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In response to DOD Army solicitation A95-095, SQI proposed a new type of Trauma Care Decision System considerably enhancing efficiency of prehospital trauma care. The greatest advantage of SQI's triage support system is the capability of accepting multiple sensors data, and provide fast decision, identify high risk patients, estimate patients' survival time and identify the most efficient and effective treatment. The decision algorithms is based on the use of neural assemblies and SQI's proprietary bi-radial bases neural networks. In SQI methodology, identification of high risk patients and prediction of their survival time is reduced to prediction of the values of the danger functions, which characterize the patients' conditions and their survival time.

The preliminary prototype software was integrated in hand-held personal computer from Texas Microsystems Inc., and adapted for multiple medical sensors logging. The decision making algorithm is capable to accept data from pH tissue analysis, oxygen tissue analysis, cardiac analysis, and other sensors and will be capable to work with different combinations of input parameters without redesigning the algorithm and retraining the neural network. This SQI developed preliminary algorithm has high potential greatly enhance the Army's Casualties Life Support during Trauma and Transport.

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Irm Katz 10-11-96

PI - Signature Date

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1.0 INTRODUCTION

In modern warfare, approximately 40% of all combat casualties die of exsanguination on the battlefield, forward of any type of medical station. Although prompt resuscitation of hypotensive post-trauma patients with plasma volume expansion is preferred, optimal fluid resuscitation requires physiological assessment both to improve patient outcome and minimize usage of limited fluid resources. We believe that above and beyond the clinical information obtainable from a dataset derived from a combination of invasive and non-invasive sensors coupled with personal status monitors (PSM) and/or personal computer assistants (PCA), clinical logic and decision making based on a Fast Neural Network Decision Algorithm (FNNDA) is necessary to both minimize loss of life and to enable medical personnel of limited training and capability (i.e. military medics or civilian paramedics) to find the best strategies for preservation of life and function, in the pre-hospital setting.

During the SQI Phase I study we recognized that in a combat situation the time delay before a casualty arrives at a site capable of providing definitive medical care may be many hours, accentuating the need for prolonged high level medical decision making in the absence of tertiary medical personnel and facilities. (viz. army concept for trauma and transport (TAT)). The use of a FNNDA based system under such circumstances will improve patient outcome, minimize usage of limited fluid resources, and greatly enhance the performance of the available medical personnel.

During Phase I Science Quest Inc. (SQI) developed a prototype of a fast neural network decision algorithm for combat casualty care. This algorithm provides fast, computer-based decisions using data from physiological sensors (preferably non-invasive), such as: pH, oxygen, blood pressure, temperature, respiratory rate, cardiac rhythm, etc., and based on SQI's proprietary Bi-Radial Neural Network (BRNN). Clinical and scientific discussions were held with our various consultants and co-workers including Bert Rosenthal M.D. (SQI), Walid Ghurabi M.D. (UCLA Medical Center, Trauma Care Unit), Professors Albert Lutterman M.D. and Seth Isenberg M.D. (Department of Surgery, University of South Alabama Medical School, Mobile Alabama), Frederick Pearce Ph.D. (Acting Director of Surgical Research, Walter Reed Army Institute of Research), Dr. Tammy Doherty (US Army Institute of Surgical Research, Fort Sam Houston, Tx), Dr. Paul Kizakevich, and Dr. Michael L. McCartney (Research Triangle Institute, Research Triangle Park, NC), Richard C. Hunt Associate Professor (Department of Emergency Medicine, East Carolina School of Medicine Greenville, NC), Michael V. Scanlon, Army Research Laboratory at Adelphi, MD), and other scientists working in areas related to combat casualties and trauma care support.

Based on the data received SQI developed a flexible (easily upgradeble) neural network structure which works with different sets of input parameters. It is capable of decision making under conditions when part of the input data is missing and provides simultaneous continuous quality assessment of the input data. The success of early resuscitation and critical care of combat casualties in modern warfare under field conditions may require continuous control of the injured, up to 40 hours or more, by low level medical personal, thereby making algorithm driven "smart decisions" a critical issue in military application scenarios where high level medical treatment is only available after large delays.

State-of-the-art medical hardware (Protocol Systems Inc. Beaverton OR, BCI International Waukesha, WI, etc.) allows the acquisition of vital data such as invasive (non invasive) blood pressure, CO_2, pulse oxymetry, ECG, body temperature, respiratory rate, etc. The clinical work station (CWS) recently introduced by Protocol Systems Inc. allows for the collection of such data from PSM's, without any ability to interpret the data or recommend intervention based on the continuously acquired variables. The addition of FNNDA technology allows this hardware to be part of a test bed for our envisioned treatment system in an Intensive Care Unit setting, and also allows us a glance at how a miniaturization of this hardware might perform in the military and civilian settings in which we intend to operate.

We see four major components of present and future modern warfare casualty support:

- Novel non-invasive sensors allowing more rapid deployment of clinical assessment techniques
- Novel personal computer assistant devices (presently represented by devices such as Propaq from PSI, or Escort from Medical Data Electronics Arleta, CA);
- Improved Life support systems for Trauma and Transport (TAT);
- Improved objective Neural network decision algorithm driven clinical capability in the field, allowing for the evaluation and treatment of casualties and/or accident victims in a proactive manner with a substantial reduction in mortality and an enormous increase in preservation of function.

1.1 Phase I Technical Objectives.

The main goal of Phase I was to demonstrate the reliability of SQI's proposed FNNA trauma triage algorithm. To achieve this goal, the following technical objectives were proposed for Phase I.

1. Based on scientific literature and government reports, to identify a set containing a minimum number of sensors that will be used for trauma care and decision making.

2. To develop pattern recognition / prediction algorithms based on neural network processing of the data-stream provided by the set of sensors.

3. To develop algorithms, prototype software and architecture for the proposed system. Provide an example of preliminary demonstration based on portable IBM PC 486DX 50 Mhz platform.

2.0 PHASE I TECHNICAL EFFORTS

The work performed in this Phase I program and the discussion of the theory of SQI's FNNDA approach is given in the following sections.

2.1 Highlights of The Phase I Results

Main results of Phase I include development and testing of the neural network based diagnostics methodology that is characterized by the following advantages:

- Fast training and fast restructuring of the neural network utilized as a key tool in computer-assisted triage. Fast restructuring is especially important under conditions where new information becomes available so that a training dataset may be expanded and the efficiency of the computer-assisted diagnostics may be enhanced.
- Neural networks utilized as a key element in the SQI developed methodology for computer-assisted diagnostics may be trained with the use of the training data-sets of a limited size. This will allow us to design computer-assisted diagnostics software for narrowly-oriented specialized applications characterized by smaller available information in the form of training patterns.
- The neural network is designed in such a way that clinical evaluation and diagnosis may be produced in conditions when some of the input parameters are unavailable.
- Additional advantages of the proposed diagnostics methodology include utilization of parameters of a different nature with variations at a vastly different time-scale and a joint use of quantitative and qualitative parameters.

SQI met all proposed objectives and demonstrated a working prototype based on a set of data obtained from Walter Reed Army Research Institute.

2.2 Research of Market Potential

The medical information technology and health data management market is one of the largest and fastest growing commercial markets $4.9 billion in 1994 [31], according to International Data Corporation' market analysis of medical application software. SQI's FNNDA is specially designed to support casualties and to help medical personnel predict an impending medical crisis before it happens, and turn available therapy into a proactive rather than a reactive intervention. The estimated medical infotech market in 1996 is > $ 10 billion [35], and will grow about 25% per year. SQI performed market analysis and identified several very promising commercial applications of the computer-assisted diagnostics technology developed during Phase I of this project.

- **Personal Status Monitor (PSM).** The next-generation physiologic sensing and monitoring device. The PSM will include new types of physiological sensors and sensor-to-network interfaces, a fiber optics and a wireless communication scheme, a microprocessor/memory (1 Gigabit) module, a patient card (Smart Card), etc. Its function is to provide trauma care professionals with the ability to remotely monitor patients and provide rapid determination of their medical status. Addition of microprocessor based decision technology will allow both the ability to monitor patients and to treat them via closed loop feedback systems, as well as perform remote trauma analysis and diagnostics.

- **Personal Clinical Assistant (PCA) with decision making software incorporated on microprocessor chip.**

  Hand-held portable computer (Soldier Individual 21st Century computer) to be carried by military medical personnel. The PCA will be capable of remotely interrogating PSMs worn by combatants or attached to civilian trauma patients. The PCA will be used to help determine the casualty's status, assign a triage category to each casualty based on the sensor data, and rank the casualties in the most appropriate order for medical treatment. As each patient is examined and treated, the PCA's anatoglyph screens will be used to record the location and extent of wounds/injuries and additional screens to record, and optimize the use of the limited medical resources, treatment(s) rendered. As casualties are evacuated, the PCA will be a part of LSTAT efforts.

- **Clinical Workstation System (CWS):**

  State-of-the-art workstation with functionality to provide selected administrative support and access to medical and logistic decision support systems and databases. It will interact with the clinician using a simple, consistent, and intuitive graphical user interface and present the provider with a unified view of the entire patient record. It will encode medical knowledge such as diagnostic guidelines and treatment protocols and act as an intelligent agent between existing data sources and the health care provider. Decision making algorithms and software designed for workstation applications will include identification of high risk patients, prediction of the patient's survival time and optimization of medical treatment.

2.3 Computer-Assisted Pre-Hospital Trauma Diagnostics

To operate in combat, or in environmentally harsh pre-hospital conditions, - computer-assisted trauma diagnostics should be:

- Robust
- Designed to have minimum latency
- Designed to be useful in fast-changing field conditions
- User friendly, i.e., allowing for operation by low level medical personnel.

In addition, the following criteria should were met for computer-assisted triage to be useful as a tool for battlefield and pre-hospital trauma care:

1. Computer -assisted triage should be based on a "fast training" neural network.
2. The neural networks should be trained with the use of limited size training data-sets.
3. Assessments and diagnoses should be produced in conditions when some of the input parameters may be unavailable or recorded with considerable error.
4. The neural network should be able to utilize parameters of different natures exhibiting vast variations of time-scale.
5. The neural network should be able to use both quantitative and qualitative parameters and variables.
6. The neural network should be able to assimilate any human acquired data with the sensor/computer generated data in performing clinical assessments and clinical diagnoses.
7. The neural network should be able to function under two different conditions of data unavailability:

(a) long-term unavailability of the data, when some of the parameters which define patterns from
the training data-set are unavailable;
(b) current partial unavailability of data due to time limitations and/or field conditions.

In some cases, the long-term data unavailability may be compensated for by careful analysis of the training data-set via use of additional co-variable information and/or exclusion of incomplete or partially defined patterns. As for current partial unavailability, in many cases it can not be avoided and the system should continue to operate with the available data albeit with quantifiable and reported reduced precision.

Recordable parameters and variables may be only partially available for both trauma-patterns from the training data-set and for the new patient to be evaluated. In this case this means that only certain information may be available with respect to the desired output of the neural network. This information taken into account via introduction of priority constraints on the output probability vector.

2.4 State-of-the-Art of a Current Neural Network Based Diagnostics Technology

Development of the methodology for medical diagnostics and pattern recognition is based on neural network processing of multi-spectral data. Neural network algorithms, theory, and applications have been under extensive development during the last ten to fifteen years. Two classes of networks are of special importance in terms of development of flexible and reliable pattern recognition algorithms:(1) global-approximation, multi-layered feed-forward neural networks with error backpropagation, and (2) local-approximation, radial-basis neural networks and their generalizations. Neural networks of the first type have been successfully used in pattern recognition algorithms during last 10 years (e. g. [5, 6, 30, 31, 32, 33]). There are multiple examples of their testing on medical data when outcome of medical procedure was predicted or current state of the patient was correctly identified. Examples of successful testing of the neural networks in the framework of medical diagnostics include outcomes assessment in common general surgical conditions, clinical decision making and diagnosis of acute coronary occlusion [1], identification of the patients that may fail to survive after hospital cardiopulmonary resuscitation [3], prediction of an outcome after liver transplant [2], and in cancer diagnostics [22, 23, 28] et al.. Efficiency of the neural networks of this type is due to their complex structure and their ability to identify complex patterns. Nevertheless their use in practical medicine has been so far limited. Their drawbacks are related to time-consuming procedures of retraining the neural network when additional information is available, necessity to use large training data-sets in the case of complex patterns described by a large number of input parameters, and inability to operate without time-consuming retraining when some of the expected data relevant to a diagnosed patient in not available.

Radial-basis neural networks is a new development. Main principles and examples of their application in approximation and pattern recognition is given in a number of publications [22, 23, 28, et al]. Similar to multi-layered feed-forward neural networks, the radial-basis neural networks are capable of classifying complex patterns and of picking up hidden phenomena. Their additional advantages are related to comparative simplicity of the neural network restructuring, when new

information is available or part of the expected input data are temporarily inaccessible, and to their ability to produce results with limited approximation/
identification error even in the case of small training data-sets.

Limitations of all currently available neural network based medical diagnostics methodologies are mostly related to:

(a) rigidity in treating information from the training data-set and information related to the current and former state of a patient to be evaluated

(b) inability to use jointly computer-generated diagnosis and a human-produced diagnosis for the purpose of generating a final diagnosis and/or evaluation,

(c) difficulties in assessment of reliability of the computer-generated diagnosis,

(d) absence of a neural network assisted methodology in identification of an optimal strategy of treating a patient.

Methodology of fast and flexible trauma diagnostics developed in the framework of this project was based on the use of several major concepts developed by PI during last five years:

- Adaptive bi-radial-basis neural networks designed to work with incomplete training patterns and capable of fast restructuring when new information becomes available;
- Cascading neural assemblies constructed as an open architecture combination of neural elements with the necessary number of the elements in the assembly estimated automatically during training session;
- New methods of computer-assisted medical diagnostics when patterns with censored data are involved;
- Methods of neural bootstrap designed for estimation of reliability of computer-assisted medical diagnosis and identification of an optimal set of input covariates;

SQI has been actively involved in development of neural networks of new type including cascading neural assemblies[13], bi-radial-basis neural networks for processing incomplete patterns[18], neural networks for processing of censored data[19, 20], and methods of neural bootstrap[11, 15, 21].

Neural networks and algorithms of medical diagnostics develop by PI were utilized for prediction of operational heart valve related complications and identification of high risk patients [19, 12, 14] and for earthquake prediction [16, 17].

During Phase I SQI developed a prototype of a computer-assisted methodology for trauma diagnostics predicated on the use of bi-radial-basis neural networks. The prototype version of the diagnostic software was developed and tested on a database compiled by SQI, the main advantages of the proposed diagnostic techniques were verified and guidelines for development of the working prototype of the neural network trauma diagnostics were formulated based on results of computer experiments.

2.5 Flexibility of the Computer-Assisted Trauma Diagnostics

Major limitations of the computer-based pre-hospital trauma diagnostics include:

(1) necessity for fast training of the neural networks,
(2) limitations on the size of the training data-set,
(3) the necessity to make diagnosis in conditions when some of the input parameters may be unavailable or recorded with considerable error.

Another group of problems related to the pre-hospital trauma diagnostics include:

- utilization of parameters of different nature and with variations at vastly different time-scale (e.g. age and pulse rate),
- joint use of quantitative and qualitative parameters. (examples of qualitative parameters: eye opening to pain, no verbal response, flexion to pain),
- joint use of static parameters and dynamically evolving parameters of the patients,
- desirability to combine personnel-produced diagnosis with computer-generated diagnosis with recorded weights of both components in the final diagnosis.

There are several major specific features of the pre-hospital computer-assisted methods of trauma diagnostics that should be taken into account in developing a successful pre-hospital trauma diagnostics techniques:

- Different time-scales for decision making. Computer-based diagnosis conducted in hospital conditions may take several hours or even days and, nevertheless, give helpful results, whereas pre-hospital trauma diagnostics should be conducted within several minutes, at most.
- Difference in professional qualification of the personnel utilizing software. Professional qualification of medical personnel that will presumably utilize trauma diagnostics hardware/software will be generally lower compared to that of personnel available in hospital conditions
- Difference in the character and amount of the available data. In conditions of pre-hospital trauma diagnostics, a smaller amount of information will be, generally, available.

During Phase I, SQI developed diagnostics methodology capable to process trauma patterns of different types including:

(1) fully defined patterns,
(2) patterns with missing parameters, and
(3) patterns with censored parameters.

For each of these patterns, bi-radial-basis functions of a special type are constructed and utilized as a component of the bi-radial-basis neural network. The following is a brief review of the patterns of different type that may be processed by bi-radial-basis neural networks.

2.6 Fully Defined Patterns

Each fully-defined pattern is presented as a pair of two components: (1) the input data-vector $\mathbf{x}_i$ and (2) the respective prediction/diagnostic outcome μ_i:

$$\omega_i = (\mathbf{x}_i, \mu_i) \qquad (2.6.1)$$

μ_i may be either a scalar or a vector (diagnostic vector), depending on a type of a prediction/diagnostic outcome. In the cases when μ_i is defined as a diagnostic vector, its coordinates characterize a probability of possible diagnostic outcomes. In accordance with its definition, all components of the fully-defined pattern are assumed to be known.

2.7 Incomplete, Partially-Defined Patterns with Missed Parameters

In incomplete patterns, some of the coordinates of the vector x_i and vector/scalar μ_i may be unavailable.

An incomplete pattern from the training set is described by a pair

$$\omega_i = (\mathbf{x}_i, \mu_i) \qquad (2.7.1)$$

$$\mathbf{a}_i = (\mathbf{a}_i^x, \mathbf{a}_i^\mu) \qquad (2.7.2)$$

where,
ω_i is data-pattern,
$\mathbf{a}_i$ is the availability pattern consisting of two elements:

(1) $\mathbf{a}_i^x$ - input availability vector corresponding to the input data-vector $\mathbf{x}_i$

(2) $\mathbf{a}_i^\mu$ outcome availability vector corresponding to prediction/diagnostic outcome vector μ_i. If μ_i is a scalar and its value is unavailable the pattern ω_i is useless in terms of neural network synthesis. In the case of vector μ_i, with some of its coordinates unavailable the partially defined pattern (2.7.1, 2.7.2) may be efficiently utilized to synthesize a bi-radial-basis neural network.

In the case of incomplete diagnosed pattern, it is presented as a combination:

$$\omega_{diagn} = \mathbf{x} \qquad (2.7.3)$$

$$\mathbf{a} = \mathbf{a}^x \qquad (2.7.4)$$

According to Eqs. 2.7.3 and 2.7.4, the incomplete diagnosed pattern consists of the input data-vector, $\mathbf{x}$, and a respective availability vector $\mathbf{a}^x$.

In the case of the pattern from the training set, the coordinates of the availability vectors are of the form:

$$a_i^x(k) = \begin{cases} 1; & \text{the coordinate } x_i(k) \text{ is available} \\ 0; & \text{the coordinate } x_i(k) \text{ is unavailable} \end{cases} \tag{2.7.5}$$

$$a_i^\mu(k) = \begin{cases} 1; & \text{the coordinate } \mu_i(k) \text{ is available} \\ 0; & \text{the coordinate } \mu_i(k) \text{ is unavailable} \end{cases} \tag{2.7.6}$$

The elements of the data-pattern from the training set are of the form:

$$x_{i,k} = \begin{cases} x_{i,k}; & \text{the coordinate } x_{i,k} \text{ is available} \\ arbitrary; & \text{the coordinate } x_{i,k} \text{ is unavailable} \end{cases} \tag{2.7.7}$$

$$\mu_{i,k} = \begin{cases} \mu_{i,k}; & \text{the coordinate } \mu_{i,k} \text{ is available} \\ arbitrary; & \text{the coordinate } \mu_{i,k} \text{ is unavailable} \end{cases} \tag{2.7.8}$$

In the case of an incomplete diagnosed pattern that does not belong to the training set, the coordinates of the input data-vector and its availability vector are of the form:

$$x_k = \begin{cases} x_k; & \text{the coordinate } x_k \text{ is available} \\ arbitrary; & \text{the coordinate } x_k \text{ is unavailable} \end{cases} \tag{2.7.9}$$

$$a^x(k) = \begin{cases} 1; & \text{the coordinate } x_k \text{ is available} \\ 0; & \text{the coordinate } x_k \text{ is unavailable} \end{cases} \tag{2.7.10}$$

According to Eqs. 2.7.5 to 2.7.10, coordinates of the availability vectors and elements of a data pattern are formed in such a way that

$$x_{i,k} \cdot a_i^x(k) = \begin{cases} x_{i,k}; & \text{the coordinate } x_{i,k} \text{ is available} \\ 0; & \text{the coordinate } x_{i,k} \text{ is unavailable} \end{cases} \tag{2.7.11}$$

$$\mu_{i,k} \cdot a_i^\mu(k) = \begin{cases} \mu_{i,k}; & \text{the coordinate } \mu_{i,k} \text{ is available} \\ 0; & \text{the coordinate } \mu_i(k) \text{ is unavailable} \end{cases} \tag{2.7.12}$$

Similarly, following relations hold for the elements of incomplete diagnosed pattern:

$$x_k \cdot a^x(k) = \begin{cases} x_k; & \text{the coordinate } x_k \text{ is available} \\ 0; & \text{the coordinate } x_k \text{ is unavailable} \end{cases} \tag{2.7.13}$$

Equations 2.7.6 and 2.7.7 are used to design bi-radial-basis neural networks that can deal with incomplete patterns in a systematic and a simple way.

2.8 Training Patterns with Censored Parameters

In some cases, precise values of parameters of the patterns from the training dataset or parameters of the diagnosed pattern may be unknown, although their upper or lower boundaries may be available. Parameters of this type are called censored parameters. One example of a censored parameter is the survival time of medical patients when monitoring of a patient does not continue up to the patient's death. In that case, it may be known that the patient survived longer than the length of the monitoring period.

In the training patterns, $\omega_i = (\mathbf{x}_i, \mu_i)$ with censored input data-vector, $\mathbf{x}_i = \left(x_{i,1}, \ldots, x_{i,k}, \ldots, x_{i,K}\right)$, some of the coordinates of the vector, $\mathbf{x}_i$, may be unknown. Instead constraints of the form:

$$x_{i,k} \le a_{i,k}^{+} \tag{2.8.1}$$

$$x_{i,k} \ge a_{i,k}^{-} \tag{2.8.2}$$

$$a_{i,k}^{-} \le x_{i,k} \le a_{i,k}^{+} \tag{2.8.3}$$

may be available.

If the outcome diagnostic vector, $\mu_i = \left(\mu_{i,1}, \ldots, \mu_{i,n}, \ldots, \mu_{i,N}\right)$, is censored, then the expected output $\mu_{i.n}$ is unknown for at least one index n. Censoring of the outcome $\mu_{i.n}$ assumes, that instead of an unknown parameter $\mu_{i.n}$, constraints of the form:

$$\mu_{i,n} \le b_{i,n}^{+} \tag{2.8.4}$$

$$\mu_{i,n} \geq b^{-}_{i,n} \tag{2.8.5}$$

$$b^{-}_{i,n} \leq \mu_{i,n} \leq b^{+}_{i,n} \tag{2.8.6}$$

are available.

Similar constraints may be available for input parameters of a new, to be diagnosed pattern, that is presented by its input data-vector, $\mathbf{x}$. Censoring of the input data-vector means that some of the coordinates of the input data-vector are unknown, but the constraints of the form:

$$x_k \leq c^{+}_{k} \tag{2.8.7}$$

$$x_k \geq c^{-}_{k} \tag{2.8.8}$$

$$c^{-}_{k} \leq x_k \leq c^{+}_{k} \tag{2.8.9}$$

are available for unknown input parameters.

A training pattern with censored parameters is described by a combination of data-pattern

$$\omega_i = (\mathbf{x}_i, \mu_i)$$

and censoring vectors a_i^{+}, a_i^{-}, b_i^{+}, b_i^{-}, that define upper and lower boundaries for the censored components of input data-vector, $\mathbf{x}_i$, and outcome diagnostics vector, μ_i.

2.9 Bi-Radial-Basis Neural Networks

Diagnostics methodology developed during Phase I of this project is predicated on the use of bi-radial-basis neural networks. The bi-radial-basis neural networks are constructed as a further iteration of the radial-basis-neural networks whose output is of the form:

$$\mu^{r} = \sum_{i} \mu_i D_i\left(\mathbf{x}_i, \mathbf{x}\right) \tag{2.9.1}$$

where $\mathbf{x}_i$, is the input data-vector for the patterns from the training data-set, $\mathbf{x}$ is the input data-vector for a diagnosed pattern, μ^r is the output parameter, μ_i is the outcome corresponding to the input vector $\mathbf{x}_i$, $D_i(\mathbf{x}_i,\mathbf{x})$ are radial-basis functions of the form:

$$D_i(\mathbf{x}_i,\mathbf{x}) = \exp\left(-\sum_k g_{i,k}\left(x_{i,k} - x_k\right)^2\right); \quad g_{i,k} > 0 \tag{2.9.2}$$

According to Eqs 2.9.1 and 2.9.2, if the distance between vectors $\mathbf{x}_{i_1}$ and $\mathbf{x}$ is small, whereas distances between vectors $\mathbf{x}_i$ ($i \neq i_1$) and $\mathbf{x}$ are large, then $\mu^r \approx \mu_i$. Therefore the output of the radial-basis neural network is close to the outcome of the pattern from the training set which vector of input parameters is most similar to that of the classified pattern. The neural network structure defined by Eqs. 2.9.1 and 2.9.2 does not allow for some of the input parameters $x_{i,k}$, x_k, or μ_i to be missed or censored. Bi-radial-basis neural networks designed as a generalization of the radial-basis neural networks are free from this limitations.

Similarly to the radial-basis neural networks, the bi-radial-basis neural networks are presented as a linear combination of several basis functions. These basis functions are called aggregate bi-radial-basis functions $H_i(\mathbf{x}_i,\mathbf{x},\mu_i,\mu)$ and are taken in the form:

$$H_i(\mathbf{x}_i,\mathbf{x},\mu_i,\mu) = \eta(\mu_i,\mu)D_i(\mathbf{x}_i,\mathbf{x}) \tag{2.9.3}$$

where $\eta(\mu_i,\mu)$ and $D_i(\mathbf{x}_i,\mathbf{x})$ are respectively output and input basis functions. Their product forms the bi-radial-basis function $H_i(\mathbf{x}_i,\mathbf{x},\mu_i,\mu)$. In some cases, the input basis function in Eq. 2.9.3 may have the same structure as the radial-basis function in Eq. 2.9.1. Generally the structure of both input and output basis functions may be different from the structure of the basis functions utilized to construct radial-basis neural networks.

Each bi-radial-basis functions corresponds to a certain pattern from the training dataset. . If a pattern from the training set is fully defined, then the output bi-radial basis function $\eta(\mu_i,\mu)$ characterizes the difference between the possible output μ of the currently processed pattern and the output μ_i corresponding to the $i-$th pattern from the training data set. The input basis function $D_i(\mathbf{x}_i,\mathbf{x})$ characterizes the difference between the input data-vector $\mathbf{x}$ of the currently diagnosed pattern and the input $\mathbf{x}_i$ corresponding to the pattern from the training data set. If the pattern from the training set is only partially defined then the values of both input and output bi-radial-basis functions characterize a degree of similarity between the pattern from the training set and diagnosed pattern. The degree of similarity is calculated based on incomplete available information.

The set of possible outputs of the bi-radial-basis neural network is defined by a set of maximum points of the following function

$$u(\mu) = \sum_i d_i^2 \eta(\mu_i, \mu) D_i(\mathbf{x}_i, \mathbf{x}) \tag{2.9.4}$$

In Eq. 2.9.4:

$u(\mu)$ is the bi-radial-basis output function of the expected outcome vector μ for the classified pattern;

d_i^2 is a bi-radial weight which value is defined by a reliability of the data presented by the training pattern $\omega_i = (\mathbf{x}_i, \mu_i)$; this parameters may be either predefined or iteratively calculated during the process of a synthesis of the bi-radial-basis neural network;

$\mathbf{x}_i$ and μ_i are input and output data-vectors for the patterns from the training data-sets; $\mathbf{x}$ input data-vector for to be classified pattern with unknown outcome.

The output of the bi-radial-basis neural network has two components:

$$\omega_{outp} = \left(u(\mu_{opt}), \mu_{opt}\right)$$

The first component called the reliability factor, is the maximum value of the bi-radial-basis output function defined by the following equation:

$$u(\mu_{opt}) = \max_{\mu} \sum_i d_i^2 \eta(\mu_i, \mu) D_i(\mathbf{x}_i, \mathbf{x}) \tag{2.9.5}$$

The second component is the estimated outcome μ_{opt} for which the bi-radial-basis output function attains its maximum. The component $u(\mu_{opt})$ characterizes a reliability of the outcome μ_{opt}. The greater is $u(\mu_{opt})$ the greater is the reliability of the diagnosis defined by the estimated outcome μ_{opt}.

The bi-radial-basis output function $u(\mu)$ may have several local maxima as a function of the outcome vector μ. In this case, each local maximum defines a possible version of the diagnostics outcome.

To be able to process incomplete patterns, patterns with censored parameters, and over-defined patterns, and utilize training sets containing patterns of this type, the input and output bi-radial-basis functions constituting the aggregate bi-radial-basis function are presented as the products of several elementary basis functions:

$$\eta(\mu_i, \mu) = \prod_n \eta_n(\mu_{i,n}, \mu_n) \tag{2.9.6}$$

$$D_i(\mathbf{x}_i, \mathbf{x}) = \prod_k D_{i,k}(\mathbf{x}_{i,k}, \mathbf{x}_k) \tag{2.9.7}$$

where, $\mu_{i,n}$, μ_n are n-th coordinates of the vectors μ_i and μ; $\mathbf{x}_{i,k}$ and $\mathbf{x}_k$ are k-th coordinates of the vectors $\mathbf{x}_i$ and $\mathbf{x}_k$ respectively; $\eta_n(\mu_{i,n}, \mu_n)$ and $D_{i,k}(\mathbf{x}_{i,k}, \mathbf{x}_k)$ are elementary basis functions.

In the case of fully defined patterns or patterns with missed parameters the elementary basis functions satisfy the following equations:

$$\max_{\mu_n} \eta_n(\mu_{i,n}, \mu_n) = \eta(\mu_{i,n}, \mu_{i,n}) \tag{2.9.8}$$

$$\max_{x_k} D_{i,k}(\mathbf{x}_{i,k}, \mathbf{x}_k) = D_i(\mathbf{x}_{i,k}, \mathbf{x}_{i,k}) \tag{2.9.9}$$

In Eqs. 2.9.6 and 2.9.7, there is an elementary basis function for each coordinate of vectors $\mathbf{x}_i$ and μ_i. Depending on whether the coordinate of these vectors are known, unknown or censored, the elementary basis functions take different form.

2.10 Elementary Basis Functions For The Paterns Of Different Types

Two groups of elementary basis functions were utilized to construct bi-radial-basis neural networks to deal with a combination of fully-defined, incomplete, and patterns with censored parameters.

2.10.1 Elementary Basis Functions For Fully-Defined Patterns

Basis input and outcome functions for fully defined patterns are defined by the following equations:

$$D_{i,k}(x_{i,k}, x_k) = \exp\left(-g_{i,k}(x_{i,k} - x_k)^2\right); \quad g_{i,k} \geq 0 \tag{2.10.1}$$

$$\eta_{i,n}(\mu_{i,n}, \mu_n) = \exp\left(-h_{i,n}\left(\mu_{i,n} - \mu_n\right)^2\right), \quad h_{i,n} \geq 0 \tag{2.10.2}$$

In Eqs. >> and >> $x_{i,k}$, x_k are the k-th coordinates of the vector $\mathbf{x}_i$ (training dataset) and vector $\mathbf{x}$ (data-pattern to be diagnosed); $\mu_{i,n}$, μ_n are the coordinates of the outcome vector μ_i (pattern from the training set) and a vector μ (unknown diagnostics vector for the pattern to be diagnosed).

2.10.2 Elementary Basis Functions for Patterns with Censored Data

To utilize censored parameters for the purpose of medical diagnostics we introduce basis functions of special type that allow to take into account available information in the form of a priory constraints on censored parameters.

Following elementary cost functions for a parameter o_p:

$$Q_p^{+}(o_p) = \exp(+\alpha_p^{+}(o_p - b_p^{+})) \tag{2.10.3}$$

$$Q_p^{-}(o_p) = \exp(-\alpha_p^{-}(o_p - b_p^{-})) \tag{2.10.4}$$

$$Q_p(o_p) = u_p^{(+)} Q_p^{+}(o_p) + u_p^{(-)} Q_p^{-}(o_p) \tag{2.10.5}$$

are used as building blocks in construction of the input and output elementary basis functions for censored data. In Eq. 2.10.5, $u_p^{(+)}$ and $u_p^{(-)}$ are non-negative constants.

The cost functions 2.10.3 - 2.10.5 satisfy the following relations:

$$\text{If } Q_p^{+}(o_p) \leq 1 \text{ then } o_p \leq b_p^{+} \tag{2.10.6}$$

$$\text{If } Q_p^{-}(o_p) \leq 1 \text{ then } o_p \geq b_p^{-} \tag{2.10.7}$$

$$\text{If } Q_p^{+}(o_p) \leq 1 \text{ and } Q_p^{-}(o_p) \leq 1 \text{ then } b_p^{-} \leq o_p \leq b_p^{+} \tag{2.10.8}$$

Parameters α_p^{+} and α_p^{-} may be interpreted as measures of fuzziness of the constraint: the smaller the value of the parameters α_p^{+} or α_p^{-}, the fuzzier the respective constrain is. An elementary cost function is small in absolute value and positive, if the constrain on the output of the neural network is satisfied. If the constraint is not satisfied, the respective cost function may increase unlimitedly.

2.10.3 Input and Output Basis Functions for Incorporation of Censored Input Data for the Patterns from the Training Set

Using equations 2.10.3 - 2.10.8 the following input basis functions are constructed to incorporate censored input data into the structure of the bi-radial-basis neural network.:

$$D_{i,k}^{+}\left(x_{i,k}\right) = \frac{\exp\left(+\alpha_i^{+}\left(x_{i,k} - b_k^{+}\right)\right)}{1 + \exp\left(+\alpha_i^{+}\left(x_{i,k} - b_k^{+}\right)\right)} \tag{2.10.9}$$

$$D_{i,k}^{-}\left(x_{i,k}\right) = \frac{\exp\left(-\alpha_i^{-}\left(x_{i,k} - b_k^{-}\right)\right)}{1 + \exp\left(-\alpha_i^{-}\left(x_{i,k} - b_k^{-}\right)\right)} \tag{2.10.10}$$

$$D_{i,k}^{(+,-)}\left(x_{i,k}\right) = D_{i,k}^{+}\left(x_{i,k}\right) + D_{i,k}^{-}\left(x_{i,k}\right) \tag{2.10.11}$$

Similarly, the outcome basis functions for incorporation of censored outcome data for the patterns from the training set are taken in the form:

$$\eta_n^+(\mu_{i,n}) = \frac{\exp\left(+\alpha_n^+\left(\mu_{i,n} - b_n^+\right)\right)}{1 + \exp\left(+\alpha_n^+\left(\mu_{i,n} - b_p^+\right)\right)} \tag{2.10.12}$$

$$\eta_n^-(\mu_{i,n}) = \frac{\exp\left(-\alpha_n^-\left(\mu_{i,n} - b_n^-\right)\right)}{1 + \exp\left(-\alpha_n^-\left(\mu_{i,n} - b_n^-\right)\right)} \tag{2.10.13}$$

$$\eta_n^{(+,-)}(\mu_{i,n}, \mu) = \eta_n^+(\mu_{i,n}, \mu) + \eta_n^-(\mu_{i,n}, \mu) \tag{2.10.14}$$

2.11 Input Basis Functions for Processing of Diagnosed Patterns with Censored Input Parameters

Similarly to Eqs. 2.11.12 - 2.11.14, the input basis functions for incorporation of censored data in the input data-vector of the diagnosed pattern are of the form:

$$D_k^+(x_k) = \frac{\exp\left(+\alpha_k^+\left(x_k - c_k^+\right)\right)}{1 + \exp\left(+\alpha_i^+\left(x_k - c_k^+\right)\right)} \tag{2.11.15}$$

$$D_k^-(x_k) = \frac{\exp\left(-c_k^-\left(x_k - c_k^-\right)\right)}{1 + \exp\left(-\alpha_k^-\left(x_k - c_k^-\right)\right)} \tag{2.11.15}$$

$$D_k^{(+,-)}(x_k) = D_k^+(x_k) + D_{ik}^-(x_k) \tag{2.11.16}$$

2.12 Elementary basis functions for patterns with missed parameters:

Patterns with missed parameters and fully-defined patterns have the elementary basis functions of the similar structure. Missed parameters are taken care of via a special choice of factors $g_{i,k}$ and $h_{i,k}$ in Eqs. 2.11.1 and 2.11.2.

If a pattern $\omega_i = (\mathbf{x}_i, \mu_i)$ is fully-defined, then parameters $g_{i,k}$ and $h_{i,k}$ are all positive.

If a pattern $\omega_i = (\mathbf{x}_i, \mu_i)$ is partially-defined, then parameters $g_{i,k}$ and $h_{i,k}$ are of the form:

$$g_{i,k} = g_{i,k}^0 a_i^x(k) a^x(k) \tag{2.12.1}$$

where $a_i^x(k)$, $a^x(k)$ are the coordinates of the availability vectors defined by Eqs. 2.7.5, 2.7.10 and $g_{i,k}^0 > 0$.

$$h_{i,k} = h_{i,k}^0 a_i^\mu(k) \tag{2.12.2}$$

where $a_i^\mu(k)$ is the coordinate of the availability vectors defined by Eqs. 2.7.6 and $h_{i,k}^0 > 0$.

According to Eqs. 2.10.1, 2.10.2, 2.12.1, and 2.12.2

$$D_{i,k}(x_{i,k}, x_k) = \begin{cases} \exp\left(-g_{i,k}^0 (x_{i,k} - x_k)^2\right); & \text{values of } x_{i,k} \text{ and } x_k \text{ are both known} \\ 1; & \text{value of } x_{i,k} \text{ or / and } x_k \text{ are unknown} \end{cases} \tag{2.12.3}$$

$$\eta_{i,n}(\mu_{i,n}, \mu_n) = \begin{cases} \exp\left(-h_{i,n}^0 \left(\mu_{i,n} - \mu_n\right)^2\right); & \text{value of } \mu_{i,n} \text{ is known} \\ 1; & \text{value of } \mu_{i,n} \text{ is unknown} \end{cases} \tag{2.12.4}$$

It follows from the Eqs. 2.11.3 and 2.11.4 that the output of the bi-radial-basis neural network does not depend on the parameters of the patterns from the training data set and the diagnosed pattern that are unavailable and is totally defined by the currently available parameters.

2.13 Examples of the Basis Functions for Training Patterns of Different Types

Utilization of the basis functions of different structure, chosen in accordance with a character of available information makes the bi-radial-basis neural networks especially valuable as a tool for fast pre-hospital trauma diagnostics under conditions when only part of the expected input parameters may be available or additional information on the patient to be evaluated becomes available and the neural network needs to exhibit fast adaptation.

Examples of input basis function $D_i(\mathbf{x}_i, \mathbf{x}_m)$ for a two dimensional input data-vector and for different character of information available for two coordinates of the input data-vector are shown in Fig. 2.1. The function $D_i(\mathbf{x}_i, \mathbf{x}_m)$ is plotted as a function of the coordinates of the classified vector $\mathbf{x}_m$. Examples presented at this Figure show the 2D input bi-radial-basis function for conditions when: (a) one parameter is known and the other one is unknown, (b) a numerical estimate is available for one parameter and one-side constraint is available for another parameter (censored parameter), (c) a numerical estimate is available for one parameter and a two-side constraint of the form, $a_{i,k}^- \le x_{i,k} \le a_{i,k}^+$, is available for another parameter, (d) values of both parameters are unknown but for both of them two-sided constraints are available.

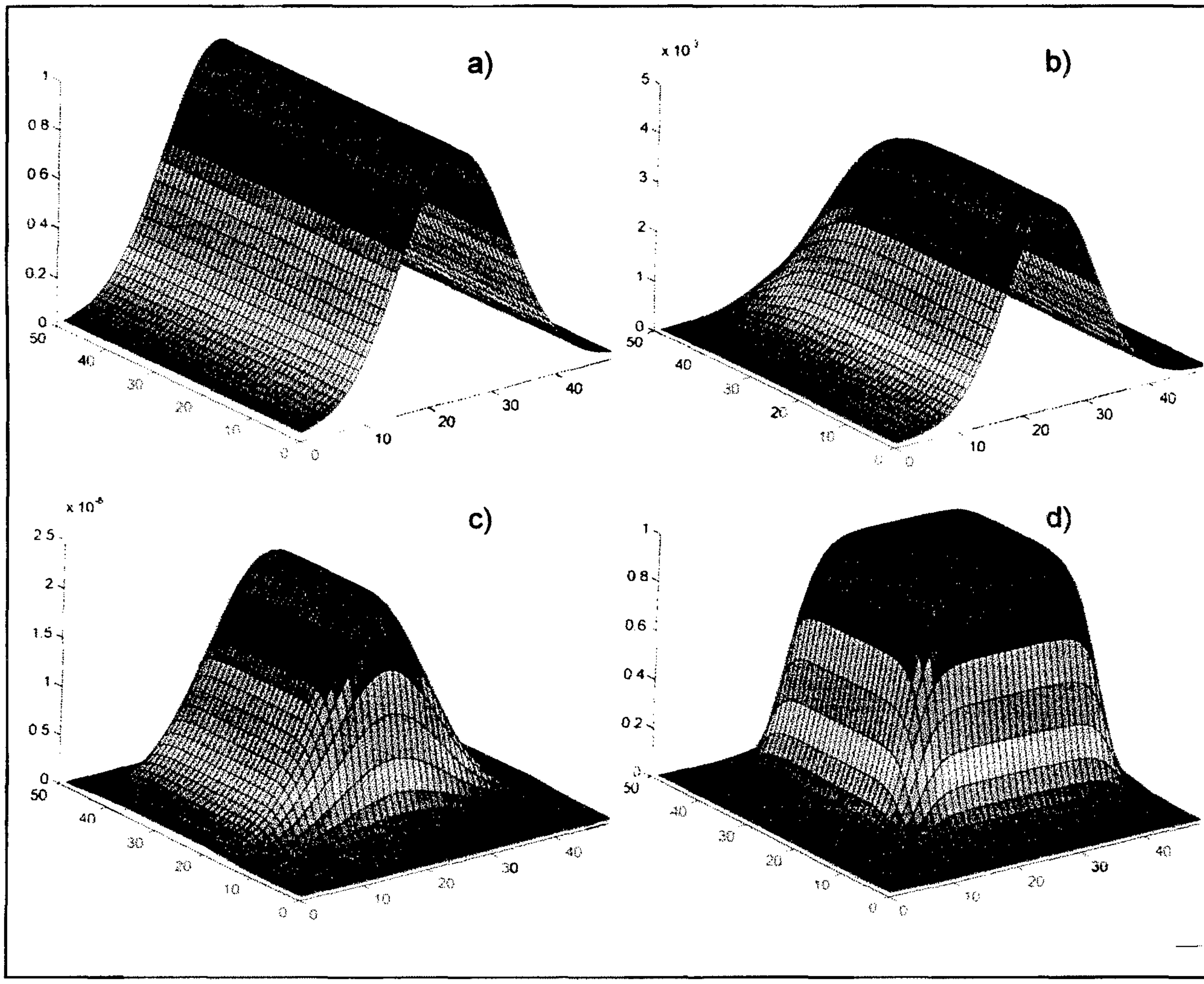

Figure 2.1. 2D input bi-radial-basis functions for four types of information available for the coordinates of the 2D input data-vector.

(a) one parameter is known and the other one is unknown; (b) a numerical estimate is available for one parameter and one-side constraint is available for another parameter (censored parameter); (c) a numerical estimate is available for one parameter and a two-side constraint of the form, $a_{i,k}^{-} \leq x_{i,k} \leq a_{i,k}^{+}$, is available for another parameter; (d) values of both parameters are unknown, but for both of them two-side constraints are available.

2.14 Experiments with Bi-Radial-Basis Neural Networks

Figures 2.2 and 2.3 present two examples of experiments with the bi-radial-basis neural networks. We used data obtained with rats in laboratory experiments conducted by Dr. Pearce. Dr. Pearce kindly supplied SQI with a data file containing information for 22 animals.

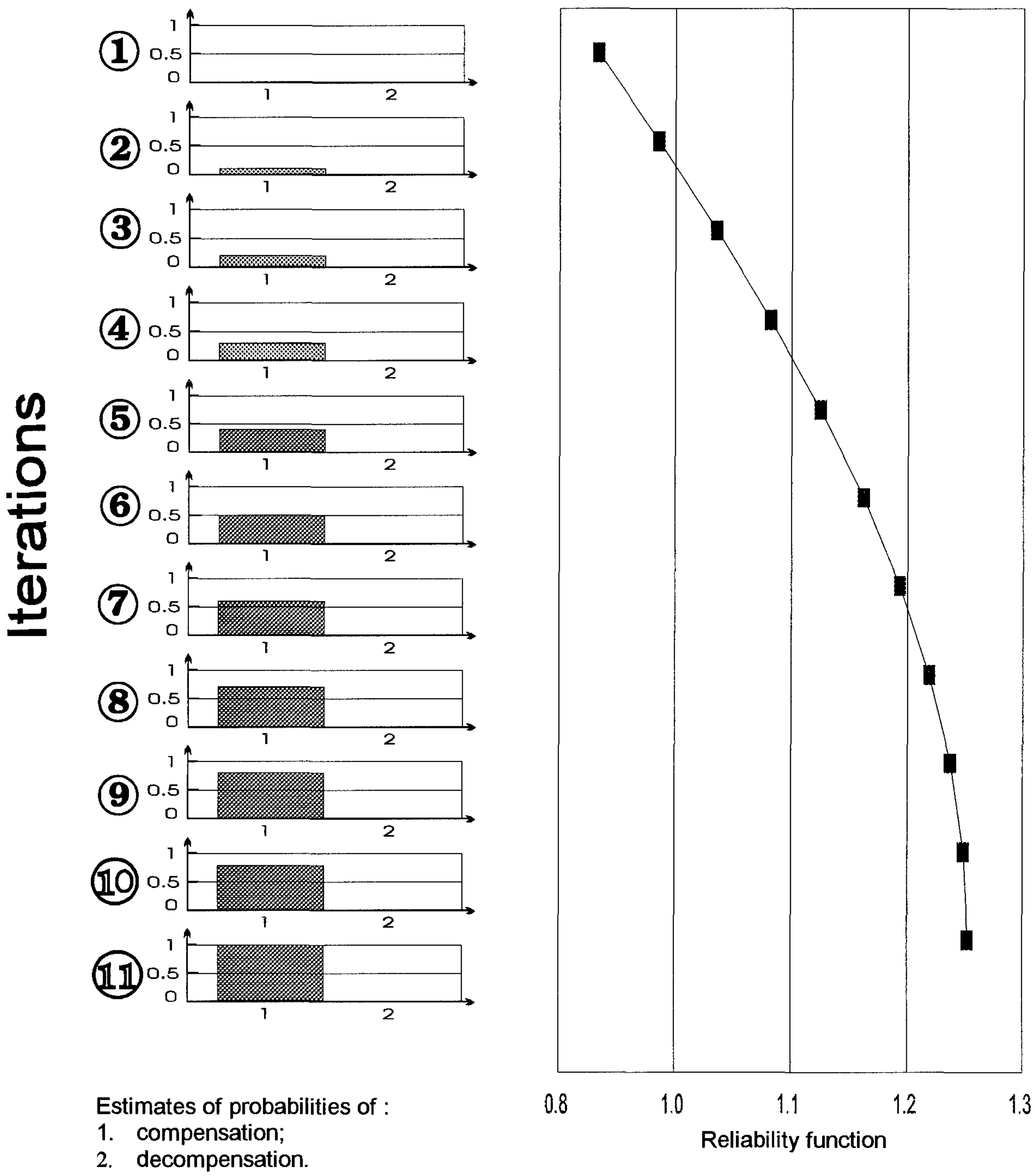

Figure 2.2. Sequence of iteratively produced diagnoses for the hemorrhaging animal in the compensation stage.
a. Neural network outcome, μ. b. Reliability factor, $u(\mu)$.
Expected neural network output (correct diagnosis) is $\mu = (1;0)$.

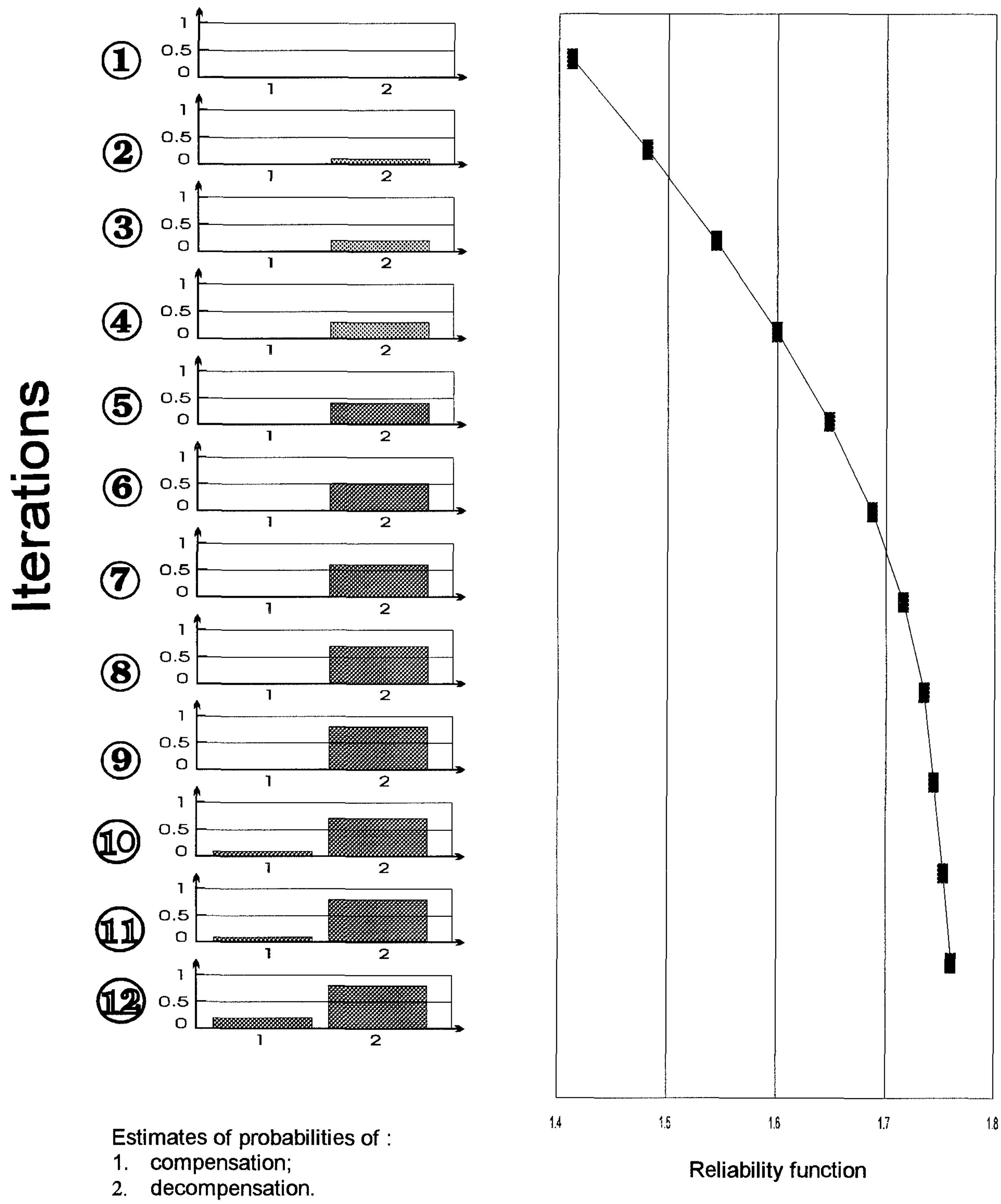

Figure 2.3. Sequence of iteratively produced diagnoses for the hemorrhaging animal in the decompensation stage.
a. Neural network outcome, μ. b. Reliability factor, $u(\mu)$.
Expected neural network output (correct diagnosis) is $\mu = (0;1)$.

The goal of the experiments was to estimate ability of the SQI diagnostics to identify a current state of the animal (compensation/decompensation) using a limited number of input parameters with no information on a time period from the beginning of the hemorrhage loss. Four parameters: SBV (Shock Blood Volume), RSBV (Reinfused Shock Blood Volume), pH , and pCO_2 were taken as input data. To take into account a character of variations of these parameters in time, finite differences of the form:

$$\Delta SBV(t_n) = SBV(t_n) - SBV(t_{n-1});$$

$$\Delta RSBV(t_n) = RSBV(t_n) - RSBV(t_{n-1})$$

$$\Delta PH(t_n) = PH(t_n) - PH(t_{n-1})$$

$$\Delta PCO2(t_n) = PCO2(t_n) - PCO2(t_{n-1})$$

were calculated and used as additional input data.

The compensation stage was marked by the vector $\mu = (1,0)$ whereas the decompensation stage was marked as $\mu = (0,1)$.

Results of experiments clearly demonstrated the ability of the bi-radial-basis neural network to pick up the difference between the two states and to identify the current state of the animal.

In the examples shown in Figs. 2.2 and 2.3, the diagnosed animals were not included in the training dataset and the neural network did not utilize any information on an actual state of the diagnosed animal besides the above input parameters. Each diagnosis included two components: (1) reliability factor. $u(\mu_{opt})$, and (2) Neural Network output, μ_{opt} .The diagnostics process included iterative search for an outcome vector μ_{opt} for which the reliability factor $u(\mu_{opt})$ attains its maximum. Iterative diagnostics consisted of the iterative search for the maximum of the reliability factor and identification of the outcome vectors corresponding to iteratively found values of the reliability factor. The process of optimization took about 3 sec, when a Pentium 133 MHz computer is utilized.

2.15 Basic Features of A Preliminary Version of a Prototype Bi-Radial-Basis Neural Network

SQI developed the prototype version of a flexible and robust bi-radial-basis neural network and tested the prototype version. The designed neural network satisfies the following conditions:

1. The neural network is fast-trained so that new data may be easily integrated.
2. Training data-sets of a limited size may be used for synthesis of the neural network. This allows the syntheses of neural networks of general and subsequent type, specialized neural networks efficiently performing narrowly-defined tasks.
3. The bi-radial-basis neural network is capable of conducting clinical evaluations under conditions, when some of the input parameters are unavailable or recorded with considerable error.
4. It allows the utilization of parameters of different types and with variations at vastly different time-scales (e.g. age and pulse rate).

5. It gives an opportunity to use jointly, both quantitative and qualitative parameters (examples of qualitative parameters: eye opening to pain, no verbal response, flexion response to pain).
6. The neural network produces estimates of the probabilities for all possible outcomes.

The block-diagrams of training procedures of the bi-radial-basis neural network and medical evaluation done by a trained bi-radial-basis neural network are shown in Fig. 2.4 and 2.5. An important part of both training and diagnosis is identification of available parameters, including real-time recorded parameters and demographic parameters, such as age, sex, and parameters related to medical history of the patient.

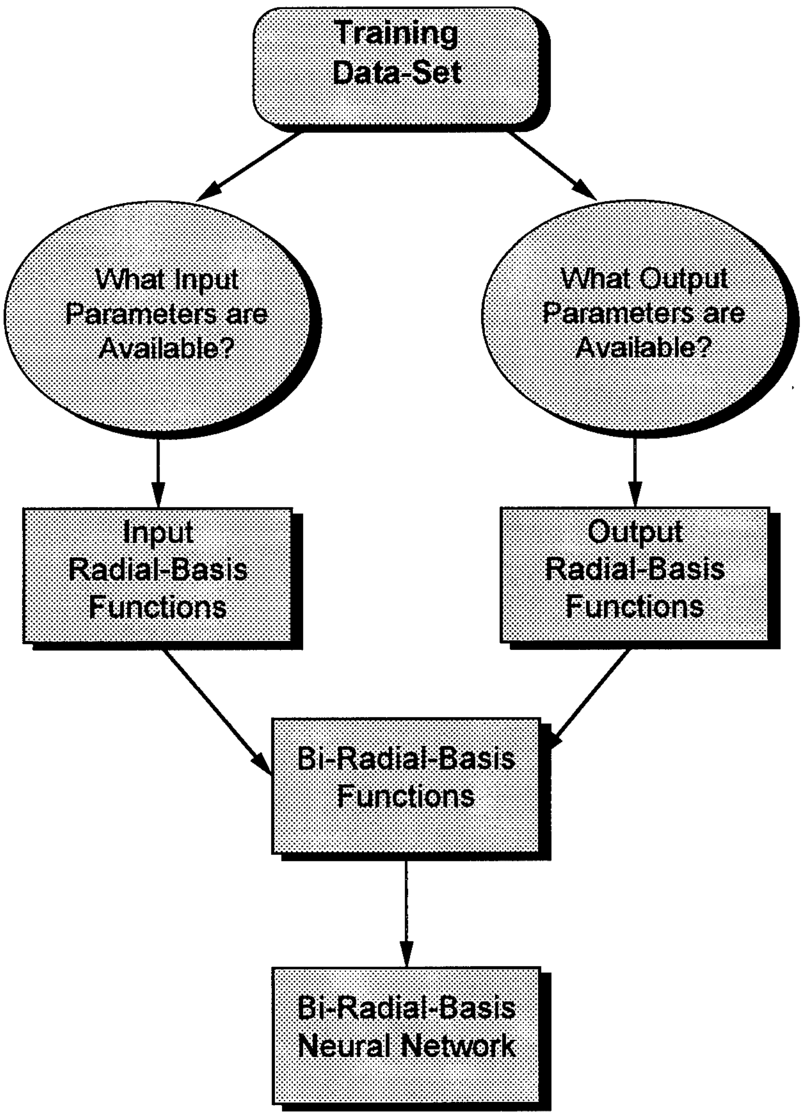

Figure 2.4. Synthesis of Bi-Radial-Basis Neural Networks.

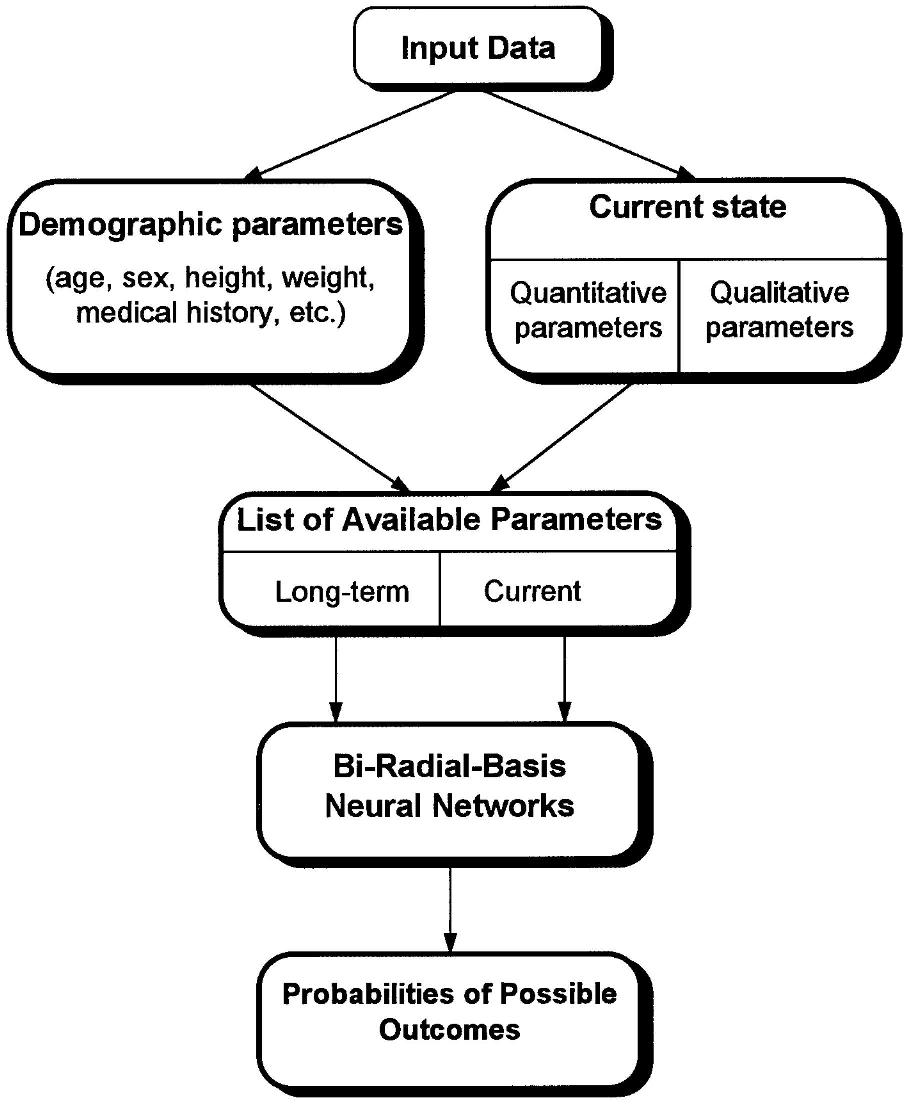

Figure 2.5. Medical Diagnostics by the Bi-Radial-Basis Neural Networks.

Figures 2.6 and 2.7 show the first results of testing of a prototype bi-radial-basis neural network designed to identify high risk patients undergoing extracorporeal shock wave lithotripsy (data acquired at University of Southern California County hospital). The training data-set consisted of 113 patterns. Each pattern included a set of 9 patient parameters and information on the outcome of the procedure (whether the patient had or didn't have cardiac arrhythmia during the procedure). The neural network was designed to predict a probability of cardiac arrhythmia. Figure 1.6 shows the neural network output for the patient identified as a high-risk (estimated probability of cardiac arrhythmia is 0.88). Figure 2.7 shows the neural network output for the patient identified as low-risk (estimated probability of cardiac arrhythmia is 0.19). In both cases, neural network's diagnosis was correct: the patient identified as a high risk did have cardiac arrhythmia and the low risk patient did not.

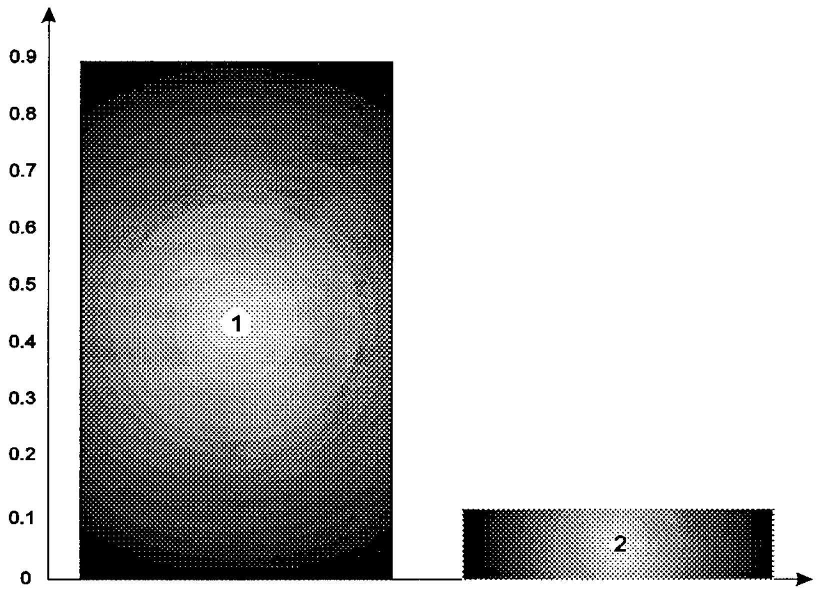

Figure 2.6. Bi-Radial-Basis Neural Networks.
Estimation of a probability of Cardiac arrhythmias during extracorporial shock wave lithotripsy based on preoperative data.
1. Cardiac arrhythmia will occur.
2. No cardiac arrhythmia

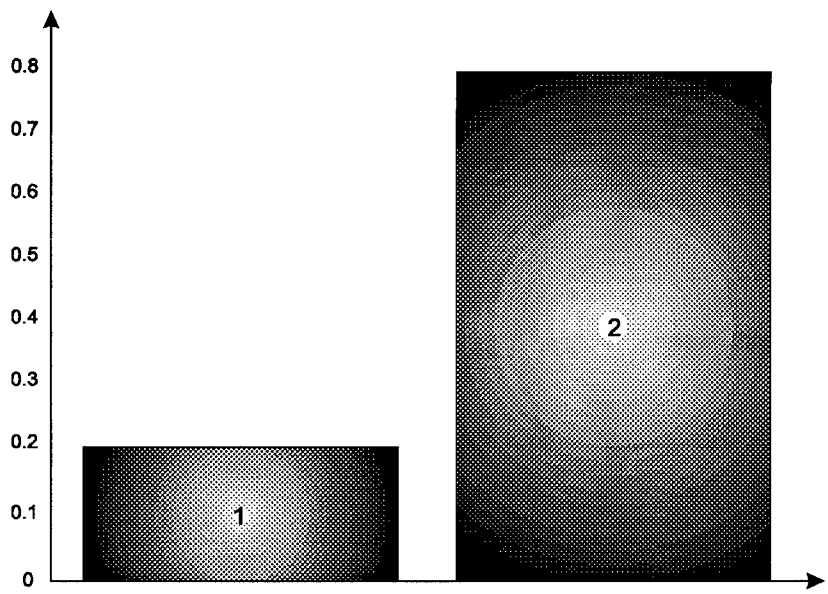

Figure 2.7. Bi-Radial-Basis Neural Networks.
Estimation of a probability of Cardiac arrhythmia during extracorporial shock wave lithotripsy based on preoperative data.
1. Cardiac arrhythmia will occur.
2. No cardiac arrhythmia.

2.16 Modular Bi-Radial-Basis Neural Networks for Medical Diagnostics

During Phase I algorithms of medical diagnostics based on the use of bi-radial-basis neural networks were developed and successfully tested. The developed prototype has a number of advantages compared to multi-layered feed-forward neural networks:

- It is much faster to synthesize compared to the feed-forward, multi-layered neural networks,
- It is much more robust and needs smaller training sets for their synthesis,
- It can work with incomplete data sets with randomly missing parameters,
- It allow for a simple way to use information related to the errors in the parameter defining patterns from the training data set and a diagnosed pattern,
- It can naturally accommodate censored data both in a training data-set and in a new, to be diagnosed, trauma-pattern.

The above advantages make the bi-radial-basis neural networks especially valuable as a tool for fast pre-hospital trauma diagnostics in conditions when only part of expected input parameters may be available or when additional information on the patient becomes available and the neural network needs to be adapted rapidly.

2.17 Two Types of Modular Neural Structures for Adaptive Trauma Diagnostics

To guarantee additional improvement of flexibility and enhancement of efficiency of the computer-assisted diagnostics, SQI began development of modular neural structures consisting of bi-radial-basis neural elements. Modularity of the neural structure will allow for better adaptability of the decision-making algorithm and faster restructuring in accordance with changing conditions and changing diagnostics needs.

The modular neural structures of the first type are designed for medical diagnostics in conditions characterized by a small number of expected diagnostic outcomes (generally, not larger than six different outcomes). The neural structures of the second type will be efficient in conditions which permit a large number of possible outcomes (the number of possible outcomes may be as large as several dozen in a case of a training data-set containing several thousands patterns).

The first layer of both of these structures contains bi-radial-basis nodes such that each node corresponds to a certain pattern from the training data-set. The total number of nodes equals the number of the patterns in the training set. The nodes are divided into node groups so that each group corresponds to a certain diagnostics outcome.

2.18 Modular Structure of Bi-Radial-Basis Neural Elements with Threshold Optimization

The neural structure of the first type produces an output diagnostics vector which ranks all possible diagnoses in accordance to their likelihood. The likelihood is characterized by the values of the outputs of the bi-radial-basis neural elements and by the similarity between likelihood distributions obtained by three diagnostics algorithms. The threshold applied to the outputs of the bi-radial-basis elements is iteratively modified to minimize the difference in likelihood distributions for the three diagnostics algorithms. The first layer of this neural structure contains neural modules with multi-dimensional outcome. Each module corresponds to a certain pattern in the training set. The number of modules is equal to the number of training patterns. All diagnostics outcomes in the training patterns are indexed with the index r and all training patterns are grouped into groups with the same outcome. So the patterns with the outcome μ_r are presented in the form:

$$\omega_{i(r)} = (\mathbf{x}_{i(r)}, \mu_r) \tag{2.18.1}$$

where μ_r is a vector of dimension P with coordinates, $\mu_r(p)$, of the form:

$$\mu_r(p) = \begin{cases} 1; & p = r \\ 0; & p \neq r \end{cases} \tag{2.18.2}$$

In accordance with grouping of the patterns in the training dataset, the bi-radial-basis functions are grouped into groups of the elementary basis functions with the same respective outcome. The elements of the r-th group of the bi-radial-basis functions correspond to the outcome μ_r.

Training of the three-level modular bi-radial-basis structure is illustrated by Fig. 2.8. The first level of the modular bi-radial-basis structure contains P groups of the bi-radial-basis functions where P is the total number of possible diagnostics outcomes represented by the patterns from the training set. Each group outputs two parameters:

(a) the sum, λ_r, of the values of the bi-radial basis functions in the group corresponding to the diagnosed pattern $\mathbf{x}_m$: $\mathbf{g}_1 = \sum_r \lambda_r \mu_r$

$$\lambda_r = \sum_{i(r)} D\left(\mathbf{x}_{i(r)}, \mathbf{x}_m\right) \tag{2.18.3}$$

(b) thresholded sum of the form

$$U_r = \begin{cases} \lambda_r; & \lambda_r \geq threshold \\ 0; & \lambda_r < threshold \end{cases} \tag{2.18.4}$$

The second layer produces three versions of the estimated diagnosis with the output diagnostics vectors of the form:

$$\mathbf{g}_1 = \sum_p \lambda_p \mu_p, \quad \mathbf{g}_2 = \lambda_{r(opt)} \mu_{r(opt)}, \quad \mathbf{g}_3 = \sum_p U_p \mu_p \tag{2.18.5}$$

where $r(opt)$ is such that $\lambda_{r(opt)} = \max_r \lambda_r$

The diagnosis processor finds such a value of the threshold that minimizes the diagnostics error using neural bootstrap and chooses the optimal diagnostics strategy among those defined by Eqs. 2.18.3 to 2.18.5.

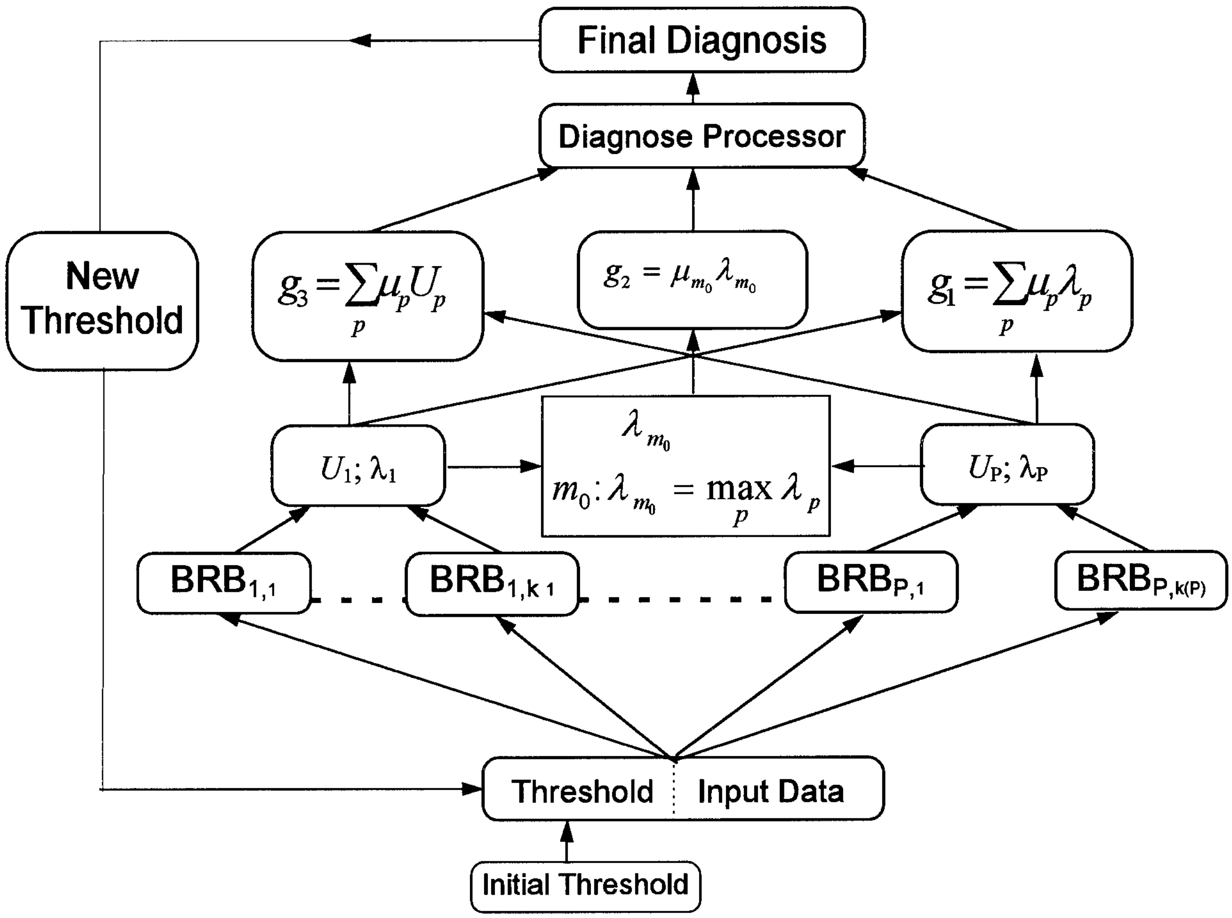

Figure 2.8. Modular structure of bi-radial-basis neural elements with threshold optimization.

2.19 Modular Bi-Radial-Basis Neural Structure with Recursive Optimization of Diagnostics Reliability

Bi-Radial-Basis neural networks with recursive diagnostics produce diagnostics vectors with coordinates equal to a likelihood of a certain diagnosis. Coordinates of the diagnostics vector are obtained via recursive maximization of the output of the neural network. The flow-chart of the modular structure of this type is shown in Fig. 2.9 The input layer contains an input vector of parameters of the to be diagnosed patient and recursively modified diagnosis. The second layer contains bi-radial-basis elements that output the values of reliability functions

$$R_i(\mu) = \eta(\mu_i, \mu) D_i(\mathbf{x}_i, \mathbf{x}_m) \qquad (2.19.6)$$

The sum of the reliability functions is calculated in the gating element, (+). The diagnosis, defined by the vector of diagnostics probabilities, μ, is iteratively modified and sent back to the first layer to start the next iteration.

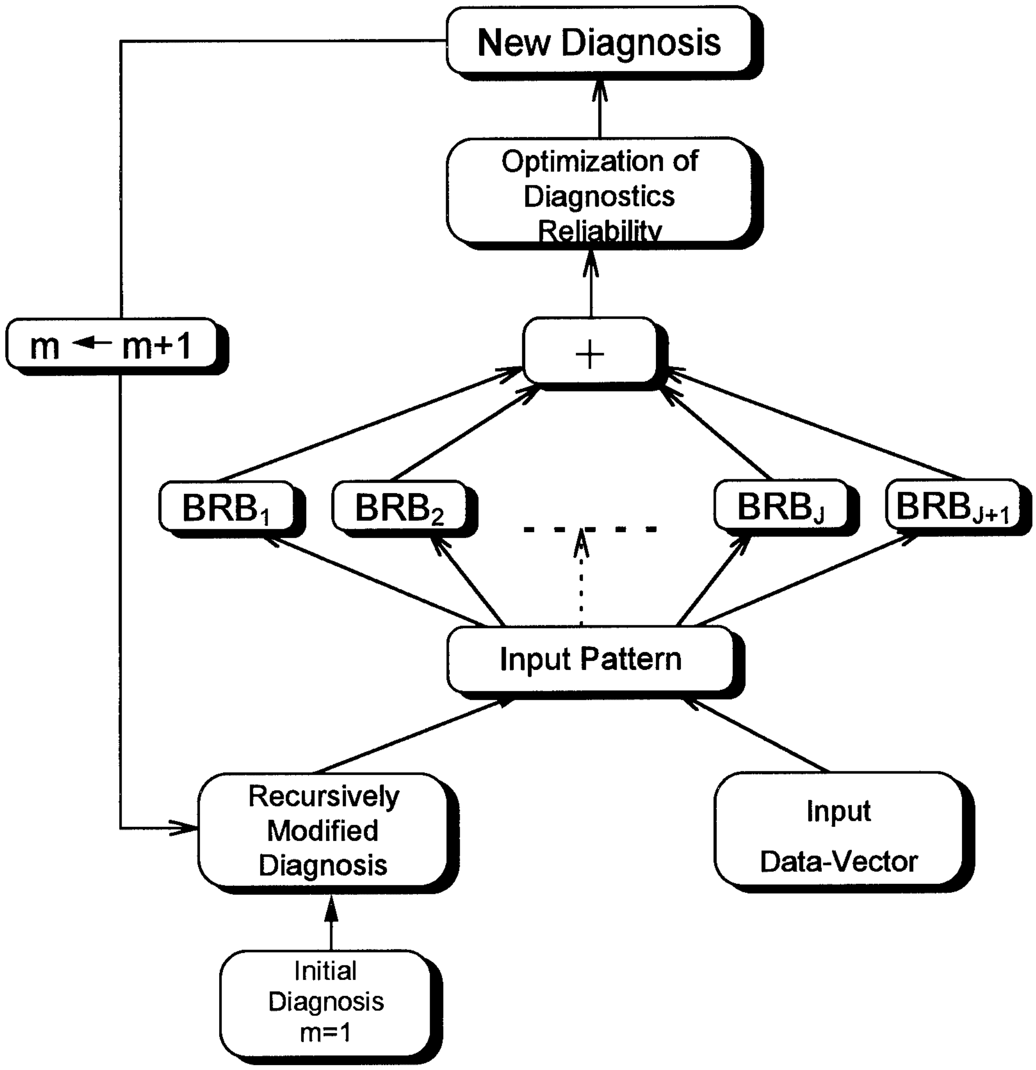

Figure 2.9. Modular bi-radial-basis neural structure with optimization of diagnostics reliability

2.20 Neural Bootstrap as a Tool for Assessment of Diagnostics Reliability

Neural bootstrap was initially developed by the Principal Investigator as a tool for analysis of of specialized neural networks called "neural assemblies". This methodology was tested on medical data and proved to be an important tool in assessing efficiency and reliability of the performance of neural networks. In the neural bootstrap, available dataset Ω consists of pairs (input, expected output) $(\bar{x}_i, \bar{z}_i)$. During bootstrap testing, the dataset Ω is randomly divided into two non empty training and test subsets, $\Omega_{tr,j}$ and $\Omega_{ts,j}$. Here, j is the index of a pair training and test subsets. Bootstrap training and testing samples $\omega_{tr}(j)$ and $\omega_{ts}(j)$ are independently generated from $\Omega_{tr,j}$ and $\Omega_{ts,j}$. Using bootstrap samples of the training set, $\omega_{tr}(j)$, the neural net is initialized and trained to minimize the approximation error

$$\varepsilon_j = \sum_{\mathbf{x}_i \in \omega_{tr}(j)} \| \mathrm{F}(\mathbf{u}_{j,i}, \mathbf{x}_{j,i}) - \mathbf{z}_{j,i} \|^2 \tag{2.20.1}$$

After the neural network is synthesized, the prediction error is estimated using testing samples:

$$\xi_{\mathrm{j}} = \sum_{\mathbf{x}_i \in \omega_{ts}(j)} \| \mathrm{F}(\mathbf{u}_{j,l}, \mathbf{x}_{j,l}) - \mathbf{z}_{j,l} \|^2 \tag{2.20.2}$$

After generating bootstrap samples $\omega_{tr}(j)$ and $\omega_{ts}(j)$ of the training and testing sets for $j \in [1, J]$, and estimating the network's prediction errors ξ_{j}, random variable statistics are computed and distribution parameters for ξ_{j} are estimated and analyzed.

Depending on the size of the training set and the empirical distribution of the measure of interest (prediction error $\xi(\mathbf{u}_j)$ in our case), confidence intervals may be estimated by different methods. Using the bootstrap percentile method, if $\xi^{*(\alpha)}$ is the $00 \cdot \alpha$ percentile of J bootstrap replications $\xi^*(j)$, j=1,...,J, then the interval of intended coverage -2α is obtained by

$$(\xi_{lo}, \xi_{up}) = (\xi^{*(\alpha)}, \xi^{*(1-\alpha)}) \tag{2.20.3}$$

Neural network -- bootstrap cycle is schematically shown at Fig. 2.10. The cycle includes selection of training and testing datasets, neural network training, and prediction error estimation.

During Phase I, we concentrated on:

(1) Development of a bootstrap-based methodology for assessment of the importance of individual input parameters and their influence on the reliability of medical diagnostics.

(2) Development of the methodology for identification of a group of input parameters that guarantee the most reliable computer-assisted diagnostics.

Selection of an appropriate set of input parameters is especially important when the size of the training dataset is comparable to a number of possible input parameters so that the network's adaptive training is impeded by the size of the input data-vector. In addition, a reasonable decrease in the number of input parameters may cut the cost of medical diagnostics and may make it more usable under harsh field conditions. The question that should be answered based on the developed neural bootstrap methodology is: given an initial sample of medical data, how do we determine which input variables are the most important from the point of view of computer-assisted diagnostics and which could be safely dropped from the model.

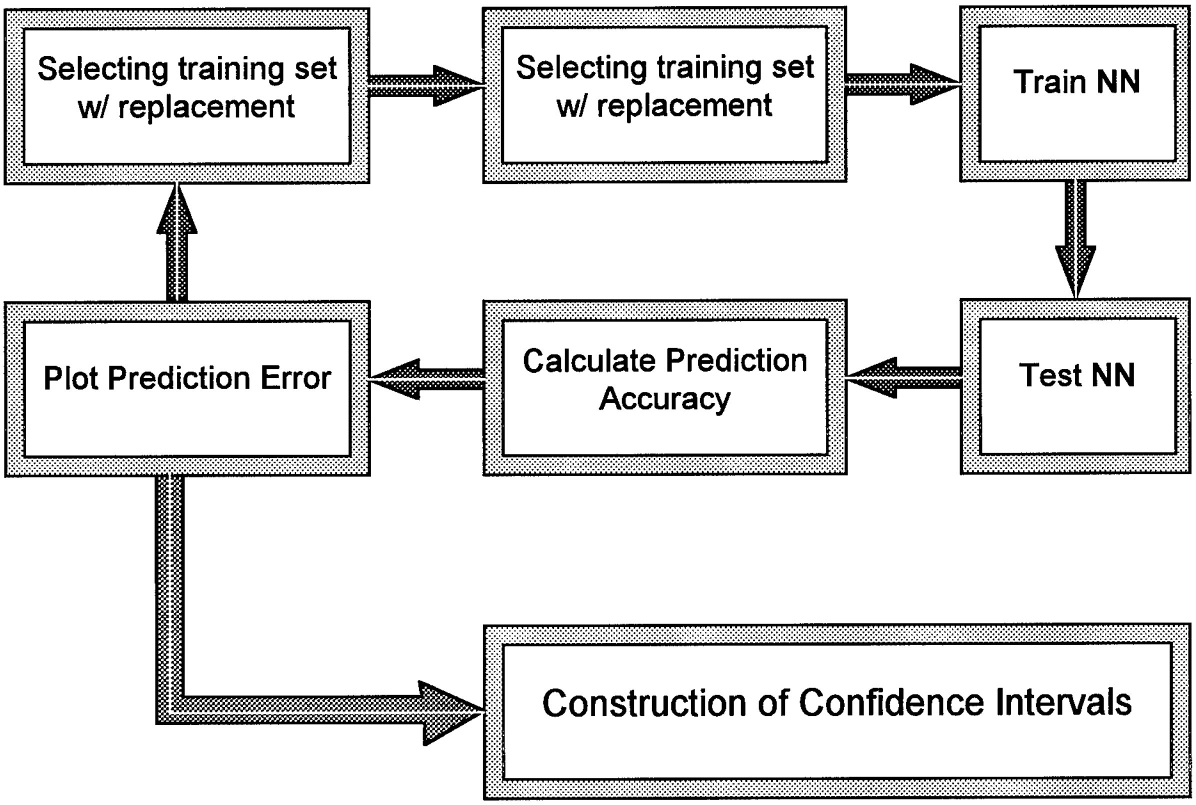

Figure 2.10. Neural Network -- bootstrap cycle

Examples of testing of neural bootstrap methodology for identification the optimum set of input parameters is shown in Figs. 2.11 and 2.12.

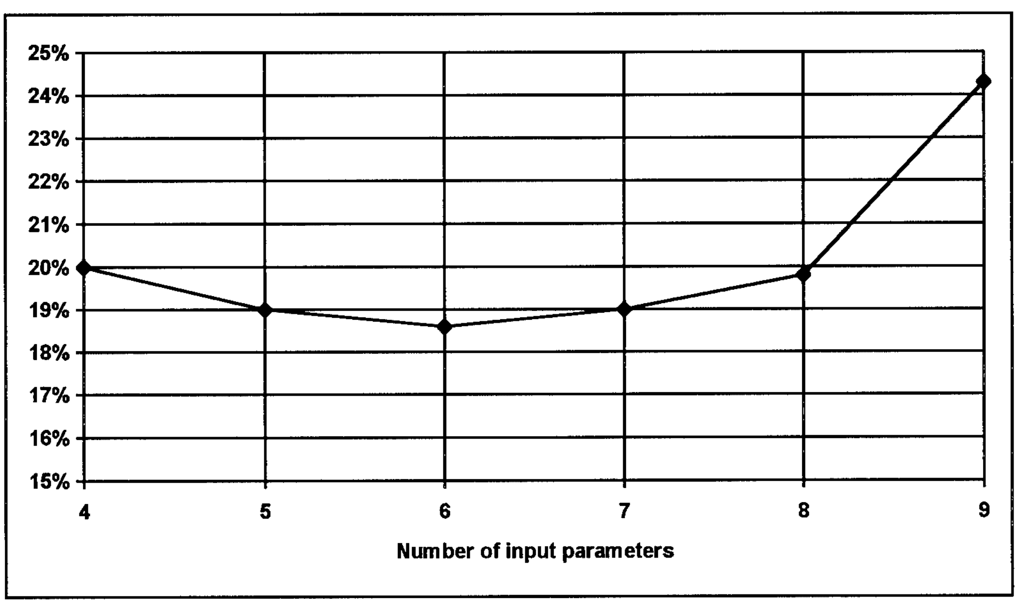

Figure 2.11. Percentage of false diagnosis as a function of a number of input parameters.

Figure 2.11 presents the percent of diagnostics errors versus the number of input parameters in the model. For each fixed number of input parameters - from nine to four - the average error for the best combination of parameters is plotted. There is a clearly visible trend of the percent of errors decreasing along with the number of parameters entered into model until the number of predictors becomes so small, that some of the predictive power starts getting lost. One can observe that when the number of predictors becomes less than six the percent of errors starts increasing. The error function seems to reach its minimum with six predictors in the model.

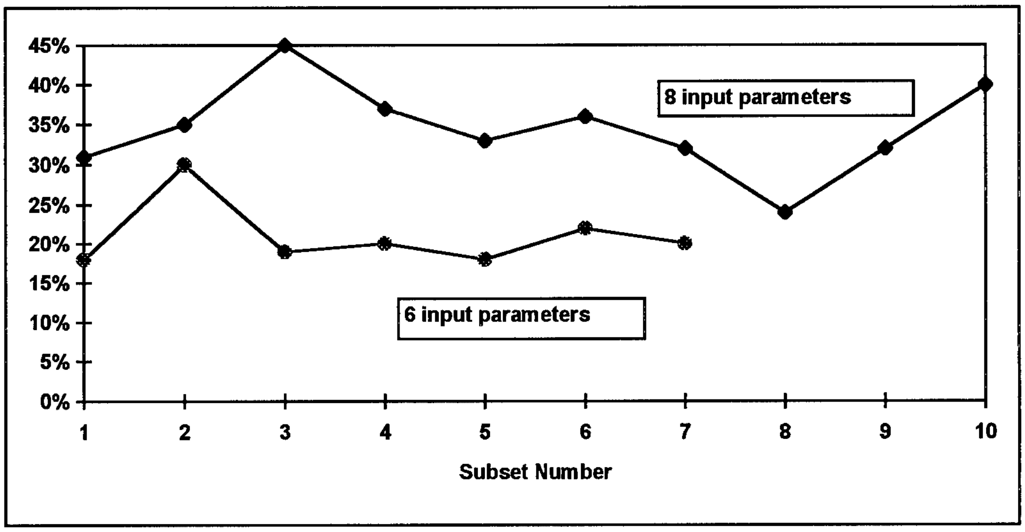

Figure 2.12. Percent of false diagnoses for various subsets of input parameters.

In Fig. 2.12 two curves demonstrate the results of a search for the best combination of input parameters when the number of predictors in the model is correspondingly nine and six. Each point on the curve plots the percent of diagnostics errors for a particular combination of nine (the top curve) and six input parameters (the bottom curve) . One can observe that combinations of six parameters systematically give better results compared to combinations of eight input variables.

2.20.1 SQI's Portable Computer Setup

All commercially available medical equipment for Pre-Hospital Trauma Care, including ECG monitors, oxymeters, carnographs, thermometers, etc. has RS232 interfaces for data acquisitions by the user's Personal Digital Assistant. Virtually all information displayed on the display is available for serial transmission including parameters, values, alarm status, leads status (ECG), remote status, etc. The configuration for serial data transmission is different, for example ESCORT 100 ECG monitor has a configuration 9600 baud, one start bit, eight data bits, two stop bits and no parity; Nellcor Oxymeter N-180 has configuration 2400, 4800, 9600 or 19200 baud (selectable), no start bit, because N-180 transmits a data string every 10 seconds, eight data bits, one stop bit and no parity bit. N-180 interface is active when power is plugged in and does not operate at battery mode.

SQI's N-180 computer setup is shown in Figure 2.13. The listing of RS 232 interface program is shown in Appendix A. The Nellcor OEM factory manufactures a replaceable board available under a licensing agreement. This module performs the SaO_2 functions of determining blood oxygen content, computing heart rate through pulse pickup and providing a pulse waveform.

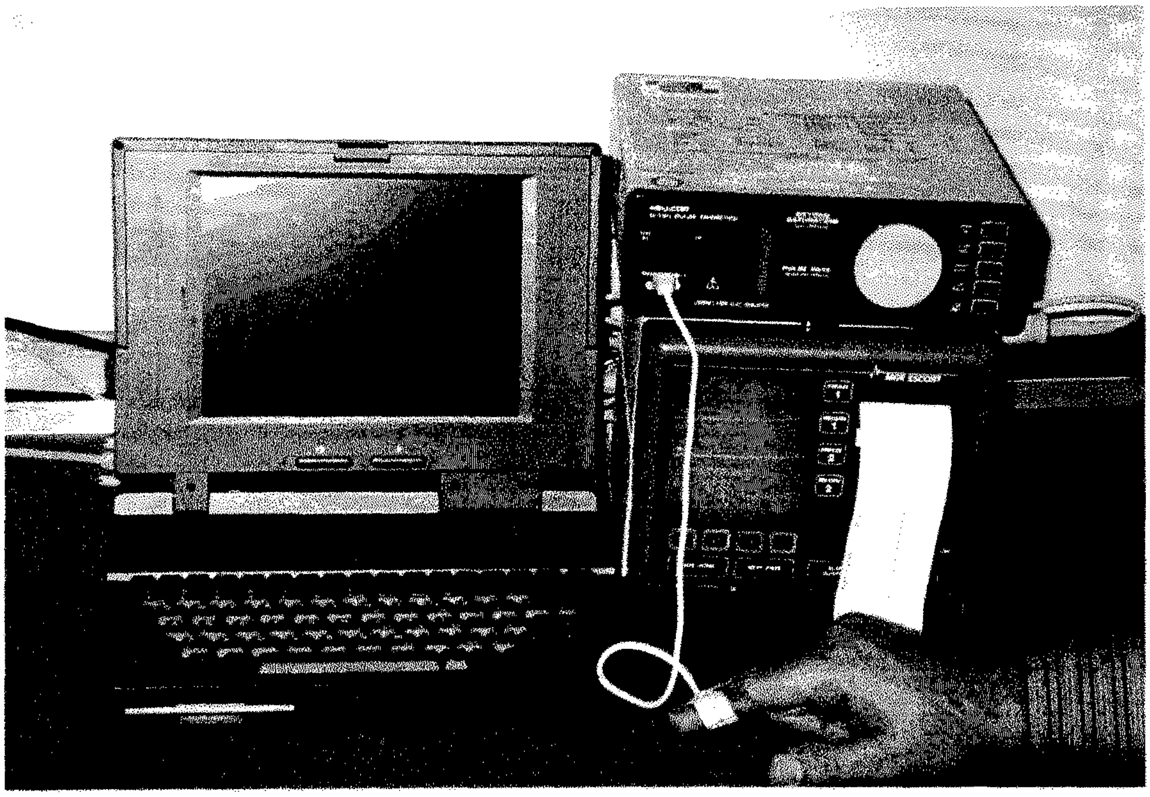

Figure 2.13. SQI N-180 computer setup.

The Nellcor OEM module requires only three RS232 signals Rx, Tx, and CTS. The serial communications connector pit assignment is shown below:

Computer (DB-9, female)		Oxymeter Module (DB-9, male)
Tx 3	←→	2 Rx
Rx 2	←→	3 Tx
RTS 7	←→	7 CTS

The oxymeters, carnographs, temperature and non invasive blood pressure OEM modules are commercially available under licensing agreement, therefore they can be easily integrated into a single chassis in order to provide the desired measurements. SQI will integrate the Propaq PSM from PSI. PSI has expressed a high level of interest in cooperation with SQI.

3.0 CONCLUSIONS AND RECOMMENDATIONS

3.1 Phase I Conclusions

During Phase I SQI has effectively developed FNNDA, utilizing bi-radial-neural networks. The following advances in trauma triage have been achieved:

- Bi-radial-basis neural network with fast training and fast restructuring were designed. Fast restructuring is especially important under conditions where new information becomes available so that a training dataset may be expanded and the efficiency of the computer-assisted diagnostics may be enhanced.
- Neural networks utilized as a key element in the SQI developed methodology for computer-assisted diagnostics may be trained with the use of the training data-sets of a limited size. This will allow us to design computer-assisted diagnostics software for narrowly-oriented specialized applications characterized by smaller available information in the form of training patterns.
- The neural network is designed in such a way that clinical evaluation and diagnosis may be produced in conditions when some of the input parameters are unavailable.
- Additional advantages of the proposed diagnostics methodology include utilization of parameters of a different nature with variations at a vastly different time-scale and a joint use of quantitative and qualitative parameters.
- Flexibility, fast training, and fast restructuring of the developed neural networks allows for their efficient integration into trauma monitoring equipment such as Propaq and Aquity Trauma Clinical Station.

3.2 Recommendations

In light of the successful results obtained in Phase I we offer the following recommendations for the Phase II effort

- The FNNDA must be integrated into trauma care monitoring equipment (Propaq, Aquity Trauma Clinical Station, Portable Hardbody Computer.
- FNNDA must be easily upgradeble, allowing for triage with new sensors.
- The FNNDA algorithm must be enhanced in accordance with the existing and future data base (will be available from Protocol System Inc., and Research Triangle Institute from Research Triangle Park at North Carolina)
- The new commercial product will be introduced into commercial market jointly by SQI, Protocol System Inc., Vista Group of Hospitals, Texas Microsystems, and Israeli Investment Company Ha Tehiya Ltd.

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APPENDIX A

Publications

1. Simon Katz, Alex Katz, *"Supervised neural networks capable of training on censored data and incomplete patterns", 1996 World Congress of Neural Networks, San Diego, CA, International Neural Network Society, pp. 1221-1226, 1996.*

Abstract

Existing methods of supervised training of neural nets use iterative minimization of cost functions, obtained as a sum of quadratic errors for individual patterns from the training set. We introduce a modification of the backpropagation methodology that allows for minimization of a wide class of non-quadratic general-form cost functions. A generalized cost function is presented as a combination of elementary cost functions. Its structure depends on features of individual patterns from the training set and output nodes of the neural network. This methodology allows neural networks to train on data sets containing censored or incomplete data patterns, and has been successfully tested on clinical cardiovascular data. A Cascading Assembly of Neural Elements (CANE) with a generalized cost function was trained to predict the time from implant to dysfunction of medical devices in cardiovascular patients. The average prediction error as a function of the proportion of incomplete training patterns indicated that inclusion of large subsets of censored data may improve predictive properties of the system. Correlation analysis of predicted failure times versus clinically observed ones corroborated this finding. The described technique of inclusion of censored or incomplete data patterns into training sets may be applicable to various lifetime, reliability, and survival analyses problems dealing with censored data.

APPENDIX B

SQI Personnel Receiving Pay from Contract No. DAMD17-96-C6029

1. Simon Katz Ph.D	Principal Investigator
2. Vladimir Katsman Ph.D.	
3. Bert Rosenthal MD	
4. Alex Tartakovskiy Ph.D.	
5. Lev Katsman MS	Contract Administrator

DEPARTMENT OF THE ARMY
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Phylis Rinehart

PHYLIS M. RINEHART
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