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Diagnostic Models Based on Personalized Analysis of Trends (PAT)

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***Abstract*—Many changes have taken place in medicine over the last century. In the first half of the Twentieth Century physicians were faced with the challenge of making diagnoses with too little information, often resorting to exploratory surgery to confirm the presence or absence of a condition. Due to rapid technological advances during the second half of the Twentieth Century, and continuing to this day, the position of the physician has now shifted from an information-poor environment to an environment with too much information, often exceeding the limits of human decision-making capabilities. To take full advantage of all available information, a new approach based on refined automated decision support methods is needed to assist the physician in the decision-making process. Medical decision-support systems need to evolve from stand-alone systems to cooperative systems in which the physician becomes the decision maker but relies on the decision-support system to sift through information to determine relevant trends. In this article, a decision support system that combines a number of methodologies for trend analysis is described, along with examples in cardiology. The methods have also been used in applications in neurology as well as cancer diagnosis and prognosis.**

***Index Terms*—Diagnostic Computer Models, Hybrid Systems, Medical Decision Making, Trend Analysis**

I. Introduction

At the beginning of the Twentieth Century, physicians were faced with challenges in arriving at a diagnosis based on too little information. As a result exploratory surgery was often necessary to confirm or rule out diagnoses; many conditions remained undiagnosed. During the latter part of the century, technological advances changed the face of medicine, beginning in the early Twentieth Century with x-rays [1], heart monitoring [2], and pacemakers [3], followed by advanced imaging methodologies such as CT [4], SPECT [5], MRI [6], and PET [7] in the latter part of the century. Imaging technologies became feasible in large part due to the increasing power of computers upon which all methods for image reconstruction rely. In the Twenty-First Century we are now seeing practical applications in the emerging field of bioinformatics applied to diagnosis and treatment of disease [8]. The end result of these rapid advances has been a change in the physician's perspective from having too little information to having more information than can be accommodated in the human decision-making process. Since multi-parameter decision-making is not a strong point of human reasoning, the assistance provided by computer-based analysis is crucial to take full advantage of the available information [9].

Technology has already dramatically advanced the state of medicine. To move to the next step in the integration of multiple types of information, universal availability of the electronic medical record (EMR) is crucial. Interoperability standards must be established so EMRs with different formats can readily exchange information [10]. Perhaps the most important long-term goal is the establishment of a personal health record (PHR) that would contain the complete medical record of each patient beginning at birth. The PHR would form the basis for a shift from population-based diagnosis and prognosis to individual analysis for each patient.

In this paper a general framework is described for automated trend analysis using the PHR. It is illustrated using three methods of analysis based on symbolic, numeric, and signal analysis methods which can be combined using a hybrid system approach that includes all data types. Comprehensive trend analysis will require many additional methods and the work of many researchers before reaching the goal of true personal health analysis.

II. Computer-Assisted Decision Support

In the last forty years, numerous medical decision support systems have been developed but have rarely been used in practice. Multiple reasons can be put forth for this failure [11]. In the beginning, most of the problems that were addressed were too simple. Although many systems functioned well within their domains, these domains were often well-understood by the physician, removing the motivation for their use. The stated goal of many systems that were developed by domain experts was to provide support to general practice physicians who have broad general knowledge but not necessarily domain-specific knowledge in medical specialties. Many of the problems addressed by early expert systems were too simple in the sense that physicians could make appropriate decisions on these problems without computer assistance. An

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allied problem with expert systems was that, in some cases, the reasoning ability of the system did not adequately express the complexities of the problems. Finally, many medical decisions have critical implications so physicians are naturally reluctant to trust decisions that can have far-reaching consequences if incorrect.

The approach described here is based on personal analysis of trends (PAT) and takes a different approach in that the computer-based analysis does not make decisions on its own but rather provides additional information on which the physician can base a decision. Crucial components include trend analysis that results in automatic alerts and notifications to the physician based on changes in the patient's parameters.

III. Personal Health Records

The creation of standards for electronic medical records would permit interoperability and would also make possible the personal health record (PHR) [12, 13]. The universal health record containing the complete patient history including biomedical signal and imaging results could be accessed via a secure web link or through a USB device that the patient retains. The existence of the PHR will change the way in which medicine is practiced. Instead of relying on population-based statistics to determine if certain treatments are relevant, the PHR will allow trend analysis for each individual patient to provide treatment and follow-up that is focused on the individual [14]. The resulting paradigm shift will change the diagnosis focus from population-based statistics to individual analysis.

The goal of PAT is not to provide diagnoses but rather to alert the physician when something has changed that may impact the patient's health. The computerized system has the advantage of being able to scan large amounts of data that the physician does not have time to examine and also to form an overall picture based on analysis in a multi-parameter space of high dimensionality. Unlike traditional expert systems that provide diagnostic advice, this approach provides structured information that can better help the physician in making decisions [15]. Specific objectives include the creation of an alerting system for:

- Changes in trends
- Emergence of new symptoms
- Worsening or improvement of existing symptoms and conditions.

The physician receives the alerts and notifications and decides on actions to be taken.

Because a number of categories of data exist in the medical record, a number of different methods of analysis are required. These categories will no doubt expand in the future to include detailed information on genetic markers as well as unforeseen areas that will provide more in-depth knowledge on the functioning of the human body. PAT must be based on a flexible software design that incorporates known methods while allowing the seamless integration of new methods as they become available. In the remainder of this article, a basic structure for trend analysis is described, followed by specific implementations for symbolic, numeric, and signal analysis data. The structure can be easily expanded to include new data types as they become available and can also include other analytic methods in addition to the examples provided here.

IV. Health Alerts and Trend Analysis

The overall structure of PAT relies on a method developed by the authors that provides information on changes in the patient's condition, both positive (notification) and negative (alert) [9]. The general algorithm does not specify methodology and thus can invoke a variety of techniques depending on the data and the condition. A comprehensive trend analysis system will require the use of many methods of analysis and validation of the methods on medical data for a broad range of conditions.

The Alerting and Notification Algorithm (ANA) is shown in Fig. 1. The algorithm compares current data to previous data to determine if a significant change has occurred in either a positive or negative direction. If the change is negative, three levels are considered based on the level of change.

Types of Alerts

- Level 1: Informational (issued when a result has changed in a negative direction, but not significantly)
- Level 2: Warning (issued when a result has changed significantly and should be addressed)
- Level 3: Urgent (issued when results indicate immediate action is required).

In the case of a positive change in a condition, or the complete resolution of a condition, a notification rather than an alert is issued

Types of Notifications

- Positive change in existing condition
- Resolution of existing condition

The method is based on the computation of degree of confidence $\delta_C(t)$ that indicates the degree of certainty that the condition exists at time t. The method for determining $\delta_C(t)$ depends on the data type. Examples are given in the following sections for symbolic, numeric, and signal analysis data. The approach requires the determination of threshold values for the alert levels for new or worsening conditions and the threshold for which a notification would be sent indicating an improvement in an existing condition. The determination of these thresholds can be quite complex and will vary greatly depending on the type of data. Two different scenarios need to be considered:

- The values for which a level 1, 2, or 3 level alert would be triggered for a new condition or worsening condition;
- The difference between the current value of a parameter and a previously recorded value that would trigger a level 1, 2 or 3 alert.

These values must be derived for each condition; the values will also depend on the methodology. The process is simplified by the normalization of all values to the interval [0, 1].

Methods for computing normalized values for $\delta_C(t)$ are shown in the next section.

Fig. 2 illustrates the alerting and notification process. While the process described here illustrates only comparisons to the immediate previously recorded values, it can be applied iteratively to n previous values in two ways:

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For all currently confirmed conditions
If condition i is present at time t_n with $\delta(t_n)=a$
If condition n previously present with $\delta(t_{n-1})=b$ set $\alpha = a-b$
If condition n was not previously present set $\alpha = a$
If $\alpha > 0$
if $(x_1 < \alpha < x_2)$ then send alert 1
if $(x_2 < \alpha < x_3)$ then send alert 2
if $\alpha > x_3$ then send alert 3
For all previously-confirmed conditions
If condition is not currently present send notification
If condition i is present with $\delta(t_n)=a$
If condition i previously present with $\delta(t_{n-1})=b$ and $(b-a)>x$ then send notification of change in degree

Fig. 1: **Alert and Notification Algorithm (ANA)**

- Identifying the first previous occurrence of significant change;
- Comparing the current value to an average of previous values over a specified time frame.

Both of these procedures are implemented as recursive algorithms.

V. Trend Analysis Models

In this section diagnostic models are discussed based on the type of data which they analyze: symbolic, numeric, signal analysis, or imaging. Each model is used to evaluate information that is then utilized in *ANA* as described in Fig. 1.

A. Information in Symbolic Form

For symbolic data, the EMERGE system developed by the authors is used [16]. EMERGE uses approximate reasoning and evidence aggregation to determine if a rule is substantiated. The rule comprises:

a_i: symbolically stated antecedents
w_i: relative importance of i^{th} component
s_i: degree of presence of i^{th} component
T: threshold for rule substantiation.

This format is an extension of the original EMERGE system which utilized binary logic [16]. Antecedents were combined as conjunctions, disjunctions, or counts, the latter of which consisted of confirming n out of m antecedents. In the approximate reasoning form used here, each antecedent has a weight w_i determined using expert input [17]. This format has the advantage of more closely representing the human decision-making process in which some factors are usually considered more important than others. The degree of presence s_i allows the physician or other medical professional to indicate the severity of each symptom or condition. To incorporate these more subtle measures, evidence aggregation must be used to determine rule substantiation, as represented by the equation:

$$E = \max[(\sum_{i=1}^{n} c_i \wedge s_i) \wedge \min_{i=1,...,n} (w_i^{c_i \wedge s_i})] \quad (1)$$

where $\wedge$ indicates min, $c_i \in \{0,1\}$, and n is the number of antecedents. The rule is substantiated if $E > T$, the threshold value that has been pre-determined for each rule. The degree to which E exceeds T indicates the strength of the supportive evidence that the condition exists. Thus two types of information are derived from this process:

- Substantiation or non-substantiation of the rule
- The degree of confidence in the result defined as the normalized value:

$$\delta_C(t) = (E-T)/(1-T) \quad (2)$$

where E is the evidence aggregation value in the interval [0, 1] determined from equation (1), T is the threshold value for the current rule, and t is the time of occurrence. If the condition is confirmed, aggregated evidence is greater than the threshold value and thus the confirmation range is a subset of the unit interval. For example, if the threshold T for substantiation is 0.6, a substantiated condition will have a $\delta_C(t)$ value in the interval (0.6, 1.0], Thus a 0.1 change in value of $\delta_C(t)$ is equivalent to 25% of the range of presence of the condition. As an example, consider the 25% value for issuing alerts:

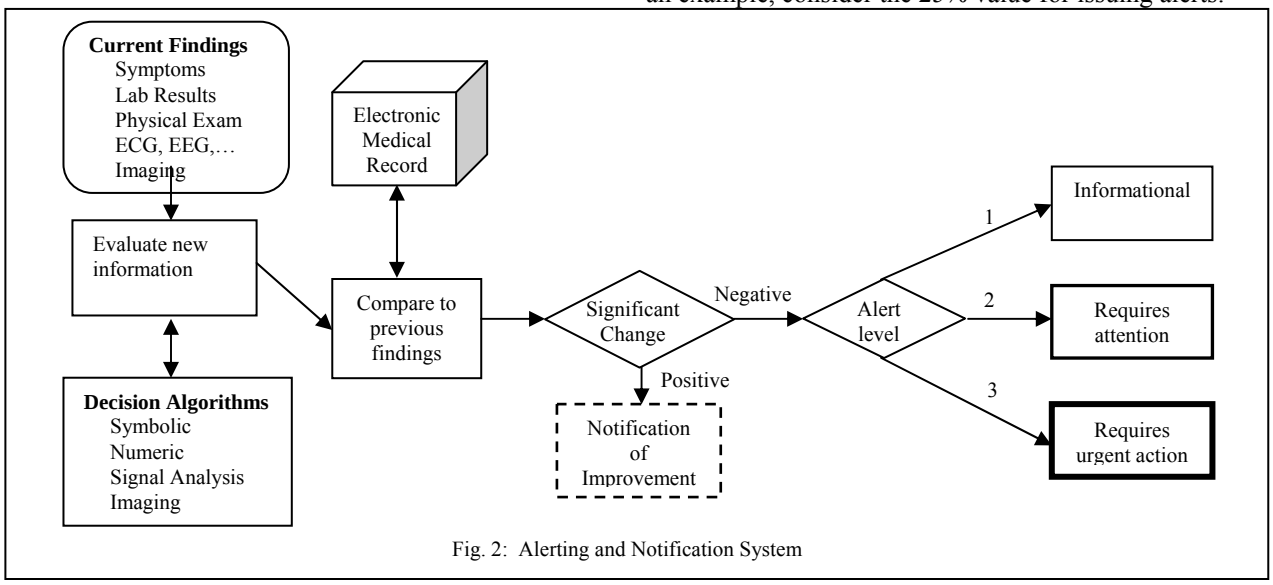

Fig. 2: Alerting and Notification System

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$\delta_C(t) - \delta_C(t-1) \leq 0.25\ (1-T)$	No Alert
$0.25\ (1-T) < \delta_C(t) - \delta_C(t-1) \leq 0.5\ (1-T)$	Alert 1
$0.5\ (1-T) < \delta_C(t) - \delta_C(t-1) \leq 0.75\ (1-T)$	Alert 2
$\delta_C(t) - \delta_C(t-1) \geq 0.75\ (1-T)$	Alert 3

The same method of alerting is also used for the current value $\delta_C(t)$ for a new condition for which $\delta_C(t-1)$ would be 0. The 25% rule is subjective; this value can be modified based on information specific to each rule.

Similar procedures are used for the neural network and signal analysis models with appropriate adaptation based on the ranges of these methods. Note that this process simply alerts the physician who decides if action is necessary. It should also be noted that this process will send a notification if a condition improves or no longer exists which may result in re-evaluation of treatments. A degree of confidence for non-substantiation $\delta_N(t)$ is obtained using the equation:

$$\delta_N(t) = (T-E)/T \tag{3}$$

B. Information in Numeric Form

Pattern recognition methods comprised most of the early approaches to computer-assisted medical decision making [18]. Most early methods were statistical but were quickly later followed by nonlinear neural network models [19]. In this work, a neural network model is utilized based on the Hypernet system developed by the authors [20]. In Hypernet, an n-dimensional feature vector **x** contains all parameters that are potentially relevant to the diagnosis. Each component, x_i, i=1,…,n can be any ordered data type including, integer, continuous, binary, or ordered categorical. The network is trained on suitable data sets for each application using a four-step process for each application: training, testing, classification, and determination of degree of confidence.

Hypernet is an extension of the potential function approach to pattern recognition [21]. Rather than using the Euclidean distance formula, the potential function is used:

$$P(\mathbf{x},\mathbf{x}_k) = \sum_{i=1}^{\infty} \lambda_i\, \Phi_i(\mathbf{x})\, \Phi_i(\mathbf{x}_k) \tag{4}$$

for k = 1,2,3..., where $\Phi_i(\mathbf{x})$ are orthonormal functions and λ_i are non-zero real numbers. The orthogonal functions of mathematical physics may be used as potential functions [22]. P_1 is computed by substituting the values from the first feature vector for case 1, $\mathbf{x}_1$. Subsequent values for P_k are then computed by

$$P_k = P_{k-1} + r_k\, P(\mathbf{x},\mathbf{x}_k) \text{ where} \tag{5}$$

$$r_k = \begin{cases} 1 & \text{If } P_i < 0 \text{ and class 1} \\ -1 & \text{If } P_i > 0 \text{ and class 2} \\ 0 & \text{If } P_i > 0 \text{ and class 1 or } P_i < 0 \text{ and class 2} \end{cases}$$

The functions used in Hypernet are chosen from the set of multidimensional orthogonal functions developed by Cohen [23], represented by the general class:

$$C_n(x_1,\ldots,x_m) = m!/[\,n!(m-n)!] \sum_{k=1}^{n} (-1)^k (m-k)!/\,[(n-k)!(m-n)!]\,\cdot$$

$$\sum_{i_k=k}^{m} \sum_{i_{k-1}=k-1}^{i_k} \cdots \sum_{i_1=1}^{i_2} \sum_{p=1}^{k} x_i^{\,a(n,i_p)}\, [a(n,i_p) + v_{i_p}]/\, v_{i_p} \tag{6}$$

where m is the dimensionality of the data, a_i, i=1,...,k are parameters which may be arbitrarily selected, and v_{i_p}, i=1,...,m are assigned values corresponding to the components of the first feature vector. Note that while high-order equations can be obtained using this method, in general only linear and second-order terms are used to prevent over-determination of the decision surface.

Implementation

1. Training

In the training phase, data of known classification are used to determine weighting factors w_i and w_{ij} in the decision equation:

$$D(\mathbf{x}) = \sum_{i=1}^{n} w_i x_i + \sum_{i=1}^{n} \sum_{j=1}^{n} w_{i,j}\, x_i x_j \qquad i \neq j \tag{7}$$

Each x_i represents a diagnostic parameter which is coupled with its weight w_i that is determined in this training phase. All parameters as well as all first-order combinations of parameters are included in this nonlinear decision function.

2. Testing

In the testing phase, a new data set is used to test the classification ability of D(**x**) using sensitivity, specificity, and accuracy measures.

Sensitivity: number positives classified correctly/TP

Specificity: number negatives classified correctly/TN

Accuracy: number correctly classified/(TP+TN)

where TP and TN represent true negatives respectively.

3. Classification

In the classification phase, D(**y**) is used to determine if a condition exists using the feature vector **y** that contains values for the current visit, with a positive value indicating presence and a negative value indicating absence. These results parallel the symbolic approach: D(**y**) > 0 substantiation, D(**y**) < 0 non-substantiation of the condition and D(**y**) = 0 no decision.

4. Degree of Confidence

In the neural network approach, the degree of confidence $\delta_C(t)$ is determined by comparing results from the decision equation D(**y**) where **y** represents the values for each parameter for the current patient visit with D(**x**), the decision surface. The further D(**y**) is from D(**x**) the more certain that the classification is correct. The degree of confidence for this method is thus defined by the normalized value:

$$\delta_C(t) = |D(\mathbf{y}) - D(\mathbf{x})|/D(\mathbf{z}) \tag{8}$$

where **z** is the vector whose components result in the greatest distance from D(**x**). $\delta_C(t)$ is then compared to $\delta_C(t-1)$ as

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described above for the symbolic analysis. If the condition is not substantiated, this method also provides a degree of confidence in the negative finding $\delta_N(t)$obtained from equation (7) when D(**y**) is negative.

The training and testing phases must be repeated for each new disease. It is necessary to have a large enough data set for sufficient training as well as data that has been collected in an environment that corresponds to the population being evaluated.

C. Signal Analysis

Medical records contain special data types in addition to symbolic and numeric information. These include routine biomedical signals for diagnostic purposes such as the ECG and EEG. For the ECG, two basic types of studies are routinely done: short time-duration studies for detection of arrhythmias and long-duration studies for determination of heart rate variability based on the R-R interval, or time between heartbeats. In general, the appearance of variations of the normal QRS pattern are automatically detected and listed according to type, such as ST depression, T waves, bigeminy and others. These are handled by rules in the symbolic processor. Long-term studies such as Holter recordings also detect the appearance of arrhythmias as well as heart rate variability. A method developed by the authors for nonlinear analysis of time series is used. The theoretical basis is the logistic equation, sometimes called the Poincaré equation:

$$a_n = A\, a_{n-1}(1 - a_{n-1}) \quad 2 \le A \le 4 \tag{9}$$

where A is a constant whose value changes the behavior of the function. The recursion is dependent on the selection of a_0, which must be chosen between 0 and 1. This equation appears chaotic if only discrete values are taken for a_n. A method for analyzing time series relies on the continuous solution of the equation (9) previously derived by the authors [24]. Results show a continuous progression rather than a precise point that indicates the onset of chaos. The Poincaré differential space was defined using the second-order difference between values in a time series. For point a_n that occurs at time n, the second-order difference plot is produced by computing a_{n+2}-a_{n+1} vs. a_{n+1}-a_n for all points in the time series. Using this space, points in the time series can be summarized using the Central Tendency Measure (CTM):

$$CTM = \left[\sum_{i=1}^{t-2} \Delta(d_i)\right]/(t-2) \tag{10}$$

where $\Delta(d_i) = 1$ if $[(a_{i+2}-a_{i+1})^2+(a_{i+1}-a_i)^2]^{1/2} < r$
0 otherwise

This measure calculates the percentage of points that fall within the specified radius around the origin. The CTM method has been shown to be useful in summarizing Holter recordings for the diagnosis of congestive heart failure (CHF) [25]. In general, normal subjects have a CTM measure between 0.90 and 0.99, indicating that most points are centered near the origin. Patients in the study with CTM < 0.5 all had CHF.

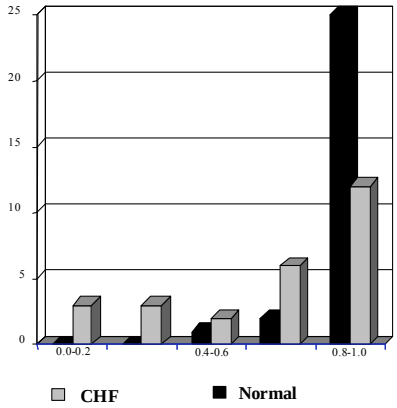

Fig. 3
Distribution of Normal and CHF Patients Based on CTM Measure

Thus the CTM on its own has some degree of diagnostic power. Neural network models were developed using data from a number of studies. A comparison of CHF vs. normal patients using only the CTM with a value of r = 0.1 in equation (10) resulted in sensitivity of 69%, specificity of 91%, with overall accuracy of 74%, (Fig. 3).

Using the CTM as the sole measure:

- Substantiation of a condition is determined by the CTM exceeding a threshold.
- The certainty of the classification increases with an increase in the CTM with a maximum value of 1.

Since a high value of the CTM is indicative of the healthy state, the degree of confidence of the presence of CHF is defined as:

$$\delta_C(t) = 1 - CTM \tag{11}$$

The degree of confidence for non-substantiation is

$$\delta_N(t) = CTM. \tag{12}$$

The CTM measure alone is useful as an indicator of CHF; its diagnostic power is significantly improved by combination of CTM with other parameters in a hybrid model described below.

D. Imaging

Automated analysis of medical images presents challenges. Comparison of new images to previous images for the same patient requires the use of image registration techniques [26]. The process is further complicated with functional imaging techniques [27] and 4-D imaging [28]. Image registration is an active area of research that is outside the scope of this article. In addition to the direct comparison of images in the patient record, textual interpretations are also provided by the radiologist who interpreted the image. These textual descriptions can be processed using the symbolic approach.

E. Hybrid System with Multiple Data Types

A hybrid system is used to combine the above methodologies for evaluation of mixed data types. As an example, consider the use of the neural network in conjunction with the CTM method for biosignal analysis. The CTM measure can be used as one input parameter in the neural network along with other findings such as blood test results. In addition, different

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measures using the same CTM methodology can be included as separate parameters in the neural network model.

While the CTM on its own can identify most cases without CHF, many of the CHF cases overlap the normal range. If CTM is combined with other parameters using a neural network model, accuracy is greatly increased. Using the same group as study 1, additional clinical parameters were added to the CTM: edema, rales (abnormal respiratory sound), HR (heart rate), and BUN (concentration of nitrogen in the form of urea in the blood), resulting in the following measures: sensitivity = 84%, specificity = 82%, and accuracy = 84%. A second study which combined several CTM-related parameters (CTM (r=0.05), CTM (r=0.1), # of RR intervals (time between heartbeats), lowest value of r for which CTM > 0.99) the neural network model resulted in sensitivity: 83%, specificity: 88%, and accuracy: 85%. These studies are summarized in Table I [29].

Using the decision models generated from the above data, the substantiation is determined as described above under neural networks using the values for the variables in Table I to produce a value at time t for D(**y**) and deriving $\delta_C(t)$ from equation (11). The alerts are reported using $\delta_C(t) - \delta_C(t\text{-}1)$.

A study was also done by the authors for prognosis of survival in patients with CHF [30]. The CTM measure was combined in a neural network model that included BUN (concentration of nitrogen in the form of urea in the blood), orthopnea (inability to breathe except in an upright position), dyspnea (difficult or labored respiration), heart rate, edema, functional impairment, and PND (paroxysmal nocturnal dyspnea). This study is summarized in Table II. These studies are based on the Hypernet model and form the basis for the decision algorithm with the dichotomous decision predicting survival. Note that although this is a yes/no decision, the value for D(**y**) indicates the strength of the conclusion which must be taken into account in treatment strategies.

VI. Example: Patient with Shortness of Breath

Patient A, 67 year-old woman complains about recurring shortness of breath (not present at time of visit). This example shows the use of the different components and also illustrates the importance of considering more than one diagnosis.

TABLE I
CTM Studies based on Holter Tape Analysis for Detection of CHF

Study #	Sensitivity	Specificity	Accuracy	Variables
1	69	91	74	A
2	84	82	84	B
3	80	89	85	C
4	83	88	85	C

Number of Patients/Group (X: CHF, Y: Other heart disease, Z: Normal)
A CTM Alone (r=0.1), X(32), Y(20)
B CTM, (r=0.1), Edema, rales, Heart Rate, BUN, X(32), Y(20)
C CTM (r=0.05), CTM(r=0.1), # of RR intervals, lowest value of r with CTM > 0.99, X(25), Z(27)
C CTM (r=0.05), CTM(r=0.1), # of RR intervals, lowest value of r with CTM > 0.99, X(52), Z(32)

Table II
Survival Study of CHF Patients Using Holter Recordings

Surviving (22), Deceased (22)	Sensitivity	Specificity	Accuracy
	80%	94%	88%

CTM (r=0.1), Symptom status, BUN, orthopnea, dyspnea, HR, edema, functional impairment, PND

Data from a number of sources are listed below:

History: Borderline high glucose 115
High cholesterol: 200 total, 52 HDL
ETT normal
Holter: CTM=0.99, no significant arrhythmias

Physical Findings: Rales present
Slight edema in ankles
Height: 64”
Weight: 145 lb
Temperature: 99.2°F

ECG: ST depressions
Incidents of bigeminy

Blood Analysis: Total cholesterol: 20/46
Glucose: 125
C-Reactive Protein (CRP): 5.8
BUN 29

(CRP is an indicator of severe inflammation that may indicate heart disease as well as other disorders such as infection.)

Chest Radiograph: Left-sided infiltrate

ETT HR beginning: 88
HR end: 120
BP beginning: 138/85
BP end: 150/95
Max ST depression: 1.5

Holter CTM measure: 0.82
Occasional bigeminy

Findings: Pneumonia
Potential CHF

These results were analyzed in the following manner:

- Changes in numerical values on individual variables
- Application of rules relevant to current findings
- ECG analysis for ECG arrhythmia detection
- Neural network model for cardiac analysis

The following are selected detailed results for this case.

A. Symbolic Analysis

The EMERGE system described above is used to determine probable diagnoses in patients complaining of chest pain when data are symbolic in nature. An example is given using the following rule for determination of possible pneumonia:

IF	Chest Pain	0.2	w_1
	Difficulty breathing	0.3	w_2
	Rales	0.3	w_3
	CRP elevated	0.2	w_4

Then Pneumonia probable, T = 0.7

The weights are entered by the user and indicate the degree of presence of each symptom. The following steps then occur:

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Using equation (1), the evidence is aggregated. *ANA* is then invoked.

If E > T, the condition is confirmed.

The database is then searched.

If the condition did not previously exist an alert is issued.

If the condition is pre-existing and $\delta_C(t)$ is significantly greater than the average of previous values, an alert is issued.

If the condition is pre-existing and $\delta_C(t)$ is significantly less than the average of the previous values, a notification is issued.

If E ≤ T, the condition is not confirmed.

If the condition previously existed, a notification is issued.

From this rule, it appears probable that the patient has pneumonia.

A level 2 alert is issued and a chest radiograph is ordered and confirms the diagnosis.

B. Neural Network Analysis

A previous study of exercise treadmill tests (ETT) using Hypernet identified parameters that separated normal subjects from patients with heart disease with high degrees of sensitivity, specificity, and accuracy[31]. These parameters are:

x_1: Blood pressure (BP) at beginning of test
x_2: BP at end of test
x_3: Heart rate (HR) at beginnings of test
x_4: HR at end of test
x_5: Double product at end of test (HR x BP)
x_6: ST depression during test

Values for the current ETT are used in Hypernet to produce a value for D(**y**), with a positive value indicating presence of heart disease. The normalized distance from the decision surface indicates the strength of the decision. *ANA* is then invoked following the same procedure as outlined above for the symbolic method with $\delta_C(t) = |D(\mathbf{y})-D(\mathbf{x})|/D(\mathbf{z})$. $\delta_C(t-1)$ is compared with $\delta_C(t-1)$ associated with the previous ETT to determine alerting and notification options. The current values show that the patient's cardiac health is less certain than on the previous test with $\delta_C(t) - \delta_C(t-1) = 0.1$. The difference is minimal and a level 1 alert is issued.

C. Signal Analysis

Because of the level 1 alert issued it is decided to obtain a 24-hour Holter recording for the patient [32]. CTM analysis resulted in a value of 0.82, which although normal, is in the low normal range. The patient had a previous Holter in her PHR showing a value of 0.99. The difference represented a significant change and resulted in a level 2 alert determined by looking at the normal range (0.7, 0.99). The shift of o.17 is approximately 59% of the range. Using the CTM value in the neural network model along with edema, rales, heart rate, BUN confirms a probable early stage congestive heart failure.

VII. Discussion

The alerting and notification methods described here provide a basis for the development of a comprehensive system for trend analysis. The specific methodologies developed by the authors for symbolic, numeric, and signal analysis data can be expanded to include other methods such as statistical, Bayesian, genetic algorithms, clustering, image registration and image comparison. The challenge of collecting sufficient information on which to base each disease model remains. For knowledge-based systems this requires the participation of multiple experts and requires a considerable time commitment. For data-based systems sufficient amounts of data are required to assure the accuracy of the decision model. The creation of standards for electronic medical records will facilitate the analysis of data for large populations and permit the development of sound data-based decision-making. Data need to be available for research, without patient identifiers. The practical implementation of the methods described here must be done in a distributed and cooperative atmosphere as the development of each new model will require time commitments as well as access to the appropriate data sources, whether expert or data-based. The potential for personalized healthcare is receiving attention from many researchers. The availability of interoperability standards for the patient record [33] will permit the use of electronic methods of evaluation including web-based clinical support [34] and the inclusion of broad-based biomedical information including genetic information [35]. Personal healthcare workgroups based on information technology are actively pursuing new methods to make these possibilities a reality [36].

In the neural network studies cited, the sensitivity, specificity, and accuracy are always less than 100%. Historically, the argument has been made that it is not suitable to use such models, as mistakes will be made, with the hidden assumption that human decision-making is never in error. The same is true of the expert-system approach and the signal analysis approach. Whatever the decision process, absolute certainty is never possible. The advantage of the approach taken in this work is that the decision is not made by the computerized system alone; rather it is a cooperative effort between the modeling mechanism and the human decision maker. The computer is using multi-parameter analysis to supply additional information that the human decision maker would not otherwise have; the physician can then add the repertoire of information that he or she already has available.

VIII. Conclusion

Information technology has permitted the evolution of medicine over the last forty years, particularly in the area of medical imaging. Technological advances are focusing in new directions, including the expansion of genomic information that will be important in the realm of personalized health care. Due to the increasing amount of diagnostic information it will be increasingly difficult for the physician to analyze this highly multi-dimensional space to form a comprehensive picture of the patient's health status. It is time to apply technology to the sophisticated analysis of medical records to determine personal trends that can lead to improved treatment at earlier stages of disease. It will however require both technical advances and changes in the structure of the electronic medical record to form a comprehensive life-time record that can be accessed by the patient.

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