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PROBLEMS OF DESIGNING AN INFERENTIAL MEDICAL CONSULTING SYSTEM

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'Medicine is a science of uncertainty and an art of probability.'

Sir William Osler

ABSTRACT

The paper gives an outline of basic problems involved in designing an inferential medical computer consultant, and then discusses the methods of implementing deductive and inductive capabilities of such a system. To implement the latter capabilities the paper advocates logical methods (specifically methods employing concepts of a variable-valued logic system) rather than statistical or syntactic methods which are currently most common.

1. INTRODUCTION

The amount of diagnostic and therapeutic knowledge existing today surpasses by far what a single physician or a group of physicians can encompass even if they have a sizable library in their offices. The situation is becoming worse as this knowledge grows rapidly. An augmentation of a physician's memory by developing computer medical data bases is an important step forward, but in the long run it will not be sufficient. To improve the quality of his decision making a physician will need a medical computer consultant with significant inferential and learning capabilities.

By 'inferential capabilities' we mean deductive and, as well, inductive capabilities. The deductive capabilities will allow such a medical computer consultant (MCC) to apply various decision rules, stored in its data base, to the specific new situations in order to come up with a diagnostic, therapeutic or other advice. The inductive capabilities will allow the MCC to modify, generalize or determine various decision rules from new facts, observations, feedback information, 'experience', etc. By 'learning capabilities' we mean capabilities to accept various facts and rules, and to link them with already known facts and rules.

A need for such an inferential computer consultant is clearly seen from the following.

A data base without inferential and learning capabilities would just be a bank of known specific facts about diseases, therapy, disease-symptom, therapy-symptom, and other relationships.* Such a system could answer only the questions directly related to the situations identical to those stored in its memory, and would be useless for answering questions related to any new situations. A system with deductive capabilities would be able to answer questions related to new situations, but only if decision rules pertinent to these new situations were available. To formalize and program, however, all the known, usually very informal, intuitive, and sometimes contradictive rules developed by the medical profession is a monumental task. But even if such a task was achieved in a certain point in time, the system would become quickly obsolete, if it would not have inductive and learning capabilities. The latter capabilities will enable a system to learn rules from examples, specific cases, to modify and update rules, using feedback information to make new generalizations, etc.

2. OUTLINE OF BASIC PROBLEMS OF DESIGNING A MCC

Designing an inferential medical computer consultant is a very complex task consisting of many different problems:

- Development of a system of programs for executing learning and inferential processes, i.e., programs which

  (1) can accept, 'comprehend', and easily handle, and also update medical knowledge about 'symptom-disease', 'cause-effect', 'disease-therapy' and other relationships (learning capabilities)

  (2) can infer decision rules expressing these relationships from given single facts, examples, cases, etc. (inductive capabilities)

  (3) can advise, based on the directly obtained or inferred decision rules and the given information about a patient, about diagnosis, therapy, tests to assign or other medical action (deductive capabilities)

*There are approximately 6000 diseases and 20,000 medical symptoms and measurements.(1) With each disease, there can be associated a large number of known cases and facts, thus the development of a complete medical data base presents a very serious problem by itself.

. Development of very convenient, simple and attractive methods, devices, terminals and computer language(s) for interactive communication between physician(s) (also researchers and other users) and the MCC.

. Development of a computer medical base consisting of

(1) data about patients (medical history, physical examination, laboratory tests, special tests, diagnostic decisions, prescribed therapy, resulting changes of a patient's health, etc.),

(2) diagnostic and therapeutic and other knowledge obtained from physicians and medical books,

(3) diagnostic and therapeutic knowledge (in the form of decision rules) which MCC acquired itself from given cases and examples (using its learning and inductive capabilities).

An important property of such a data base must be that the above knowledge is represented in a form which is well suited for implementing deductive, inductive and learning processes. It should be noted, that the data bases being developed presently are not well suited for such processes.

. Design of overall hardware configuration of the system.

. Design of overall software configuration of the system (operating system, supporting programs, etc.).

. Security problems (different types of access to the system for different users (doctors, researchers, laboratory technicians, computer operators, etc.).

. Communication of the system with external computer data bases.

. Other problems, in particular legal problems.

3. CRITICAL REVIEW OF BASIC METHODS FOR IMPLEMENTING INFERENTIAL AND LEARNING PROCESSES

The problems which are most theoretically difficult are the problems of implementing inferential and learning processes for medical decision making. In this paper we will restrict ourselves to a discussion of only these problems. Basic known methods which may be used for solving these problems can be divided into 4 groups:

(1) statistical methods, i.e., methods based on statistical decision theory, in particular on the Bayesian theorem,

(2) analytical methods, which employ techniques such as regression analysis, factor analysis, multiple discriminant analysis, linear and polynomial discriminant functions, etc.

(3) syntactic methods, which employ the concept of formal grammars and parsing techniques

(4) logical methods, which describe decision processes in terms of concepts developed in formal logic (binary and multivalued).

The statistical methods are of quite limited usefulness for our task. Some of the difficulties with these methods with regard to diagnostic decisions were expressively described by Edwards*:

> "...My friends who are expert about medical records tell me that to attempt to dig out from even the most sophisticated hospital's records the frequency of association between any particular symptom and any particular diagnosis is next to impossible -- and when I raise the question of complexes of symptoms, they stop speaking to me. For another thing, doctors keep telling me that diseases change, that this year's flu is different from last year's flu, so that symptom-disease records extending far back in time are of very limited usefulness. Moreover, the observation of symptoms is well-supplied with error, and the diagnosis of diseases is even more so; both kinds of errors will ordinarily be frozen permanently into symptom-disease statistics. Finally, even if diseases didn't change, doctors would. The usefulness of disease categories is so much a function of available treatments that these categories themselves change as treatments change -- a fact hard to incorporate into symptom-disease statistics.
>
> All these arguments against symptom-disease statistics are perhaps somewhat overstated. Where such statistics can be obtained and believed, obviously they should be used. But I argue that usually they cannot be obtained, and even in those instances where they have been obtained, they may not deserve belief."

We can summarize these difficulties as follows. These methods

(1) require usually too much data to estimate all the necessary class conditional probabilities**

(2) do not provide goal oriented descriptions of decision classes, e.g., descriptions which use only variables (symptoms, measurements, signs, etc.), which are most adequate for describing each individual decision class. (They use descriptions which use the same variables for describing all the classes, i.e., these methods are 'constant decision space methods', rather than 'variable decision space methods').[3]

*In ref. 2, pp. 139-151.

**It can be shown that in some situations these methods may require more disease cases then number of people who ever lived or live on our planet (!).

(3) ignore 'cause-effect', structural and other relationships which often exist among symptoms, signs, results of medical tests, etc.

(4) produce decision rules which are difficult to comprehend by humans; the rules do not relate well to human inferential processes.

(5) are often feasible only when independence of tests, symptoms, etc., is assumed, which is often too strong an assumption in real situations.[4]

(6) do not give any insight how to divide decision problems into subsystems, which, as indicated by Patric,[1] would be a necessity for a large-scale system.

(7) produce decision rules which are not easy to modify (in order, e.g., to accommodate new information) or to correct (e.g., when some errors were introduced in gathering statistics).

(8) are primarily oriented toward situations described by absolute and ratio variables; they are not well suited for situations where ordinal or nominal variables are used.

Analytical methods also are not particularly promising, since they share many of the above disadvantages. As an example of a rule produced by such methods, consider thyroid index developed by Overall and Williams[5] using a factor analysis method:

$$
\begin{aligned}
Y= & 0.8380X_1+1.4070X_2+1.1780X_3+1.6810X_4 \\
& +0.8440X_5+1.8450X_6+1.3940X_7+1.0690X_8 \\
& -0.8780X_9-0.8700X_{10}-2.7400X_{11}-0.1630X_{12} \\
& -0.4800X_{13}-1.2790X_{14}-1.0900X_{15}-0.9010X_{16} \\
& +2.4350X_{17}+1.6610X_{18}+0.0251X_{19}+0.0043X_{20} \\
& +0.0067X_{21}-0.0036X_{22}-0.0075X_{23}+0.0260X_{24} \\
& +0.0491X_{25}+0.0456X_{26}.
\end{aligned}
$$

where X_i are various measurements and symptoms, such as 'recent increase of sweating', 'dry puffy coarse skin', 'blood glucose', etc.

The value of Y, computed for given X_i, is compared with two thresholds, and based on the result of this comparison the patient is assigned one of the three diagnosis -- hypothyroid, euthyroid or hyperthyroid.

Disregarding other features of this method, let us observe that the above decision process has little in common with the way humans make decisions. Such a decision rule seems to be dogmatic, it does not give 'reasons' for a given decision, it is difficult to check correctness of the rule, to have the 'confidence' in such decisions.

Syntactic methods also seem to be not very promising. They require that each decision class be described by a formal grammar.* But it is not clear how to construct such grammars. It is quite difficult to construct the grammars from the knowledge in medical books, and, on the other hand, it seems unrealistic that grammatical inference methods could be advanced sufficiently to construct grammars automatically. Grammars are also not easy to modify, they require a sequential process for evaluation, they don't give a 'degree of confidence' in a decision, they are not adequate for handling numerical information, etc.

*See, e.g., paper by R. S. Ledley, p. 152 in the book.[2]

The methods from the above 3 groups can, of course, be quite useful in various specific situations, but they do not seem to be adequate for providing the basic philosophy for development of a large-scale inferential MCC.

The methods which the author considers most promising here stem from the development of logic, specifically multi-valued logic.

In the next chapter we will give a brief outline of inferential methods which are based on logical concepts, in particular on the concept of a 'variable-valued logic system'.

4. A LOGIC-BASED APPROACH TO IMPLEMENTATION OF INFERENTIAL PROCESSES

4.1 General Remarks

In the logic-based methods decision rules are expressed as statements of a logic system. A deduction process consists of testing whether a specific input information satisfies conditions implied by the logical decision rules. An inductive process consists of creating the general decision rules (hypotheses) from the specific examples of decisions and available problem knowledge.

A logic system which seems to be very adequate for implementing such processes is a variable-valued logic system called VL_1.[6-8,11] This system assumes that logic formulas and the variables in them can be assigned independent domains from which they draw their values. Thus, the domains of formulas and variables may have different numbers of elements and the elements may have different meaning. Below are examples of VL_1 variables (x_i) and formulas (v_i), and their domains.

Variables	Domains
x_1='body temperature'	$D(x_1)$={below normal, normal, above normal}
x_2='sex'	$D(x_2)$={male, female}
x_3='age'	$D(x_3)$={numbers of years}

Formulas	
v_1='biliary cirrhosis'	$D(v_1)$={not present, present}
v_2='chronic hepatitis'	$D(v_2)$={not present, moderate, severe}

The definition, properties and VL_1 formula synthesis algorithms are described in papers[11-13]. Here we will give only an informal outline of VL_1 and then, in the next section, will illustrate its application by some results from an experiment on the diagnosis of 3 liver diseases.

The VL_1 system uses the following operators: min($\wedge$), max ($\vee$), inverse ($\neg$), exception ($\setminus$), separation ($|$) and arithmetic addition.* A VL_1 formula is constructed by applying these operators to the constructs called selectors and elements of the output domain of the formula.

A simple form of a selector is a unary condition which tests whether a value of a given variable belongs to a certain subset of the domain of this variable. For example:

$$[x_2 = 1,2,6]$$

is a selector which is satisfied if a value of x_2 is 1, 2, or 6, otherwise it is not satisfied. A satisfied selector accepts the highest and an unsatisfied the lowest value in the output domain (which has to be an ordered set). Similarly,

$$[x_5 \geq 2]$$

is satisfied when a value of x_5 is greater than or equal to 2, and

$$[x_1 \neq 3:5]$$

is satisfied when a value of x_1 is not between 3 and 5, inclusively. A more complex form of a selector permits one to have an analogous condition on an arithmetic sum of variables or their inverses, or on a VL_1 formula itself.

A VL_1 formula is interpreted as a function which maps every possible sequence of input variables into the output domain. For example,

$$2[x_1=0,3][x_5\neq 2] \vee 1[x_2=2:5,7] \vee [x_3\geq 0][x_4\geq 0]$$

can be interpreted as a function which takes value

2, if x_1 is equal to 0 or 3 and x_5 is not equal to 2

1, if the above condition is not satisfied and x_2 is equal to 2,3,4,5 or 7, except when x_3 and x_4 are greater than 0.

0, in all the remaining cases.

The values of a VL_1 formula (elements of the output domain) can be names representing a decision or a set of decisions. To increase the reliability of decision making each decision (or set of decisions) can be associated with more than one formula. Also, evaluation of a formula (or formulas) can be executed in such a way that the resulting decisions can be assigned certain credibility value.

VL_1 formulas can be easily translated to English statements. Below is an example of a decision rule expressed in English which corresponds to a certain VL_1 formula.

<u>If</u> [condition i1] <u>and</u> [condition i1+1] ...

<u>or</u>

[condition i2] <u>and</u> [condition i2+1] ...

<u>except</u>

[condition i3] <u>and</u> [condition i3+1] ...

<u>then</u> the advised decisions are:

d1: 'Patient has disease...'
'with credibility value = ...'

d2: 'Patient may also have disease...'
'with credibility value = ...'

d3: 'A suggested therapy is...'

*Only inside 'selectors'.

The credibility values are assigned during the evaluation of a formula(s) for given values of variables (where variables represent various symptoms, signs, medical tests, etc.).

The VL_1 formulas can be constructed based on medical knowledge or can be inferred automatically in a process of inductive inference from specific cases of decisions made by specialists. A computer program which is able to execute such an inductive process is called AQVAL/1 and has been described in papers (1-10).

4.2 An Example of VL_1 Decision Rules Inferred by AQVAL/1 for a Discrimination Between 3 Liver Diseases

Data used in this example were supplied by Dr. James Croft from the University of Utah. These data were originally collected by Professor Klatskin at the Yale University Medical School and used by Croft to compare 10 different models of medical decision making.(14,15)

In the example we consider 3 liver diseases:

(P) Postnecrotic cirrhosis

(G) Granulomata
Sarcaidosis
Tuberculosis
Erythema nodosum
Unclassified granuloma

(F) Fat infiltration (fatty liver).

In the data, there were 111 cases of disease P, 146 cases of disease G and 123 cases of disease F. Each disease case was described in terms of 50 symptoms (Figure 1).

The given cases of individual diseases were divided into learning and testing groups (columns 3 and 4 in Figure 2). Using learning samples, the program AQVAL/1 determined two different VL_1 descriptions for each disease:

Description A: consisting of one VL_1 formula per disease

Description B: consisting of three VL_1 formulas per disease

For example, description A for postnecrotic cirrhosis (P) was:

P(A):	COV	NEW	IND	TOT
$[x_{17}=0][x_{24}=0][x_{30}=1][x_{42}=0,1] \vee$ $[x_{48}=1][x_{49}=0]$	52	52	20	52
$[x_5=0][x_{24}=0,1][x_{31}=0][x_{36}=1] \vee$ $[x_{39}=0,1][x_{48}=1]$	41	21	16	73
$[x_{27}=1,2][x_{39}=1][x_{43}=0] \vee$ $[x_{48}=1,2]$	25	7	6	80
$[x_1=1,2][x_2=1][x_8=0][x_{23}=0] \vee$ $[x_{24}=0][x_{27}=0,1][x_{42}=0]$	9	3	3	83

Substituting names for the variables and their values the formula becomes:

[liver nodules = no][albumin = low] [regeneration: bile ducts, fibrosis;diff or focal = present] [fat:diff or zonal ≠ strongly present][fibrosis: portal or central = absent]

or

[nausea = no][albumin ≠ above normal][regeneration: retic. endo. = absent][cells:central or portal, fibrosis:diff or focal = present][cells:monos. or epithel ≠ strongly present]

or

[necrosis:diff or focal, fibrosis:diff or focal = present, strongly present][cells:monos. or epithel = present][fat:1-2+ or 3-4+ = absent]

or

[age > 39][sex = female][jaundice = no][protein, albumin = low][necrosis:diff or portal < strongly present][fat:diff or zonal = absent]

Note that the description involves in toto 17 out of the original 50 symptoms and individual terms in the formula involve 6,6,4 and 7 variables, respectively. (Note that to make a 'positive' decision only 1 term of the formula has to be satisfied.) Each product of selectors (term) in the formula is assigned a sequence of 4 numbers:

(COV, NEW, IND, TOT)

which mean, respectively:

- COV -- number of cases covered ('explained') by the term out of original 83 learning cases
- NEW -- number of cases covered by the term but not covered by the terms preceding given term in the formula
- IND -- number of cases covered only by the term and not covered by any other term
- TOT -- number of cases covered by the given term and all the preceding terms (the last value of TOT must just be the total number of learning cases used)

Description B (a three-formula description) for the same disease (P) was:

P(A):

1st formula:	COV	NEW	IND	TOT
$[x_{17}=0][x_{25}=1,2][x_{34}=0][x_{42}=0,1] \vee$ $[x_{48}=1]$	61	61	19	61
$[x_{16}=0][x_{23}=0,1][x_{39}=0,1] \vee$ $[x_{42}=0][x_{43}=0][x_{48}=1,2]$	44	15	9	76
$[x_4=0][x_5=0][x_{13}=1][x_{29}=0] \vee$ $[x_{39}=0,1][x_{42}=0,1]$	30	6	6	82
$[x_2=1][x_6=1][x_{12}=1]$	3	1	1	83

2nd formula:	COV	NEW	IND	TOT
$[x_{42}=0][x_{43}=0,1][x_{48}=1] \vee$	72	72	30	72
$[x_5=0][x_{20}=1][x_{39}=0,1][x_{42}=0,1] \vee$ $[x_{48}=1,2]$	49	9	9	81
$[x_3=1][x_{30}=1][x_{39}=0]$	12	2	2	83

3rd formula:	COV	NEW	IND	TOT
$[x_{26}=1,2][x_{48}=1][x_{49}=0] \vee$	65	65	10	65
$[x_3=0][x_{20}=1][x_{32}=0,1][x_{35}=1,2] \vee$ $[x_{39}=0,1][x_{43}=0,1][x_{48}=1,2] \vee$	46	14	6	79
$[x_5=0][x_{24}=0][x_{48}=1]$	56	4	4	83

The obtained descriptions were then applied to the testing events to see how well they discriminate between diseases. The results are given in Figure 2 (columns 5, 6, and 7).

In Column 7 are listed numbers of correctly classified diseases, by the best* of 10 models used by Croft.[14] It should be noted, however, that Croft's results were obtained when the learning and testing cases were drawn from data which included cases of 20 liver diseases rather than 3, as in our example.

The classification decisions using descriptions A and B were made as follows:

Description A

Suppose V_k is a single-formula description of disease k, k = P,G,F, and e is a description of a patient to be diagnosed. The patient is assigned a diagnostic decision(s) $\hat{k}$ if

$$D(V_{\hat{k}},e) = \max_{k=P,G,F} \{D(V_k,e)\} \pm T$$

*The Bayes' formula conditional probability model.

where

$D(V_k,e)$ is a 'confidence degree' to which the formula V_k is satisfied by description e. The $D(V_k,e)$ is computed as the maximum of the degrees of matching patient description e with each term of the formula, where the degree of matching e with a term (product of selectors) is a ratio of the number of selectors satisfied by e to the number of selectors in the term. For example, suppose that formula V_k is:

$$V_k = T_1 \vee T_2 \vee T_3$$

where

$$T_1 = [x_1 \leq 2][x_3 = 4,5]$$

$$T_2 = [x_3 = 0][x_4 \neq 2][x_7 = 2:6]$$

$$T_3 = [x_1 = 4][x_3 = 0][x_7 = 0]$$

and the patient description e is

$$e = (x_1, x_2, \ldots, x_7) = (0, *, 0, 1, *, *, 7)$$

(*denotes an unspecified value; values of variables x_2, x_5, and x_6 may be unspecified because they are not needed for the evaluation of the formula V_k). The ratios of the number of selectors satisfied to the total number of selectors in each term T_i, i=1,2,3 are: 1/2, 2/3, 1/3, respectively. Thus $D(V_k,e) = 2/3$.

T is a certain threshold value, decided by the user, which determines the 'decision equivalence classes'.

Description B

Suppose $V_k = (V_{k1}, V_{k2}, V_{k3})$ is a three-formula description of disease k, k = P,G,F. A patient with description e is assigned a diagnostic decision(s) $\hat{k}$ if:

$$D(V_{\hat{k}},e) = \max_{k=P,G,F} \{D(V_k,e)\} \pm T$$

where

$D(V_k,e)$ is the average of the 'confidence degrees' computed for each component formula V_{ki}, i=1,2,3 (as in description A)

T is defined similarly as in description A.

4.3 Remarks on Advantages and Disadvantages of the VL Decision Model

Advantages of the model:

- Does not require large amount of learning data.
- Is very general. Can handle descriptors (variables) of different types (nominal, interval, ratio and absolute).
- Infers goal-oriented descriptions of decision classes (a 'variable decision space method'). Finds sufficient or most appropriate tests (symptoms, signs) for characterization of individual decision classes. Is able to produce 'cost optimal' descriptions for individual decision classes.
- Decision rules are very simple for human interpretation and comprehension (because inferential learning processes implemented in the system seem to parallel human logical learning processes).
- Does not assume independence of symptoms or mutual exclusiveness of decision classes.
- Decision rules are very efficient computationally and therefore it becomes feasible to implement large-scale consulting systems which could give diagnostic and therapeutic advice pertaining to hundreds or even thousands of diseases.

Disadvantages:

- The work is at the early stage of development. Not much is known about generalizing and learning capabilities of systems implementing concepts of variable-valued logic.
- There are not enough experimental results to make any strong judgments about the applicability of these concepts to realistic medical diagnosis and therapy decision problems.
- Certain theoretical problems have yet to be solved and computer programs to be developed or improved, in order to have an efficient and representative implementation of this model.

5. CONCLUSION

We have delineated here basic problems of implementing an inferential medical computer consultant and described briefly a new decision model which is based on the application of a variable-valued logic system. The presented example on an application of this model to the classification of three liver diseases shows that the model has significant attractiveness for a large-scale inferential medical computer consultant.

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5) Interactive Language Design and Development
6) VL Based Deductive and Inductive Diagnostic Systems
7) Data Base and Format Design
8) Comparative Study and Review of Other Systems (Similar to MIDAS)
9) Real Time Patient Monitoring, Security, and Personal Medical Data Dossier