a classifier [81], an advantage of the local nature of radial basis function networks, compared with multilayer neural networks, is that a new set of input values that falls outside all the localized receptor fields could be recognized as not belonging to any of the existing classes. Employing an RBFNN, Bezerianos et al. AQ13 [82] have approximated the nonlinearity of heart dynamics, using the local reconstruction of the dynamics in the space spanned by each basis function. Fraser et al. [83] have investigated the effectiveness of radial basis function networks for diagnosis of myocardial infarction. Their method achieved a sensitivity of 85.7%. However, as studied by Tarrassenko [84], an RBFNN AQ14 may not perform as well as a multilayer network. For example, in an electroencephalogram (EEG) application an RBFNN has shown a shortly increased misclassification (11.6%) when compared to a multilayer neural network.

Lagerholm et al. [85] employed self-organizing neural networks in conjunction with Hermite basis function, for the purpose of beat clustering to identify and classify ECG complexes in arrhythmia. As claimed by the authors, self-organizing networks benefit in interpreting ECG data, allowing to extract the most relevant information from it, outperforming other supervised learning methods.

Hu et al. [86] have studied the feasibility of neural networks applied to a patient-adaptable ECG beat classification algorithm. Their approach consists of an SOM/LVQ–based scheme, easily adapted to other existent automated patient monitoring algorithms. Their analysis reveals that the performance of the patient-adapted network was improved due to their ability to adjust the boundaries between classes, although the distributions of beats were distinct for each patient.

Several neurological disorders are routinely examined by EEG analysis and the differentiation between physiological and pathological alterations requires the flexibility and excellent capability and recognition of various EEG-complexes. In this context, Schetinin [87] has developed an algorithm to classify artifacts and normal segments in clinical EEGs. This method involves evolving cascade neural networks, ensuring a nearly minimal number of input and hidden neurons as well as connections. The algorithm was successfully applied, classifying correctly 96.69% of the testing segments. Singh [88] has developed a polygon feature selection method for the classification of temporal data from two or more sources, with emphasis on the analysis of EEG data. A feature classification, using a modified fuzzy nearest-neighbor method, was used and a recognition rate varying from 90–99% was achieved. Millan et al. [89] have proposed a local neural classifier for the recognition of mental tasks from on-line spontaneous EEG signals, allowing to recognize three mental tasks. Leichter et al. [90] have developed and applied a classification of EEG data based on independent component analysis (ICA) as a feature extraction technique, and on evolving fuzzy neural networks as a classification modelling technique.

4.3.2 Biological System Control and Prognosis

Imprecisely defined processes, for which clinical model-based control techniques are impractical but can be satisfactorily controlled by physicians, fuzzy logic is of particular interest. Fuzzy control can be described as a "control with sentences rather than equations" providing a natural-to-use sentences or rules as the control strategy written in terms of if–then clauses.

A fuzzy controller system is usually used in feedback configuration (Figure 4.22). The fuzzy controller establishes a relationship, expressed using the if–then formalism, between inputs (the desired output or set point and the actual output) and the output, the control action.

The field of anesthesia is one of the most relevant concerning applications of fuzzy control in the clinical domain [24]. It involves monitoring the vital parameters of the patient and controlling the drug infusion to maintain the anesthetic-level constant. It includes depth of anesthesia [91], muscle relaxation [46,92], hypertension during anesthesia [93], arterial pressure

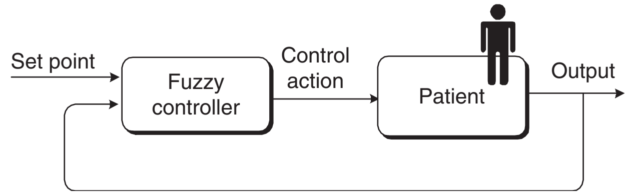


FIGURE 4.22
Fuzzy controller.

control [94], mechanical ventilation during anesthesia [95], and postoperative control of blood pressure [96].

Another example of application of fuzzy control is to develop a computer-based system for control of oxygen. Sun et al.[97] have applied a fuzzy control system delivery to ventilated infants. A successful example is VentPlan, a ventilator management advisor that interprets patients' physiological data to predict the effect of proposed ventilator changes [98] and NEOGANESH, a program for automated control of assisted ventilation in intensive care units [99].

An open-loop system for treatment of diabetic outpatients was developed for calculating the insulin dose [100]. Advisory expert systems can also be considered as an open-loop controller for advising on drug administration in general anesthesia [101]. Carollo et al. [102] have proposed a fuzzy pain control and Ying et al. [103] a fuzzy blood pressure control.

Most of the fuzzy logic control applications in the field of artificial organs are concerned with artificial hearts. In this context, a fuzzy controller has been implemented for adaptation of the heart pump rate to body perfusion demand by pump chamber filling detection [104]. A more advanced system, based on neural and fuzzy controller for artificial heart, was developed by Lee et al [105].

In Ref. 25, a combination of fuzzy logic and neural networks is used to develop an adaptive control system for arterial blood pressure using the drug nitroprusside. Another hybrid intelligent system based on a neuro-fuzzy approach can be found in Ref. 106. The system consists of an adaptive fuzzy controller and a network-based predictor for controlling the mean arterial blood pressure of seriously ill patients. The system has the ability to learn the control rules from an off-line training process as well as to adjust the parameters during the control process.

Neural networks are able to provide prognostic information based on retrospective parameter analysis. Given the ability of neural networks to identify patterns or trends in data, they are well suited for prediction or forecasting. In medical applications, neural networks can help clinicians, for example, to investigate the impact of parameter after certain conditions or treatments; they supply clinicians with information about the risk or incoming circumstances.

Patients who are hospitalized for having high-risk diseases require special monitoring. Neural networks have been used as a tool for patient diagnosis and prognosis to determine patients' survival. In this context, Bottaci and Drew [107] have investigated multilayer neural capabilities to predict survival and death of patients with colorectal cancer. Pofahl et al. [108] have implemented a neural network scheme for predicting the length of stay (more than 7 days) for acute pancreatitis patients, having achieved the highest sensitivity (75%). Ohlsson et al. [109] have presented a study for the diagnosis of acute myocardial infarction. In their study a multilayer neural network has been applied to predict whether the patient suffered from acute myocardial infarction or not.

Neural networks have also been successfully applied to other clinical problems [110]. Abidi and Goh [111] proposed a multilayer neural network as a forecaster for bacteria–antibiotic interactions of infectious diseases. Their results have shown that the 1-month forecaster produces a correct output (within occurrences of sensitivity) although predictions for the 2 and 3 months are less accurate. Prank et al. [112] have also used neural networks for predicting the time course of blood glucose levels from the complex interaction of glucose counterregulatory hormones and insulin. Benesova et al. [113] have developed a neural network scheme to predict the teratogenity of perinatal administrated drugs. Lapeer et al. [55] applied neural networks for similar predictive tasks, attempting to pick out perinatal parameters influencing birthweight.

4.3.3 Image Processing

Medical imaging has revolutionized medical practice by providing new, noninvasive, and probably, the most effective tools for diagnosis. Today any medical expert may rely on multiple imaging modalities such as ultrasound (US), projection x-ray, computer tomography (CT), magnetic resonance imaging (MRI), single positron (SPECT) and positron emission tomography (PET) AQ16
to obtain detailed morphological (structural), functional, and pathological AQ17
insight on several aspects of the human body. Besides their diagnosis function, these systems are of great help for other medical tasks such as treatment and surgery planning. To be helpful for healthcare, medical images have to be interpreted either qualitatively or quantitatively in a timely and accurate manner. In this context, medical image processing is increasingly an important tool to aid the medical professional in managing and extracting valuable information from these data sets. Typical useful processing operations on these images are as follows [36]:

Image compression. Most medical images are high-resolution images (see Table 4.5). Hence, image compression is an imperative operation in

TABLE 4.5

Some Typical Characteristics of Medical Images

Modality	Image Matrix	Bytes/Pixel	Megabytes/Study
DR	2048 × 2580	2	20
CT	512 × 512	2	30
MR	256 × 256	2	25
US	512 × 512	3	10
Mamografy	4096 × 6144	2	192
Angiografy	1024 × 1024	2	30
Fluoroscopy	1024 × 1024	1	10
PET/SPECT	256 × 256	2	2

many medical contexts to ensure fast interactivity during browsing of large sets of images (e.g., volumetric data sets, time sequences of images, and image data bases), their efficient storage management in picture archiving and communication systems (around 3.5 TB of data per year may be collected for a medium size hospital) and their application in teleradiology over low or moderate bandwidth networks such as ISDN and satellite networks. For medical image applications, special care has to be devoted to lossy compression schemes to avoid permanent loss of their diagnostic value.

Image preprocessing. The three most frequent image preprocessing operations under the medical context are image restoration in general, image reconstruction, and contrast enhancement. Distortion is an intrinsic property of most medical imaging modalities. In medical images, distortions may be both due to the electronics and the characteristics of the human body. In images where the distinction between normal and abnormal tissues is subtle, accurate interpretation may become difficult in the presence of distortions. Under these circumstances, image enhancement is usually applied to obtain clearer images for medical observation as well as for most automated or semiautomated diagnosis systems. Another common image preprocessing operation for medical applications is image reconstruction. The output from some modalities is not directly observable. For instance, the output from CT scanners are sinograms (collection of projections for different angles) that have to be backprojected to reconstruct the image. Owing to randomness, special algorithms have to be designed to avoid the cost of important details during reconstruction.

Image registration. Registration of images from different modalities is essential in several applications where the correspondence between the images conveys the desired medical information. These images may convey different information such as structural (e.g., CT) and functional (e.g., SPECT) information obtained from the same body part at different instances. Registration algorithms have to account for different types of geometrical and modality-specific distortions as well as distortions due to soft tissue elasticity to properly align the data sets for medical observation.

Image segmentation. Image segmentation is one of the most important processing steps in the analysis of patient image data. The main goal of segmentation algorithms is to divide the image into sets of pixels with strong correlation to significant structures such as organs, lesions, and different tissues that are a part of the image. These sets of segmented regions may be used to aid the medical professional in identifying important features in the image or to extract the necessary features for their automatic classification and disease diagnosis.

4.3.4 Neural and Fuzzy Applications in Medical Image Processing

4.3.4.1 Medical Image Compression

Although there is a considerable research effort concerning medical image compression, most compression approaches reported in literature do not rely on fuzzy methods. In this context, neural networks (see, e.g., Refs. 114–123) are much more common than fuzzy techniques.

Application of NN for data compression always relies on the principle of space reduction. According to Egmont-Petersen et al. [124], two different types of image-compression approaches can be identified using neural networks: direct pixel-based encoding/decoding by one ANN [114,119] and pixel-based encoding/decoding based on a modular approach [124]. Concerning architecture and principle, the major types of NNs that have been adapted for image compression are feedforward networks [116,119,120,122,123], SOMs [125,126], a learning vector quantifier [123], and a radial basis function network [126]. For a more extensive overview see Refs. 111 and 124.

A few attempts to combine fuzzy techniques for image compression have been reported. For example, Karras et al. [127] achieve higher lossy compression thresholds for wavelet coefficients in each DWT band in terms of how they are clustered according to their absolute value. Kaya [128] introduces a fuzzy Hopfield neural network for the same purpose as the one described by Karras et al. [127]. Fuzzy vector quantization for image compression is performed by Karayiannis et al. [129].

4.3.4.2 Image Enhancement

The majority of applications of ANNs in medical image preprocessing are for image restoration [121–134] and enhancement of specific image features [135]. The goal in image restoration is to compensate for the image distortion introduced by the physical measurement device. Besides noise, the major distortions introduced by the acquisition system are motion blur, out-of-focus blur, and distortion caused by low resolution (e.g., in SPECT). Image restoration is an intrinsically ill-posed problem, since conflicting criteria need to be accomplished, that is, resolution versus smoothness.

Lee and Degyvez [133] introduced color image restoration based on cellular NN (CNN). The generalized neural filter (GANF) is reported in Ref. 136, which has been applied for noise suppression. A GANF is build up on a set of neural operators, based on a stack of filters. Hopfield networks are a common use of NN for deblurring and diminishing out-of-focus effects (see, e.g., Ref. 137]). This problem is usually addressed using maximum *a posteriori* probability (MAP) and regularization. These objective functions can be mapped onto the energy function of Hopfield networks. Usually it is observed that some architecture modifications are required to enable the mapping operation.

Regarding image feature enhancement, most NN applications reported in literature are for edge enhancement. Few exist for other tasks. Usually, NN approaches for medical image enhancement rely on regression ANNs and classifiers [138,139]. In the latter, typically binary image outputs are obtained. For instance, Shih et al. [139] report an ART network for binary image enhancement. Regarding edge enhancement two approaches can be distinguished: (1) filter approximation [138] and (2) edge classification [140].

Other applications of NNs in this context are the implementation of morphological operators with modified feedforward networks [135] and the use of Grossberg's center-surround shunting feedforward network for contrast enhancement.

Fuzzy techniques have mainly been introduced for noise suppression [141–143], edge, and contrast enhancement [141,144]. Noise reduction in medical images is not a trivial task. The filter should be able to distinguish between unwanted information (noise) and image details that have to be preserved and ideally, be enhanced. From this contradictory objective, it is seen that nonlinear filters based on expert knowledge tend to outperform conventional methods. This is the main reason why fuzzy reasoning is one of the main supporting tools for fuzzy applications to noise reduction—the fuzzy inference ruled by else-action (FIRE) class of filters [145]. Another class of fuzzy filters are the fuzzy weighted filters [146,147]. This approach applies one or more fuzzy systems to evaluate weights of a weighted linear filter. These weights may be associated with the inputs (fuzzy weighted mean filters) [146,147] or with the outputs of different operators (fuzzy selection filters) [148,149]. Other fuzzy filtering approaches rely on the generalization of classical filtering methods such as median and order statistics filters [150–152]. Although a majority of these filters have not been specifically developed for medical image processing, they are very well suited for the task, given their ability to incorporate expert information. An example of their application in a medical context can be found in Zeng et al. [153]. For further information and recent reviews on fuzzy filters, see Ref. 141.

Fuzzy contrast enhancement for medical image processing has been attempted using global transformations, that is, histogram transformations and local adaptive transformations. Global contrast transformations have been reported in Refs. 154–157, whereas local contrast transformations are introduced in Refs. 158 and 159. In Ref. 144, the possibility distribution is applied together with four hard if-then-else rules to stretch the histogram of the input image. A similar approach using an intensification operator over fuzzified image pixel values is presented in Ref. 153. In Ref. 157, histogram hyperbolization is extended for fuzzy image coding. Fuzzy inference is applied in Ref. 144 to globally and locally enhance the image contrast. These techniques are local adaptations, using a small neighborhood of the global algorithms previously mentioned. A completely different approach is presented by Krell et al. [159], who combine histogram hyperbolization with a modified associative memory network to implement a local contrast enhancement algorithm for feature matching in radiotherapy.

4.3.4.3 Image Registration

The only known method for image registration using fuzzy techniques is the one reported by Maintz et al. [160]. Their algorithm is a surface-based method for registration of SPECT and MR images. In particular they propose to use the "surfaceness" computed from morphological operators as a fuzzy surface measure that is able to retain more information than concurrent algorithms based on binary segmentation. The registration is performed by optimizing the cross-correlation between the registered "surfaceness" spaces. Although several NNs applications for image registration exist in literature, few are for medical imaging purposes. A rare example is the algorithm reported by Rangarajan and Chui [161]. These authors formulate the registration problem as a feature-based matching approach with correspondences as a mixed variable objective function. Optimization is performed based on a neural-network approach.

4.3.4.4 Image Segmentation

Applications of the major fuzzy theoretical principles for image segmentation have been reported. From these, fuzzy clustering is the most straightforward and probably the most applied fuzzy technique for image segmentation in medical contexts. Typical application of this clustering principle is to divide the image into clusters and interpreting the class membership as a correlation or similarity with an ideal anatomical structure or its property. Although several variations on fuzzy clustering exist, the most applied principles for medical image segmentation are FCM [162,163] and the maximum entropy principle–based fuzzy clustering (MEP-FC) [164]. Other fuzzy algorithms applied in this context are possibilistic neuro-fuzzy c-means (PNFCM) [162] and fuzzy hidden Markov chains (FHMC) [165]. For an introduction to these algorithms see Ref. 162.

Fuzzy clustering has been extensively applied for medical image segmentation using two main strategies: (1) as the main segmentation algorithm and (2) as a preprocessing for nonfuzzy segmentation strategies or directly combined with them. In the first class of algorithms, clustering is usually performed directly on the intensity data, although other features may be applied (see, e.g., Ref. 166). A comparative performance analysis for the multimodal image segmentation problem using this approach is presented in Ref. 162. In Ref. 167, FCM is applied to extract the ventricular region in angiography images, whereas Ref. 168 uses a modified FCM to segment brain images obtained from noisy CT scans and one-channel MRI scans. Automatic identification of brain tumors using FCM is discussed in Ref. 169 (for a survey paper on fuzzy applications in brain-related topics, namely on its segmentation, see Ref. 170). Other fuzzy clustering applications to CT and MR image segmentation can be found in Refs. 171 and 172. Ghafar et al. [173] apply FCM for Pap smear image segmentation, whereas tracking of vessels in retinal images using FCM is reported in Ref. 174. Several medical domain

AQ18

applications of fuzzy clustering for unsupervised and supervised image segmentation are reviewed in Ref. 42.

In the second class of segmentation algorithms, clustering is combined with nonfuzzy approaches. For instance, a neurofuzzy segmentation technique for radiographic images is proposed in Ref. 175 based on the clustering of a feature space obtained from a wavelet decomposition of the image. Zhang et al. [176] report a multiresolution approach for cluster identification. In their work intra- and interscale properties are formulated as fuzzy functions, being significant clusters obtained from the minimization of their combined effect. A combined multiresolution FCM algorithm for breast calcifications was recently introduced by Sentelle and Sutton [177]. Fuzzy clustering is applied by Schüpp et al. [178] to initialize seed regions for active contours. Karayiannis and Pai [179] describe a hybrid algorithm for MR image segmentation based on fuzzy algorithms for LVQ, whereas Derrode et al. [165] combine fuzzy and hidden Markov chains to segment ill-defined images.

Other fuzzy image segmentation principles that can be found in literature are methods based on fuzzy integrals (e.g., applied for fuzzy feature weightening), fuzzy geometry (e.g., compactness and connectness) [178], and fuzzy entropy and divergence. However, these principles are less common for medical image segmentation. For a review on these techniques, see Ref. 37.

Algorithms for medical image segmentation using NN can be broadly divided into two classes [124]: (1) pixel-based algorithms [180–188], and (2) feature-based algorithms [189,190]. Regarding the underlying NN, most existing types of NN have been applied for the purpose: feedforward NNs [185,189], SOMs [168,183–185,189,188], Hopfield networks [186], and constraint satisfaction networks. For medical purpose, most NN-based algorithms have been trained to operate on texture [168,189] and a combination of texture and shape [187].

Regarding the application area, most of these segmentation algorithms have been developed for MR image segmentation [184,185] (a comparison between neural and fuzzy techniques for MR image segmentation is presented in Ref. 182), digital radiology [189], and multimodal images [186].

4.4 Decision Support Systems

Applications in clinical area often involve analysis and classification of the outcome of an experiment. Clinical diagnosis systems aim at offering suggestions and help in arriving at a diagnosis based on patient data. However, biosignal processing and interpretation in medicine involve a complex analysis of signals, image processing and interpretation, graphic representations, and pattern classification. Consequently, even experienced physicians could misinterpret the available data [191,192].

Diagnosis of diseases is an important and difficult task in medicine. In fact, detecting a disease from several factors or symptoms is a many-layered problem that also may lead to false assumptions with often unpredictable effects. Therefore, the attempt of using the knowledge and experience of many specialists collected in databases to support the diagnosis process seems reasonable. Fuzzy systems are well suited to tasks that heavily rely on human experience and intuition, which is the case of clinical diagnosis systems. Unfortunately in many cases, experts may not know, or may not be able to formulate, what knowledge they actually use in solving their problems. Given a set of clinical cases that act as examples, learning in soft computing can be achieved, for example, with a neurofuzzy methodology.

One of the most widely known applications of neural networks in medicine is the Papnet system [193]: a commercial neural network-based computer program for assisted screening of Pap (cervical) smears. If detected early, cervical cancer has an almost 100% chance of cure. With this system, a Pap smear test examines automatically cells taken from the uterine cervix for signs of precancerous and cancerous changes, thus enabling to detect very early precancerous changes.

Another diagnostic system is presented by Blekas et al. [194], employing a fuzzy neural-network approach, for the discrimination of benign from malignant gastric lesions. The input to the system consists of images of routine-processed gastric smears, stained by Papanicolaou technique. The analysis of the images provides a data set of cell features, being the fuzzy min–max classification network based on hyberbox fuzzy sets that can be incrementally trained. The application of the fuzzy min–max neural network has shown high rates of correct classification (both at cell- and patient level). Alonge et al. [195] presented a neurofuzzy scheme, able to perform focal lesions classification in MR images of brain tissues affected by multiple sclerosis disease. Images are first segmented using a fuzzy technique; then each cluster is processed to classify and label nonpathologic tissues and to locate all possible candidates to be sclerosis lesions. Finally, the neural classification step is implemented using a multilayer neural network, providing an estimate of the position and the shape for each lesion.

Lee et al. [196] have proposed the combination of a multimodule contextual neural network and spatial fuzzy rules and fuzzy descriptors for automatically identifying abdominal organs from a series of CT image slices. With this approach, the difficulties arising from partial volume effects, gray-level similarities of adjacent organs, and contrast media effect can be highly reduced. Basically the multimodule contextual neural network segments each image slice through a divide-and-conquer concept, and the variations in organ position and shape are addressed with spatial fuzzy rules and fuzzy descriptors, along with a contour modification scheme implementing consecutive organ region overlap constraints.

A three-dimensional (3-D) visualization fuzzy-based decision support system to timely detect glaucoma in older patients, as well as to optimize the monitoring process, allowing measuring the progress of the disease is presented in Ref. 197. The practical application of the system at the Department of Ophthalmology and the Eye Hospital of the University of Saarland in Homburg has proven that the optimized support, enhanced by fuzzy methods, for an accurate decision making in disease monitoring can offer direct benefits for the level of medical care and the interactive 3-D visualization might substantially enhance the doctor's involvement in the treatment of patients threatened by glaucoma.

The objective of the work presented by Cherrak et al. [198] was to test the performances of a computer system that was designed to analyze and quantify lesions on two-dimensional renal arteriograms. The system is based on a fuzzy automaton and performs a syntactic analysis of the arterial segment providing automatic and reproducible quantification of lesions. When compared to individual radiologists, the computer system gave a more precise estimation of percent stenosis and did not over- or underestimate the severity of the lesion.

Dutch et al. [199] have studied several systems for extraction of logical rules from data, and applied to the analysis of the melanoma skin cancer data. These systems include, among others, neural networks, enabling a very simple and accurate classification for the four types of melanoma. Clark et al. [200] have presented a knowledge-based paradigm that combines fuzzy techniques, multispectral analysis, and image-processing algorithms, to produce an unsupervised system capable of automatically segmenting and labeling complete glioblastoma-multiforme tumor volumes from transaxial MR images over a period of time during which the tumor is treated.

Zhang and Berardi [201] have investigated the potential of ANNs in diagnosing thyroid diseases. The robustness of neural networks with regard to sampling variations were examined using a cross-validation method. They have demonstrated that for medical diagnosis problems, where the data are often highly unbalanced, neural networks can be a promising classification method for practical use.

Pesonen et al. [202] have presented a neural network–based decision support system for the diagnosis of acute abdominal pain. Namely, two neural network algorithms, backpropagation and LVQ were studied, and the k-nearest neighbors in deciding the correct class for the LVQ network was used. The evaluation of the network with different databases as well as the comparison to statistical analyses has shown the effectiveness of the neural network scheme. Smith and Arabshahi [203] report the development of a fuzzy decision system to semiautomate ultrasonic prenatal examinations. The main goal is to reduce costs and minimize exposure time of the fetus to ultrasonic radiation. Varachiu et al. [204] have proposed the use of a knowledge discovery process to develop a fuzzy logic inference system for diagnosis and prediction of glaucoma. AQ19

Aphasia is a disturbance in the communicative use of language (disability to use or comprehend words), which can occur in different forms and results from brain damage. Jantzen et al. [205] have explored the capabilities of neurofuzzy system to classify several types of aphasia, showing their effectiveness for aphasia diagnosis.

Sordo et al. [206] have implemented a knowledge-based neural network for classification of phosphorus (31P) magnetic resonance spectra from normal and cancerous breast tissues. *A priori* knowledge of metabolic features of normal and cancerous breast tissues was incorporated into the structure of the neural network to overcome the scarcity of available data. The knowledge-based neural network proposed has outperformed conventional neural network, revealing that the combination of symbolic and neural techniques is more robust than a neural technique alone. AQ20

4.5 Conclusion

Computational intelligence theories have undergone important developments AQ21 during the past years. They provide techniques and tools that may support, in a very useful way, human decisions in complex contexts. Complexity here means high number of factors, changing conditions, imprecise knowledge, vagueness, lack of data, etc. The medical and healthcare domains are probably those with the highest potential for these techniques. An intense research has been and is going on worldwide concerning neural networks, fuzzy systems, and their combinations for applications covering practically all activities in these areas. This chapter provides a brief overview for these techniques and applications. The use of these techniques in the daily life of clinicians is in progress and it is expected that, with the proof of confidence, massive utilization will result in real benefits for the patients and for the clinicians.

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