

MAJOR APPROACHES TO MEDICAL DIAGNOSIS AND THEIR DRAWBACKS

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Abstract: The ability to reason within a dynamical environment is of a crucial importance in Artificial Intelligence. Medical diagnosis is a dynamic and very complex field which needs special attention. Our quest is for a system for medical diagnosis, that could model its search space efficiently and dynamically, while confronted with sequential tests. We present below some of the major approaches from literature, with their drawbacks, and conclude that a combinative hybridization of a certain type would be useful to overcome the failures.

Keywords: clinical decision making, hybrid intelligent systems, symbolic reasoning, model-based diagnosis.

1. INTRODUCTION

The present paper aims to search among the current approaches to medical diagnosis, and to suggest a best solution, considering particular problems that may arise in this field.

Section 2 introduces the main characteristics of medical diagnosis, which make it such a complex process, and illustrates the sources of difficulty through some specific examples.

Section 3 reveals the major approaches to medical diagnosis so far. In Section 3.1 we discuss the implications of bayesianism and causality in diagnosis, and show advantages and drawbacks of a classical system that uses them: CASNET. Section 3.2 is devoted to symbolic approaches to diagnosis, exemplified by MYCIN and Knowledge-Based Artificial Neural Networks (KBANN). In Section 3.3 we deal with Model-based diagnosis in first order logic and its possible medical applications (Dupres' AID and abduction), while Section 3.4 presents a combinative hybrid system (CHECK),

which we consider to be closest to an optimum solution. Section 4 concludes our study.

2. STAGES OF MEDICAL DIAGNOSIS AND POSSIBLE ERROR SOURCES

We will show following how adequate the use of computers is in the case of medical diagnosis, regarding the difficulties that usually accompany this process, where the risks and responsibilities are of a critical importance. Human reasoning is above discursive reasoning, which can be algorithmically represented, such that a human expert could only be assisted but never replaced by a computer. However, the computer could:

- Help the physician to quickly recall unusual, rare pathological states;
- Suggest alternative hypotheses and narrow down the search space faster and better than a human expert.

The medical field is complex, dynamic, and widely inaccessible, and therefore uncertainty is unavoidable as are the errors it brings along

(Russell, Norvig, 2002). As the authors notice in (Restian, 1988), the phenomena associated with human pathology are complex, nonlinear, discontinuous and highly variable, such that diagnosis is one of the most difficult problems in medical practice.

Starting with an initial symptoms' set, the physician aims at narrowing down the set of possible diseases (i.e. **clinical diagnosis**). This narrowing hides behind it a classification that completes "white spots" while ignoring "noisy" symptoms, -which means, in fact, pattern recognition under noisy conditions, in the artificial intelligence language. The purpose of the clinic diagnosis is to indicate what further para-clinical investigations have to be performed in order to make a final decision. There can exist several stages of such testing.

Clinical diagnosis should lead to **ethyologic and pathogenetic diagnosis** (the cause and the evolving mechanism of the disorder), which explain and sustain clinical diagnosis. The following stage is **differential diagnosis**, when the positive diagnostic is compared to other possible resembling diseases, in order to avoid confusions. Differential diagnosis (distinguishing among different possible alternatives) forms the basis of the diagnosis process. The final step consists in **diagnosing complications**. The whole process is based upon a combination between formal nonmonotonic logic and the internal logic of the phenomena (from the domain's model). There is one more thing to do after diagnosis: to **argue** the chosen **final diagnostic**, using the ethyologic diagnostic.

The errors of the patient, of the physician, or of the laboratory tests come in addition to the difficulties intrinsic to the domain, among which we mention (Restian, 1988):

- Few patognomonic¹ signs exists, and "diagnosis results from **the way different (more or less patognomonic) symptoms and signs combine together**" (discontinuity is a consequence of this situation: small differences between symptom sets could lead to significant diagnostic differences- that is, completely unrelated disorders);
- The majority of signs and symptoms can occur in many different disorders (discontinuity);
- The patient doesn't spontaneously present all the signs, which are to be discovered in time, on a step by step basis, by the physician (dynamism);

- One and the same disease can take one or another of many various forms, depending on the "environment" -i.e. patient- (variability).

Some of the most difficult situations are detailed following.

Disguised disorders. Clinical signs of a disorder can be so atypical that they are confused with the clinical pattern of another disorder. For instance, myocardial infarction can sometimes evolve under the form of a dispepsia (nausea, flatulence, diarrhoea), because of the circulatory disturbances that induce congestions on the organs inside the abdominal cavity. Also, gastro-duodenal ulcer can evolve under the mask of a chronic pancreatitis, and broncho-pulmonary cancer under the mask of a pneumonia, or of a hyperthyroidism, due to thyro-stimulant hormone secretion by the cancerous cells. Some forms of broncho-pulmonary cancer can manifest themselves as nephrotic syndromes, and pancreatic cancer can mimic a diabetes or a biliary lithiasis, and all these are but few examples among many other possibilities. The solution to elucidate these cases resides in finding the correct cause of the disorder(s).

Associated disorders. Often, a disorder is accompanied by its complications. Some of the above mentioned "masks" are, in fact, authentic disorders. For instance, asthma can manifest itself together with its consequence- emphysema, diabetes comes with complications such as retinopathy and glomerulosclerosis, renal lithiasis is complicated by urinary tract infection and renal insufficiency, and biliary lithiasis by acute pancreatitis.

Simultaneous disorders. Sometimes, unrelated disorders can simultaneously and independently evolve at the same patient, without important pathogenetical relations. This is probably the most confusing case for a diagnostician.

The specific features and difficulties of medical diagnosis detailed above, form a theoretical justification for the necessity and adequacy of our approach to the problem, that shall be described in the following sections.

3. MEDICAL DIAGNOSIS IN ARTIFICIAL INTELLIGENCE

The current Section aims to present the context of currently relevant (hybrid) medical diagnosis systems.

¹ signs very specific for a certain disease

3.1. Bayesianism and causality in medical diagnosis

Diagnosis can be basically treated as a classification process, which builds a set of discriminant functions for each class, and ranks diagnostic hypotheses by means of these functions. Bayes' rule (Duda, *et al.*, 2000) is one of the most frequently used statistical classification tools. Bayesian and causal nets can completely describe a diagnosis process, but they usually shortcut through the model, to achieve computational efficiency. Unfortunately, probabilistic inference remains NP-difficult in the general case (with the notable exception of noisy-OR architectures). Moreover, conditional probabilities are not suitable for causality modeling, as authors show in (Pearl, 2001b) and (Giarratano and Riley, 1994) (one of the reasons being they induce a cause-effect relationship between an evidence and the negation of a hypothesis when a cause-effect relationship exists between the evidence and the hypothesis itself, which is not always correct).

One classic example of a medical diagnosis tool using causal nets is CASNET (Weiss, 1974). If the medical field is very well-understood and allows a clear and detailed description of the physiological mechanisms that lie behind the symptoms, one has no reason to restrict himself to shallow disease-symptoms associations (like in PIP or INTERNIST, for instance). The causal net of CASNET contains dysfunctionality states (different from the disorders themselves) and tests (a test is an external information that defines the existence probability of the hidden states). Initial² and final³ states represent particular cases inside the net. Causal relations among nodes are modeled as weighted links from cause-nodes to effect-nodes, where the weight is the frequency with which the cause produces the effect (cycles are not allowed). The net is, in fact, a simplified model of the disorders, that guides the diagnosis process. Nodes can either be *confirmed* or *denied* by specific tests.

Inference is probabilistic, propagating beliefs/disbeliefs in nodes based on tests results, and creating *acceptable* (i.e. without denied nodes) paths through the net. These paths are possible explanations for the final diagnosis, and focus attention on interesting subparts of the net.

Two probabilistic measures are computed for each node: the *weight* (an estimation of its verisimilarity based on the strength of causal links between the node and the related confirmed/ denied nodes) and the *state* (an estimation of its verisimilarity based on directly relevant tests). Whenever a new test result

is available, the state of each node which is linked to the test is refreshed: if the degree of belief for the test result is lower than the degree of belief for the node, then nothing is changed, if it is greater, then the node is assigned the value of the test, and if they are equal but have opposite signs, a contradiction is reported to the user.

Drawbacks of CASNET

- A major drawback of the system is inherited from Bayesian nets: probabilistic inference is NP-difficult for multiply connected nets (i.e. with two or more paths between two nodes);
- CASNET is also not able to represent those frequent situations in medical diagnosis when a hypothesis is supported only by the conjugated presence of "several" symptoms (vague criteria);
- An important drawback is given by the way contradictions are handled. Adding and subtracting quantities to compute the score for each node can often lead to ambiguous, difficult to interpret or even completely erroneous results. (For instance, when we get score 0 for a node, by repeated additions/subtractions, a contradiction is reported to the user, because the system cannot handle it). The main conclusion here is that probabilistic reasoning is not suitable to handle contradictions, and therefore a categorical approach is needed for them.

A remarkable improvement of CASNET is realized by the CHECK system (Torraso and Console, 1989). Its advantages shall be detailed in Section 3.4.

Bayesianism is also related to medical diagnosis, viewed as a classification process, via multilayer perceptrons trained with backpropagation, because it was shown that these nets compute (when adequately trained) conditional a posteriori probabilities of the classes. Neural networks are useful when no deep causal model is available, as they use shallow disease-symptoms associations, a direct consequence being the fact that they can provide but poor explanations for the results computed. Nevertheless, their robustness and rapidity is often useful, especially when integrated in hybrid architectures.

Such a hybrid architecture, which was successfully used in diagnosing hepatic disorders, is the fuzzy multilayer perceptron (Mitra 2000). A multilayer perceptron can be extended with the ability to process fuzzy inputs/outputs. After the network is trained and pruned, one can extract diagnostic rules following the paths with greater weight, from the input to the output, and associating a rule with each

² with no causes of their own

³ with no dysfunctional consequences

subset of nodes that defines the respective paths (Mitra 2000).

3.2. Symbolic approaches to medical diagnosis

The most used symbolic structures are decision trees and expert systems. They are built around a knowledge base and inference mechanism and use heuristics that resume a human expert's knowledge (usually shallow knowledge) (Giarratano and Riley, 1994).

MYCIN (Giarratano and Riley, 1994) is an expert system, built around the model of belief factors of Shortliffe, and used to diagnose hematologic infections. The main purpose of this new model was to overcome the problems of bayesianism for medicine (i.e. a limited number of accessible tests; results obtained sequentially, on a step by step basis; too many conditional probabilities to be known apriori). Therefore, Shortliffe defines a new measure which combines beliefs and disbeliefs (conditioned by the presence of certain evidences) in a hypothesis in a single number (the "belief factor") (Giarratano and Riley, 1994). The belief factors are used to rank the diagnostic hypotheses.

The pieces of evidence from rules' antecedents are combined by fuzzy logic. The final degree of belief for a hypothesis is computed after an original model, by combining rules whose consequent is related to the hypothesis. One of the greatest drawbacks of MYCIN' evidence combination is that unexpected and incorrect interactions often occur between the rules from the knowledge-base, if this is not carefully constructed. It has been shown that the theory of belief factors is but an approximation of probabilistic reasoning and the apparent success of MYCIN is due to the simplicity of the domain's theory (short inferential paths and simple hypotheses), but theoretically some problems exist with its model.

Knowledge-Based Artificial Neural Networks (KBANN) are a hybrid neuro-symbolic architecture that can classify complex, scarce, not uniform data sets (as it is often the case with medical data). A symbolic module contains the domain's theory as a hierarchically structured set of rules, and a connectionist module associates to each concept from the domain's theory a node of a neural network, by mapping the structure of rules into the network's topology. KBANN learning algorithm takes an approximately correct domain's theory, maps it into a neural network, then trains the network with an example set, such that it shall be able to generalize. The technology was successfully used to classify tissues, in diagnosing breast cancer.

3.3. Model-based diagnosis in first order logic and its possible medical applications

Logic approaches to model-based diagnosis are appropriate for explaining conclusions and for tackling conflicts in differential diagnosis, because they offer precision, transparency and good explanation facilities (all at the cost of expensive computation techniques). Model based systems that capture deep knowledge (i.e. component subparts and relations among them) have the ability to solve problems unknown to a human expert and to rigorously explain the decisions they take during inference (which can be quite complex on such a declarative model).

There are two logic formalizations of model-based diagnosis: abduction and consistency-based. Abduction is preferred when a complete defect model (i.e. a model of the abnormal behaviour) is available for the system described. An abductive diagnostic is a minimal abnormality hypotheses set that "covers" (implies) all observations (Konolige 1992).

Abduction is a general reasoning scheme underlying diagnosis in general. The term was introduced by Peirce in 1800, and can be defined as "the process of forming an explanatory hypothesis, starting from a set of observations".

The structure of abductive reasoning is described following:

D is a set of observations, H explains D, there is no H' better than H that explains D
H is assumed true

There are three major problems in abductive reasoning: which is the data that needs to be explained, what exactly means that "H explains D" (causality or logical consequence?), and what does it mean that a set of hypotheses is "better" than another?

The logical setting for abduction says that, if T is the domain's theory and D is the formula to be explained, then an explanation for D in T is a formula E that satisfies the following conditions:

1. $T \cup E$ is consistent;
2. $T \cup E \vdash D$;
3. E is made up of assumable predicates and is the simplest that satisfies 1 and 2.

Abduction is genuine nonmonotonic reasoning. If one has (Dupre 1994):

$$p_1 \rightarrow q, \dots, p_n \rightarrow q, (3.1)$$

with p_i, q being propositions from the domain theory T , and material implication being used to model cause-effect relationships, then abductive reasoning says that, in order to explain q , we have to assume true at least one p_i (which is correct only when we have complete knowledge about q in T). Therefore, abduction represents a form of defeasible reasoning, because it depends on (possibly incomplete) knowledge available at a certain moment.

Because abductive reasoning is intractable in general, various types of heuristics/ probabilistic schemes have been used in order to focus search and improve efficiency. A specific architecture for abduction is suggested by Dupres in AID (Dupre 1994), but only monotonic models are used to describe the domain.

Direct proof techniques can also be used to compute abduction (Konolige 1992; McIlraith, 1998)), for instance, resolution-based consequence finding for a theory. Unfortunately, this approach doesn't respect the diagnosis semantics in a proper way. If we re-write $T \wedge E \vdash D$ (T - domain theory, E - explanation, D - observations), as $T \wedge \neg D \vdash \neg E$ (through contraposition), that leads to indirect (dual) abduction:

Definition.(McIlraith, 1998). E is an explanation for D iff:

- $E \subseteq T$;
- $T \cup \text{not}D \vdash \neg E$;
- From T one cannot deduce $\neg E$,

where $\neg E$ represents the conjunction of negated literals.

But in medical diagnosis the lack of some observations doesn't necessarily mean the lack of a certain diagnostic (because a disease can manifest itself in many different ways). Moreover, resolution is refutation complete (finds demonstrations) but is not deductively complete (doesn't find all the consequences). And even if deductively complete versions have been developed, they are quite prohibitive in real problems due to inefficiency (Konolige 1992). This goes with the major drawback of first order logic: semidecidability.

Consistency-based diagnosis is preferred when a normal behaviour model is available, and a diagnostic is defined as a minimal set of components assumed defect, such that the correct behaviour of the rest is consistent with the

observations (this means that an explanation for a manifestation m is everything that does not support $\neg m$, while in abduction it should have directly sustained m). The advantage of consistency-based diagnosis resides in its logical validity, regardless the completeness of the model.

3.4. Combinative hybridization in medical diagnosis: the CHECK system

Abduction and consistency-based diagnosis were conjoined in a single model in (Torraso and Console, 1989), where a diagnosis problem is viewed as an abduction problem with consistency constraints.

Definition * (Torraso and Console, 1989). A Diagnostic Problem (DP) is a tuple:

$$DP = \langle \langle BM, Comp \rangle, CXT, OBS \rangle, (3.2)$$

where BM (**B**ehavioral **M**odes) is a set of Horn clauses that describe the system's structure and behaviour, $Comp$ is the set of components that form the system, CXT is a set of contextual informations (that don't need explanation, they are auxiliary to the model), and $T = \langle BM, COMP \rangle$ is a behavioral model of the system, composed of a set of Horn clauses of the kind:

$$S_1(X_1) \wedge \dots \wedge S_n(X_n) \wedge C_1(Y_1) \wedge \dots \wedge C_m(Y_m) \wedge f(X_1, \dots, X_n, Y_1, \dots, Y_m, Z) \rightarrow S(Z) \\ (n \geq 1, m \geq 0) (3.3),$$

where:

- each S_i is a symbol that denotes either an internal or an initial state;
- C_j represents a context;
- S can either be an internal state or a manifestation;
- f is a functional mapping that describes the relation among predicates/ attributes' values inside the body of the clause and those in the conclusion.

The clauses of the behavioral model can be viewed as cause-effect relationships (very close to Pearl's structural equations (Pearl, 2001a; Pearl 2001b)), and can easily be transformed into a causal net. An unknown element/cause α can be added to incomplete (and therefore unsure) causal relations (which means the implication " \rightarrow " changes its interpretation into "MAY imply").

Using the above definitions, Torraso and Console have described a causal diagnosis theory as following.

Definition. A causal specification of a diagnosis theory is given by the frame $C=(DFS, OBS, CM)$, where:

- DFS is a set of possible hypotheses or defect literals,
- OBS is the set of (negative/ positive) observable manifestations;
- CM (Causal Model) is a set of axioms of the form:

$$d_1 \wedge \dots \wedge d_n \rightarrow o \quad (3.4)$$

(these are called abnormality axioms, the logical implication denotes a causality relation, and d_i -s are defects or intermediary abnormality states, situated between the root and the final –leaf-symptoms);

$$d_1 \wedge \dots \wedge d_n \rightarrow d \quad (3.5)$$

(these are classification axioms: a defect is defined in terms of a set of states).

$$d_1 \wedge \dots \wedge d_n \wedge \alpha_o \rightarrow o \quad (3.6)$$

$$d_1 \wedge \dots \wedge d_n \wedge \alpha_d \rightarrow d \quad (3.7)$$

(these are uncertain causal relations, where α is the literal of "incompleteness hypothesis").

The authors implement this theory inside the CHECK system (Torraso and Console, 1989). CHECK is a combinative hybridization between shallow and deep reasoning. The reason for shallow reasoning inside the first level of the system is to focus the search and overcome the difficulties of medical model-based diagnosis (NP-completeness). Search space pruning in model-based diagnosis can also be achieved numerically, through probabilistic/ possibilistic measures (Torraso and Console, 1989; Munteanu 2003). In CHECK, formal logic (for the deep causal model) is assisted by a symbolic intelligent technique, the whole architecture being an improved alternative to CASNET. Knowledge, (represented by means of frames with specific slots) is distributed over 3 levels: data description level (1), heuristic level (2) (shallow knowledge –based inference), deep causal knowledge level (3) (used for generating explanations). The system was successfully used in diagnosing hepatic disorders.

Each diagnosis hypothesis is assigned a plausibility degree, by matching evidences against prototypical definitions of disorders, in a given context. The

matching mechanism is controlled by some special activation rules that select possible disorders into an active list. Validation rules are then used to confirm/ exclude the generated instantiations of frames, and diagnosis is performed through breadth-first search.

The deep-knowledge causal level is used to confirm/ exclude hypotheses generated at the heuristic level, to generate alternative hypotheses or to analyse unexpected data (it can be queried). Basically, a causal network with specialized nodes is transformed into a set of logical formula, -very similar to (3.2-3.7)-, upon which qualitative reasoning can be performed (non-monotonic-based logic). Extended resolution principle is used to determine the source of an inconsistency (that is, if a manifestation caused by a state is missing, indirect abduction tries to find an explanation for this inconsistent observation). The disadvantages of this approach in medicine were briefly stated in Section 3.3.

CHECK improves CASNET in many ways. Firstly, it focuses on a sub-part of the medical model by selective, rule-based activation of hypotheses. Nonmonotonic reasoning (which is more appropriate for contradiction tackling) is applied to this sub-part only, during the generation of explanations. Secondly, the superior refinement of the model determines less contradictions to be generated during the explanation phase.

4. CONCLUSIONS

A major drawback of the first-generation artificial intelligence programs in medicine (INTERNIST/CADUCEUS, MYCIN, PIP) comes from the fact they do not use a deep causal structure for the relationship between disorders and their symptoms, while for a human expert an explanation is seen as a deduction inferred on basis of a cause-effect chain. An important consequence is that interactions among multiple disorders is impossible to approach, only by associations between phenomena, with no causal details.

The problem of complex interactions occurs when multiple disorders are present in one and the same patient, and their symptoms unexpectedly interact (see Section 2). Even CASNET, with all its causal representation, has serious problems with interacting or overlapping symptoms, and therefore resumes its utility at single-disorders cases, because of the difficulties with the probabilist treatment of uncertainty and inference.

The probabilistic approach to uncertainty is also to blame for the unappropriate tackling of

contradictions. When two rules are in conflict, this is treated –likewise concordance-, by adjusting the degree of trust in some related hypotheses. But in real world reasoning, human experts have a much deeper and complex reaction at the detection of a contradiction: they reconsider previously accepted data, and/or add new possible hypotheses to the active set (i.e. those currently taken into consideration). The conclusion is that a probabilistic model is inherently inadequate to deal with contradictions, and a categorical approach is needed.

Patil has completely replaced probabilistic measures with structural criteria in Abel (Patil, 1981), trying to surpass the difficulties described above. His system uses links of a special kind to model competition/ contradiction, and only categorical decisions are allowed. The system is based on a hierarchically partitioned data representation defined by Lynch (Lynch, 1960) (conceptual maps⁴).

And yet, the medical field is far too complex to completely give up probabilities, like Abel does. As structural and probabilistic measures complement each other, they should both be used in diagnosis. Moreover, the applicability of Abel in large fields is restricted, because general strategies are needed to initially pre-process extended medical contexts. Probabilistic / associative efficient types of reasoning would be useful exactly during this phase of pre-processing, in order to focus search. As a consequence, the solution for medical diagnosis would be to combine probabilistic/ categorical reasoning, taking advantage of the qualities of both of them, and leading to a combinative hybridization.

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⁴ “In approaching large maps it is recommended to work with partial images sets, which can be more or less inter-related or overlapped” (instead of a large, global image).

