An Empirical Comparison of Three Inference Methods

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Abstract

In this paper, an empirical evaluation of three inference methods for uncertain reasoning is presented in the context of Pathfinder, a large expert system for the diagnosis of lymph node pathology. The inference procedures evaluated are (1) Bayes' theorem, assuming evidence is conditionally independent given each hypothesis, (2) odds–likelihood updating, assuming evidence is conditionally independent given each hypothesis and given the negation of each hypothesis, and (3) a inference method related to the Dempster–Shafer theory of belief. A decision-theoretic approach is introduced for evaluating the performance of expert systems. This approach, when combined with a more traditional expert-rating method for evaluation, provides insights about various components of the inference process.

I. Introduction

Several years ago, before learning much about methods for reasoning with uncertainty, I and my colleagues began work on a large expert system, called Pathfinder, that assists community pathologists with the diagnosis of lymph node pathology. Because the Dempster–Shafer theory of belief was quite popular in our research group at the time, we developed a inference method for our expert system inspired by this theory. The program performed fairly well in the opinion of the expert pathologist who provided the knowledge for the system.

In the months following the initial development of Pathfinder, several of us in the research group began exploring other methods for reasoning under uncertainty. We identified the Bayesian approach as a candidate for a new inference procedure. We realized that the measures of uncertainty we assessed from the expert could be interpreted as probabilities and we implemented a new inference method— a special case of Bayes' theorem.

During this time, the expert was running cases through the program to test the system's diagnostic performance. One day, without telling him, we changed the inference procedure to the Bayesian approach. After running several cases with the new approach, the expert exclaimed, "What did you do to the program? This is fantastic!"

This experience was and still is in sharp conflict with the beliefs of many researchers in the artificial-intelligence community. At each of the first three AAAI uncertainty workshops, one or more researchers argued that the particular inference method used does not significantly affect performance, at least in the context of large real-world systems. In this paper, a formal evaluation of the performance of several inference methods is presented that confirms our early experience with Pathfinder and refutes the claim made at the workshops. Moreover, it will be shown that the Bayesian approach yields performance superior to that obtained with the other approaches in the domain of lymph-node pathology.

In addition to describing the comparison, a new approach for evaluating the performance of expert systems will be introduced. This method, based in decision-theory, compliments a more traditional expert-rating approach to system evaluation. Both the new and traditional approaches will be used in the experimental comparison of the inference procedures.

II. The Domain

AI researchers working on uncertain reasoning often complain that the merits of one inference method versus those of another are evaluated on the basis of only theoretical considerations. Another complaint is that evaluations of performance are limited to small or artificial domains. This study is designed to address both of these complaints. The Pathfinder program reasons about virtually *all* diseases that occur in a human lymph node (24 benign diseases, 9 Hodgkin's lymphomas, and 18 non-Hodgkin's lymphomas.) In addition, the program includes an exhaustive list of clues or features that can be used to help determine a diagnosis. Over 100 morphologic features or patterns within a lymph node that can be easily recognized under a microscope are represented. The program also contains over 30 features reflecting clinical, laboratory, immunological, and molecular biological information that is useful in diagnosis.

Because this study focuses on only one domain, these results should not be extrapolated to other domains. All that will be demonstrated is that the use of different inference methods *can* affect performance in a real-world system. Researchers interested in learning more about the relative merits of different inference methods are encouraged to begin similar investigations in other domains.

III.   The Inference Methods

The three inference methods evaluated are (1) a special case of Bayes' theorem, (2) an approach related to the parallel combination function in the certainty-factor (CF) model [?], and (3) a method inspired by the Dempster–Shafer theory of belief [?]. All three approaches take a set of observations and produce a belief distribution over disease hypotheses based on the same expert probability assessments. However, the second two approaches deviate significantly from probabilistic reasoning.

All three approachs share the assumption that the hypotheses represented by the system are mutually exclusive and exhaustive. Furthermore, all three approaches assume that the diagnostic features are, in some sense, independent. The exact nature of independence varies from method to method and is discussed in detail in a later section. It should be noted that, during the development of Pathfinder, obvious dependencies among features were eliminated by clustering highly dependent features. For example, a pattern called *necrosis* is seen in many lymph node diseases. The size of necrosis (percent area of lymph node showing this pattern) and the distribution of necrosis are two strongly interrelated features, and both are important for diagnosis. To remove the dependency, a single feature "necrosis size and distribution" was created which had the mutually exclusive and exhaustive values "nonextensive and focal," "nonextensive and multi focal," "extensive and focal," and "extensive and multi focal." These values were created by taking the cross-product of the values for individual features pertaining to necrosis size and necrosis distribution.

Before describing the inference methods, some definitions and notation are introduced. The mutually exclusive and exhaustive disease hypotheses will be denoted by the symbol d with a subscript—for example, d_j. Similarly, the symbol f_k refers to the kth feature in the knowledge base. Each feature is associated with a set of mutually exclusive and exhaustive *values*. The ith value of the kth feature is denoted by v_{ki}. A given feature and a value for that feature together constitute an *observation*. The term $f_k v_{ki}$ denotes an observation of the ith value for the kth feature. For the sake of brevity, a set of observations $f_1 v_{1i} \ldots f_n v_{ni}$ will be denoted by the symbol ξ. Finally, two conditional independence assumptions associated with the inference procedures are introduced here for reference. The first assumption is that evidence is conditionally independent on disease hypotheses. Formally, the assumption is that, for any combination of observations $f_1 v_{1i} \ldots f_n v_{ni}$,

$$p(f_1 v_{1i} \ldots f_n v_{ni}|d_j) = p(f_1 v_{1i}|d_j) \ldots p(f_n v_{ni}|d_j) \quad (1)$$

The second assumption is that evidence is conditionally independent on the *negation* of the hypothesis. Specifically, for any combination of observations $f_1 v_{1i} \ldots f_n v_{ni}$,

$$p(f_1 v_{1i} \ldots f_n v_{ni}|\overline{d_j}) = p(f_1 v_{1i}|\overline{d_j}) \ldots p(f_n v_{ni}|\overline{d_j}) \quad (2)$$

Both Equations ?? and ?? apply to each disease hypothesis d_j.

A.   Simple Bayes Method

The first inference method is Bayes' theorem under the assumption that features are conditionally independent on the disease hypotheses (Equation ??). In particular, if observations $\xi = f_1 v_{1i} \ldots f_n v_{ni}$ are made, the probability of the jth disease is given by

$$p(d_j|\xi) = \frac{p(d_j)p(f_1 v_{1i}|d_j) \ldots p(f_n v_{ni}|d_j)}{\sum_j p(d_j)p(f_1 v_{1i}|d_j) \ldots p(f_n v_{ni}|d_j)} \quad (3)$$

This inference procedure will be called the *simple Bayes method* to emphasize the conditional independence assumptions it embodies. Note that the only assessments required by this approach are the probabilities $p(f_k v_{ki}|d_j)$ for each combination of f_k, v_{ki}, and d_j, and the prior probabilities $p(d_j)$ for each disease. The other two inference methods require the same assessments.

B.   Odds–Likelihood Method

The second inference method begins with a form of Bayes' theorem under the assumption that evidence is conditionally independent on both the hypotheses and on the negation of the hypotheses (Equations ?? and ??). Under these assumptions, Bayes' theorem for the jth disease given observations ξ can be written

$$\frac{p(d_j|\xi)}{p(\overline{d_j}|\xi)} = \frac{p(d_j)}{p(\overline{d_j})} \frac{p(f_1 v_{1i}|d_j)}{p(f_1 v_{1i}|\overline{d_j})} \cdots \frac{p(f_n v_{ni}|d_n)}{p(f_n v_{ni}|\overline{d_n})} \quad (4)$$

The ratio on the left-hand side and the first ratio on the right-hand side of Equation ?? are the *posterior* and *prior* odds of d_j, respectively. In general, the odds of an event is just a simple monotonic transformation of the probability of the event, given by

$$O = \frac{p}{1 - p}$$

The remaining terms of Equation ?? are called likelihood ratios. As can be seen from Equation ??, the likelihood ratio $p(f_k v_{ki}|d_j)/p(f_k v_{ki}|\overline{d_j})$ is a measure of the degree to which observing feature value $f_k v_{ki}$ updates or changes the degree of belief in disease hypothesis d_j.

In the version of this inference method evaluated in this paper, the likelihood ratios are not assessed directly. Instead, the numerator, $p(f_k v_{ki}|d_j)$ is assessed directly, and the denominator, $p(f_k v_{ki}|\overline{d_j})$, is computed using

$$p(f_k v_{ki}|\overline{d_j}) = \frac{p(f_k v_{ki}) - p(f_k v_{ki}|d_j)p(d_j)}{p(f_k v_{ki})}$$

where

$$p(f_k v_{ki}) = \sum_j p(f_k v_{ki}|d_j)p(d_j)$$

Thus, this inference method makes use of exactly the same assessments as does the simple Bayes approach. The likelihood ratios were not assessed directly because the expert found that likelihood ratios were much more difficult to assess than were conditional probabilities $p(f_k v_{ki}|d_j)$. It

would be interesting to conduct a comparison similar to the one described in this paper using an expert who is willing to assess likelihood ratios directly.

Johnson [?] has demonstrated that the conditional-independence assumptions embodied in Equation ?? typically are not compatible with the updating of n mutually exclusive and exhaustive hypotheses, when n is greater than two. In particular, he has shown that consistently updating more than two mutually exclusive and exhaustive hypotheses under the conditional-independence assumptions used to derive Equation ?? is possible only when each hypothesis is updated by at most one observation.

In Pathfinder, this highly restrictive condition required for consistent updating is not met. Each disease hypothesis is updated by many observations in the knowledge base. As a result, Equation ?? produces an inconsistent probability distribution over diseases in which the posterior probabilities of disease do not sum to one. To circumvent this problem, the disease probabilities are renormalized after Equation ?? is applied to the evidence. This completes the description of the second approach, which will be called the *odds–likelihood method*.

It should be mentioned that the odds–likelihood approach is closely related to the parallel combination function used in the CF model. In fact, it was shown that the multiplicative combination of likelihood ratios seen in Equation ?? maps exactly to the parallel combination function when a certainty factor is identified with a simple monotonic transformation of the likelihood ratio [?]. Moreover, in MYCIN—the expert system for which the CF model was designed—certainty factors of mutually exclusive and exhaustive sets of hypotheses are renormalized to sum to unity [?]. This form of renormalization does not correspond directly to the renormalization of probabilities in the second inference method, but it is similar in spirit.

C. Naive Dempster–Shafer Method

The third inference method has an interesting history. It was developed by researchers, including myself, who at the time knew little about methods for uncertain reasoning. As the method was primarily motivated by the Dempster–Shafer theory of belief, it will be called the *naive Dempster–Shafer method*. It should be emphasized that the approach is fraught with difficulties, some of which will be addressed in the Discussion section. Perhaps the exposition will serve as a warning to the uncertainty in AI community as to what can happen when a group of novice researchers attempts to cope with the conflicting uncertainty literature.

As members of a medical information-science group, we were familiar with the inference method used by INTERNIST-1, an expert system for the diagnosis of disease across all diseases in internal medicine [?]. The inference procedure used by INTERNIST-1 incorporates two measures of uncertainty, an *evoking strength* and a *frequency*. An evoking strength for disease d_j and observation $f_k v_{ki}$, denoted $ES(d_j, f_k v_{ki})$, represents the degree to which the observation "evokes" or "confirms" the disease [?]. In contrast, a frequency for disease d_j and observation $f_k v_{ki}$, denoted $FQ(d_j, f_k v_{ki})$, represents the "likelihood" of an observation given the disease [?].

Because we initially had planned to use the INTERNIST-1 inference procedure, our expert assessed both an evoking strength and a frequency (on a continuous scale from 0 to 1) for each disease–observation pair. Before we began programming the approach, however, several members of our group argued that a more principled approach should be used to combine the measures of confirmation we had assessed. In particular, they argued that the Dempster–Shafer theory of belief should be used to combine evoking strengths.

After exploring of the Dempster–Shafer theory, we decided to construct a separate frame of discernment, $\theta_j = \{d_j, \overline{d_j}\}$, for each disease hypothesis d_j. In this framework, the evoking strength for a disease–observation pair is interpreted as a mass assignment to the singleton disease hypothesis:

$$m_{f_k v_{ki}}(\{d_j\}) = ES(d_j, f_k v_{ki}) \qquad (5)$$

The remainder of the mass, $1 - ES(d_j, f_k v_{ki})$, is assigned to θ. Mass assignments of this form follow the approach taken by Barnett [?]. With this interpretation, Dempster's rule of combination can be used to determine the mass assigned to the singleton hypothesis $\{d_j\}$, given observations ξ. In particular, Barnett showed that

$$m_\xi(\{d_j\}) = 1 - \prod_k (1 - m_{f_k v_{ki}}(\{d_j\})) \qquad (6)$$

In this framework of simple belief functions, the mass assigned to the singleton hypothesis $\{d_j\}$ is equal to the belief in d_j, denoted $Bel(\{d_j\})$. Thus, combining Equations ?? and ??, we can compute the belief in disease d_j given observations ξ, using

$$Bel_\xi(\{d_j\}) = 1 - \prod_k (1 - ES(d_j, f_k v_{ki})) \qquad (7)$$

This inference method produces a number between zero and one for each disease hypothesis.

At first, we ignored the frequencies provided by our expert. However, our expert kept insisting that his assessments of frequency were much more reliable than were his assessments of evoking strength. This led us to study the INTERNIST-1 inference method more carefully. It became clear to us and to our expert that the assessed evoking strengths were closely related to the posterior probability of disease given an observation. Also, it became apparent that the assessed frequencies corresponded to the probability of an observation given a disease. Thus, we discarded the directly assessed evoking strengths and replaced them with the calculated values

$$
\begin{aligned}
ES(d_j, f_k v_{ki}) &= p(d_j | f_k v_{ki}) \\
&= \frac{p(d_j) p(f_k v_{ki} | d_j)}{\sum_j p(d_j) p(f_k v_{ki} | d_j)} \qquad (8)
\end{aligned}
$$

where each probability assessment $p(f_k v_{ki}|d_j)$ is given by the frequency $FQ(d_j, f_k v_{ki})$. Equation **??** follows from Bayes' theorem and the assumption that diseases are mutually exclusive.

Equations **??** and **??** together provide a method for computing the posterior degree of belief in each disease hypothesis from the prior probabilities of disease, d_j, and the probabilities of an observation given disease, $p(f_k v_{ki}|d_j)$. These are the same assessments that are required by the two approaches described previously. It should be noted that the resulting belief distribution rarely sums to unity. This fact is not a problem conceptually, because the evaluation metrics used in the experimental comparison do not require probabilistic interpretations for the distributions. Nonetheless, the distributions produced by this inference method are renormalized to one, so that during the evaluation process, the expert is not able to recognize them immediately as being nonprobabilistic.

Like the odds–likelihood approach, the naive Dempster-Shafer method is related to parallel combination in the CF model. In fact, Equation **??** is exactly the parallel combination function for positive or confirming evidence if certainty factors are identified with singleton mass assignments.

IV. The Evaluation Procedure

The procedure for evaluating the inference methods is outlined in Figure **??**. Observations describing a lymph-node biopsy of a patient are presented to an inference method. The inference method, in turn, produces a belief distribution over the disease hypotheses. Finally, the belief distribution is compared with the *gold standard* probability distribution using an *evaluation metric*. The process is repeated for each of the three inference methods. In this section, the gold standard and evaluation metrics are defined.

A. The Gold Standard

An important consideration underlying the definition of the gold standard is the distinction between good *decisions* and good *outcomes*. A good decision is one that is consistent with the preferences and knowledge of a decision maker. A good outcome is one that is desirable to the decision maker. Sometimes, a good decision will, through a course of bad luck, lead to a bad outcome. Conversely, a bad decision may, with good luck, lead to a good outcome. However, the best way to achieve good outcomes in the long run, short of being all-knowing, is to make good decisions consistently. Therefore, the gold standards developed in this study are designed to identify good decisions, not necessarily good outcomes. This distinction between good decisions and outcomes is recognized in several previous evaluations including the validation experiments of Yu [**?**] [**?**], Cooper [**?**], and Wise [**?**].

Two gold standards were used to compare the inference methods. The first was derived from the probability
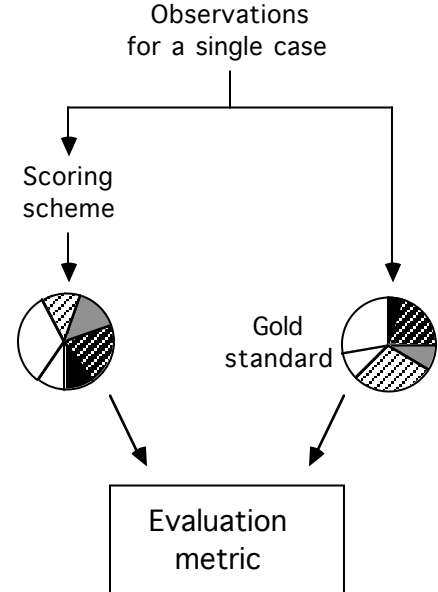

Figure 1: An schematic of the evaluation procedure.

distribution over diseases that our expert assessed using the same list of observations that was presented to the inference methods. The second was similar, except that the expert also reviewed the belief distributions generated by the three approaches.

The two gold standards each have advantages and disadvantages. Both isolate the evaluation of the inference methods from actual outcomes. The first gold standard is useful because it serves to measure how well each inference method matches the unaided reasoning of the expert. The second gold standard is useful because individuals, including experts, often make mistakes when reasoning under uncertainty in the sense that they violate highly desired principles of reasoning [**?**]. Indeed, the terms *descriptive* and *normative* often are used to distinguish how individuals actually reason and how they should reason. Of course, our expert is unlikely to appreciate his errors in reasoning, and to adjust his assessments accordingly, simply by observing the output of the three inference methods. A decision analyst would argue, for example, that a decision maker must make many iterations of the cycle comprising formulating assumptions, assessing probabilities, and inspecting the consequences of the assumptions and assessments before she can have any assurance that she is making a good decision. Such detailed iterations, however, are not possible in this experimental comparison because the principles of reasoning underlying each approach are not identical.[1] Developing a gold standard corresponding to a good decision under the principles associated with one of the inference methods would bias the results in favor of that inference method. By allowing the expert to see the

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[1] In fact, the principles underlying the odds–likelihood and naive Dempster–Shafer approaches are unclear to the author.

distributions generated by each approach, it is only hoped that gross errors in reasoning, such as lack of attention to rare hypotheses, will be reduced. To emphasize the roles played by the first and second gold standard, they will be called the *descriptive* and *informed* gold standards, respectively.

B. A Decision-Theoretic Evaluation Metric

Two evaluation metrics are used to compare the inference methods. One approach is based on direct ratings given by the expert. The order approach, described in this section, is grounded in decision theory. Although other authors have suggested similar approaches (for example, see Wise [**?**]), the comparison described in this paper is, to the knowledge of the author, the first to apply decision theory to the evaluation of a large real-world expert system.

The fundamental notion underlying the decision-theoretic metric is that some errors in diagnosis are more serious than others are. For example, if a patient has a viral infection and is incorrectly diagnosed as having cat-scratch disease—a disease caused by an organism that is killed with antibiotics—the consequences are not severe. In fact, the only nonnegligible consequence is that the patient will take antibiotics unnecessarily for several weeks. If, however, a patient has Hodgkin's disease and is incorrectly diagnosed as having an insignificant benign disease such as a viral infection, the consequences are often lethal. If the diagnosis had been made correctly, the patient would have immediately undergone radio- and chemotherapy, with a 90-percent chance of a cure. If the disease is diagnosed incorrectly, however, and thus is not treated, it will progress. By the time major symptoms of the disease appear and the patient once again seeks help, the cure rate with appropriate treatment will have dropped to leass than 20 percent.

A decision theoretic approach to evaluation recognizes such variation in the consequences of misdiagnosis. The significance of each possible misdiagnosis is assessed separately. More specifically, for each combination of d_i and d_j, a decision maker is asked, "How undesirable is the situation in which you have disease d_i and are diagnosed as having disease d_j?" The disease d_j is called the *diagnosis* and the preference assessed is called the *diagnostic utility*, denoted U_{ij}. Details of the utility assessment procedure are discussed in the following section.

Once the diagnostic utilities are assessed, it is a straightforward to evaluate each of the inference methods relative to the gold standard. The procedure for evaluation is shown in Figure **??**. First, observations for a case are presented to a inference method to produce a belief distribution over the disease hypotheses, denoted p_{ss}. In addition, the observations are shown to the expert, who then assesses the gold-standard distributions, denoted p_{gold}.

Next, a *decision rule* is used to determine the optimal diagnosis given each of the belief distributions. In many systems that employ methods for uncertain reasoning, a commonly used decision rule is to choose the hypothesis
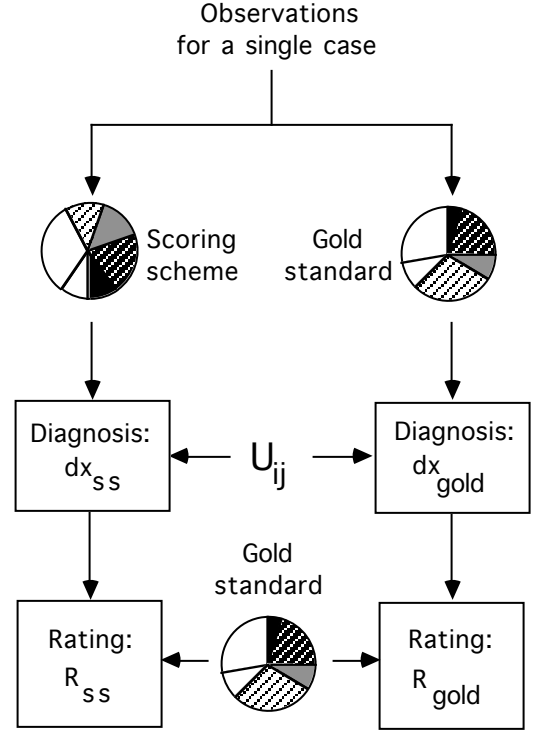

Figure 2: The decision-theoretic evaluation procedure.

with the highest degree of belief [**?**] [**?**]. Formally, the optimal diagnosis d_{ss} for a belief distribution p_{ss} is given by

$$dx_{ss} = \arg \max_i [p_{ss}(d_i)] \qquad (9)$$

where $\arg \max_i$ returns the d_i that maximizes the quantity $p_{ss}(d_i)$. This rule for choosing the optimal diagnosis is applied to the belief distributions produced by each of the inference methods. Note that the rule does not require that the degrees of belief computed by an inference procedure have a probabilistic interpretation.

The gold-standard diagnoses are then determined. The gold standards are prescribed using a decision rule different from Equation **??**. In particular, a gold-standard diagnosis is determined by finding the diagnosis that maximizes the *expected utility* of the patient. More formally,

$$dx_{gold} = \arg \max_j \left[\sum_i p_{gold}(d_i)U_{ij} \right] \qquad (10)$$

where dx_{gold} denotes a gold-standard diagnosis. For comparison, both Equations **??** and **??**, with p_{gold} replaced by p_{ss}, are applied to the simple Bayes approach. The application of Equation **??** to the simple Bayes approach is justified because the inference method produces a legitimate probability distribution over diseases.

After the gold-standard diagnoses are determined, ratings for the two distributions can be computed. In this decision-theoretic framework, the natural choice for a rating is the *expected utility* of each diagnosis, where expectation is dictated by the distributions used to derive the

gold standards. That is,

$$R_{ss} = \sum_i p_{gold}(d_i) U_{i,dx_{ss}}$$

and

$$R_{gold} = \sum_i p_{gold}(d_i) U_{i,dx_{gold}}$$

where R_{ss} and R_{gold} denote the ratings for the inference method and gold-standard diagnoses, respectively. Note that the two ratings can be different only when the diagnoses prescribed by the two distributions p_{ss} and p_{gold} are not the same.

C. An Expert-Rating Evaluation Metric

In addition to the decision-theoretic approach, an expert-rating method is used to compare the inference methods. For each probability distribution, the expert is asked, "On a scale from zero to ten— zero being unacceptable and ten being perfect—how accurately does the distribution reflect your beliefs?" The ratings given by the expert are compared using standard statistical techniques. Note that gold standards are not explicitly elicited in this approach.

The expert-rating metric is used for two reasons. First, expert-rating approaches have been used frequently in expert system evaluations. (See, for example, Cooper [?].) Therefore, it is useful to compare the approach with the decision-theoretic method introduced in this paper. Second, the expert-rating and decision-theoretic approaches evaluated different aspects of performance and are complementary.

V. Utility Assessment

In this section, several important issues surrounding the assessment of diagnostic utilities are addressed and details of the procedure for assessment are described.

An important consideration in the assessment of diagnostic utilities is that preferences will vary from one decision maker to another. For example, the diagnostic utilities of decision makers faced with the results of a lymph-node biopsy are likely to be influenced by theier age, sex, and state of health. Consequently, the ratings produced by the decision-theoretic metric are meaningful to an individual only to the degree that their diagnostic utilities match those used in the evaluation.

For this experimental comparison, the utilities of the expert on the Pathfinder project were used. The expert was chosen for two practical reasons. First, being an expert, he was reasonably familiar with many of the ramifications of correct and incorrect diagnosis. Second, a good working relationship with him had been established during the construction of Pathfinder. In future experiments, it would be useful to generate a utility model using an expert clinician who might have better insight into the preferences of a "typical" patient making a decision based on the results of a lymph-node biopsy.

It is interesting to note that our expert, because he is an expert, had biases that made his initial preferences deviate significantly from those of a typical patient. For example, many sets of diseases of the lymph node currently have identical treatments and prognoses. Nonetheless, experts like to distinguish diseases within each of these sets, because doing so allows research in new treatments to progress. That is, experts often consider the value of their efforts to future patients. In addition, experts generally suffer professional embarrassment when their diagnoses are incorrect. Also, experts are concerned about the legal liability associated with misdiagnosis. In an effort to remove these biases, our expert was specifically asked to ignore these attributes of utility. He was asked to imagine that he himself had a particular disease, and to assess the diagnostic utilities accordingly.

Another important consideration in almost any medical decision problem is the wide range of severities associated with outcomes. As mentioned previously, one misdiagnosis might lead to inappropriate antibiotic therapy, whereas another might lead to almost certain death. How can preferences across such a wide range be measured in common terms? Early attempts to resolve this question were fraught with paradoxes. For example, in a linear willingness-to-pay approach, a decision maker might be asked, "How much would you have to be paid in order to accept a one in ten-thousand chance of death?" If the decision maker answered, say, one thousand dollars, the approach would dictate that he would be willing to be killed for ten million dollars. Clearly, this is absurd.

Recently, Howard has constructed an approach that avoids many of the paradoxes of earlier models [?]. Like many of its predecessors, the model deals with determining what an individual would have to be paid to assume some chance of death, and what he would be willing to pay to avoid a given risk. Also like many of its predecessors, Howard's model shows that, for small risks of death (typically, $p < 0.001$), the amount someone would be willing to pay or would have to be paid to avoid or to assume such a risk is linear in p. That is, for small risks of death, an individual acts like an expected-value decision maker with a finite value attached to his life. For significant risks of death, however, the model deviates strongly from linearity. For example, the model shows that there is a maximum probability of death, beyond which an individual will accept no amount of money to risk that chance of death. Most people find this to be an intuitive result. [2]

In this paper, the details of the model will not be presented. For a discussion of the approach see [?]. Here, we need only to assume that willingness to buy or sell *small* risks of death is linear in the probability of death. Given this assumption, preferences for minor to major outcomes can be measured in a common unit, *the probability of immediate, painless death that a person is willing to accept to avoid a given outcome and to be once again healthy*. The

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[2]The result ignores considerations of legacy.

undesirability of major outcomes can be assessed directly in these terms. For example, a decision maker might be asked, "If you have Hodgkin's disease and are incorrectly diagnosed as having a viral infection, what probability of immediate, painless death would you be willing to accept to avoid the situation and to be once again healthy?" At the other end of the spectrum, the undesirability of minor outcomes can be assessed by willingness-to-pay questions, and can be translated, via the linearity result, to the common unit of measurement. For example, a decision maker might be asked, "How much would you be willing to pay to avoid taking antibiotics for two weeks?" If he answered $100, and if his small-risk value of life were $100,000,000, then the answer could be translated to a utility of a 1 in 1,000,000 chance of death.

Thus, the only major task in assessing the U_{ij}, aside from making the direct assessments themselves, is the determination of the decision maker's small-risk value of life. Howard proposes a model by which this value can be computed from other assessments. A simple version of the model requires a decision maker to trade-off the amount of resources he consumes during his lifetime and the length of his lifetime, to characterize his ability to turn present cash into future income, and to establish his attitude toward risk. However, our expert did not find it difficult to assess the small-risk value of life directly.[3] When asked what dollar amount he would be willing to pay to avoid chances of death ranging from 1 in 20 to 1 in 1000, he was consistent with the linear model to within a factor of 2, with a median small-risk value of life equal to $10,000,000.

Note that, with this utility model, the ratings R_{ss} assigned to the inference methods will have units "probability of death." In many cases, we shall see that the differences between ratings are small in these units (on the order of 0.001). Consequently, it is useful to define a *micromort*, a one in one million chance of death. In these units, for example, a decision maker with a small-risk value of life of $10,000,000 should be willing to buy and sell risks of death at the rate of $10 per micromort. This unit of measurement is also useful because it helps to emphasize that the linear relationship between risk of death and willingness to pay holds for only small probabilities of death.

Another important consideration is the complexity of the utility assessment procedure. There are 51 diseases represented in Pathfinder. The direct measurement of the U_{ij} therefore requires $51^2 = 2601$ assessments. Clearly, the measurment process would be tedious. Thus, several steps were taken to reduce the complexity of the task. First, the expert was asked to establish sets of disease hypotheses that have identical treatments and prognoses. An example of such a set is the collection of nine types of Hodgkin's diseases represented in Pathfinder. Patients with any of the nine types receive the same treatment and have the same prognosis.[4] The expert identified 26 such "equivalence classes," reducing the number of direct utility assessments required to $26^2 = 676$.

Next, the expert was asked to order the utilities U_{ii}— he was asked to order the undesirability of having each disease and being diagnosed correctly. After he had completed this ranking, he was asked to quantitate each U_{ii} in the manner described previously. It should be noted that the ordering of the U_{ii} was modified significantly during this process. About halfway through the procedure, he exclaimed, "The dollar is forcing me to think very carefully!" It would be interesting to determine whether most people respond in this way. The results of such a study would be interesting, particularly to reseachers in qualitative reasoning.

Finally, the off-diagonal utilities were assessed. For each disease, the expert was asked to quantify the undesirability of having the disease and being diagnosed as having a different disease. First, he identified the most similar preexisting assessment. It was then a simple matter to identify the differences between the current assessment and the preexisting assessment, and to modify the utility appropriately. For example, given a patient with the disease sinus hyperplasia, the only difference between her being diagnosed correctly and her being diagnosed with cat scratch disease is that, in the latter case, the patient would take unnecessary antibiotics for several weeks. The expert said that he would be willing to pay $100 to avoid taking the antibiotics, so this value (converted to micromorts) was subtracted from the utility of being correctly diagnosed with sinus hyperplasia.

VI.   Details of the Experiment

Whenever possible, the conditions of the experimental comparison were arranged to mimic the conditions under which Pathfinder would be used in clinical practice. For example, Pathfinder is expected to be used by community hospital pathologists to assist them in diagnosing challenging lymph-node cases. Currently, when a community hospital pathologist gets a difficult case, he refers the case to an expert, such as the expert on the Pathfinder project. Therefore, the cases selected for this experiment were chosen from a large library of cases referred to our expert from community pathologists. Relatively old cases (older than four months) were selected to decrease the chance that the memory of the expert would bias the results.

Twenty-six cases were selected at random from the referral library such that no two diagnoses were the same. Repeat diagnoses were not allowed so that the inference methods would be evaluated over a larger portion of the lymph node knowledge base. To account for the fact that some diseases are much more likely to occur than others, the ratings derived from the metrics for each case are

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[4]Prognosis for these nine types of Hodgkin's disease is determined by the clinical stage, not by the specific type of disease.

weighted by the relative likelihood of occurrence of the case. The relative likelihoods were computed by normalizing the prior probabilities of the true diagnosis of each case so that they summed to one.[5]

Although the cases were selected at random, a post-experiment analysis showed that the cases were more challenging than a set of average cases would be. The expert reported that 50 percent of the cases contained many more technical imperfections (such as tears and poor preservation) than is usual. He also thought that 70 percent of the cases were more difficult to diagnose than the average case. The deviation from normal probably occurred because the case-selection process favored the inclusion of rare diagnoses.

A pathology resident entered the observations for each case into a computer database after examining lymph-node biopsies through a microscope. A pathology resident was used for two reasons. First, our expert could not be allowed to look at the lymph nodes slides directly, because he would observe more information than is presented to the inference methods. In addition, the expertise of a resident closely matches the expertise of the users targeted for Pathfinder.

The manner in which features were selected for identification deviated from the approach typically used in Pathfinder. Specifically, a pathologist usually enters only a few salient features and then receives recommendations from Pathfinder about what additional features are most useful for narrowing the diagnostic contenders. The pathologist then provides values for one or more of these recommended features, and the process cycles. To avoid confounding the performance of the inference methods with that of the feature recommendation strategies, the resident was asked to enter all "salient features observed." At no time was the resident allowed to see what features the system recommended to be evaluated.

Once features values had been identified for each case, they were presented to the three inference methods, producing three belief distributions. The expert was then given two evaluation sheets for each case. The first sheet included a list of the observations identified by the resident, as well as list of all the disease hypotheses represented in Pathfinder. The expert was asked to assign a probability distribution to the diseases based on the observations given. The descriptive gold standard was derived from this distribution. The second sheet was identical to the first, except that it included the distributions produced by the three inference methods. The distributions were displayed in columns in a random order for each case. The expert was asked to rate each belief distribution using the 0 to 10 scale described earlier, and again to assign a probability

distribution to the diseases. He was allowed to refer to his first probability distribution during the second assignment. The informed gold standard was derived from this second distribution.

In two of the twenty-six cases, the expert found the lists of observations confusing. Also, in these same two cases, the simple Bayes and odds–likelihood inference methods produced inconsistent distributions in which all hypotheses were assigned a belief of zero. Consequently, these two cases were removed from the study.

VII.   Results

Decision-theoretic ratings for five different procedures for determining a diagnosis are shown in Table **??**. "Informed gold standard" refers to the procedure of prescribing the disease that maximizes utility under the distribution used to derive the informed gold standard (Equation **??**). "Simple Bayes-MEU" refers to the procedure of prescribing the disease that maximizes utility under the simple Bayes distribution. "Simple Bayes," "Odds–likelihood," and "Dempster–Shafer" refer to the procedures of prescribing the most likely diseases under the simple Bayes, odds–likelihood, and Dempster-Shafer distributions, respectively.

The values in the first column represent the absolute decrease in utility of a patient when faced with the result of a lymph-node biopsy and diagnosed using a particular approach. The values represent an average over the 26 cases examined, weighted by the likelihood of occurrence of each case. Notice that most of the decrease in each case is attributed to the fact that the patient is sick. Errors in diagnosis account for little of the decrease in utility. In particular, the rating associated with the informed gold standard represents the decrease in utility associated with the best possible diagnosis under the conditions of the experiment and therefore reflects solely the decrease in utility of the patient due to illness. This rating shows that a patient with a lymph-node biopsy faces a decrease in utility of 205,804 micromorts, on average. That is, the patient is as bad off as he would be facing a 0.2 chance of immediate, painless death. This quantity dominates the decreases in utility due to diagnostic error.

To highlight the effects of diagnostic error, differences between the informed gold standard rating and the rating for each diagnostic approach are shown in column 2 of Table **??**. The standard deviation of these differences is given in column 3 of the table. Note that the standard deviations are quite large relative to the mean differences. The reason for such large variances is easily appreciated. For each diagnostic approach, the diagnosis prescribed by the approach is identical to the diagnosis prescribed by the gold standard in many of the 24 cases. In particular, the simple Bayes-MEU, simple Bayes, and odds–likelihood approaches prescribe the gold-standard diagnosis in 17 of 24 cases. The naive Dempster–Shafer approach prescribes the gold-standard diagnosis in 12 of 24 cases. In these

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[5]In pathology, several methods are used to establish a true diagnosis. In some cases, a diagnosis is established through the use of expensive tests. In other cases, a diagnosis is established through observation of the time course of a patient's illness. In still other cases, a diagnosis can be established only by an expert pathologist examining tissue sections under a microscope. In this study, all three approaches, including combined approaches, were used.

cases, the ratings for the gold standard and diagnostic approaches are equal. In the remaining cases, the approaches prescribe a diagnosis that differs from the gold standard prescription. These nonoptimal diagnoses are often associated with utilities that are significantly lower than is the utility associated with the gold-standard diagnosis. Thus, differences in utility fluctuate from zero in many cases to large values in others, resulting in large standard deviations.

Although the standard deviations are high, a Monte Carlo permutation test indicates that the performance of the naive Dempster–Shafer approach is significantly inferior to that of the other methods (achieved significance level = 0.004). No other significant difference exists among the other methods.

The expert ratings for each inference method are shown in Table **??**. As in the decision-theoretic approach, the mean and standard deviation are weighted by the relative prior probability of the true diagnosis. Because the ratings apply directly to the belief distributions derived by each method, there is no distinction between the simple Bayes-MEU and simple Bayes procedures.

Using the expert-rating metric, another significant difference is detected. In particular, a Wilcoxon two-sample rank test shows that the simple Bayes inference procedure performs significantly better than does the odds–likelihood approach (achieved significance level = 0.07).

Table **??** shows a comparison of the informed and descriptive gold standards. The differences between the two standards are not significant. Thus, seeing the belief distributions generated by the inference methods did not persuade the expert to change his opinion about the cases to any significant degree. Of course, this finding should not be generalized to other experts or to other domains.

VIII.   Discussion

Before examining the results in detail, it is useful to make some general comments about the two evaluation metrics. An obvious advantage of the decision-theoretic approach over the expert-rating approach is that its results are much more meaningful. For example, the difference between the simple Bayes and naive Dempster–Shafer ratings using the expert-rating metric is 8.5 on a scale from 0 to 10 and is deemed to be "significant" by a standard statistical test. The difference of approximately 10,000 micromorts between the two approaches as determined by the decision-theoretic metric, however, carries much more force; it implies that using the naive Dempster–Shafer approach instead of the simple Bayes approach is equivalent to assuming an additional one in 100 risk of death!

A disadvantage of the decision-theoretic with respect to the expert-rating approach is that its results have limited scope. Specifically, the differences among inference methods may be highly dependent on the assessments of diagnostic utility made by our expert. Furthermore, decision-theoretic comparisons of inference methods are likely to vary from one domain to another because there is room for wide variation in utility assessments between domains. The results of the experimental comparison must be considered in this light.

An advantage of the expert-rating metric over the decision-theoretic metric, as demonstrated in this experiment, is that the former can be much more sensitive to differences. For example, the decision-theoretic ratings of the simple Bayes and of the odds–likelihood methods are identical. In contrast, the expert-rating metric shows the two inference methods to be significantly different. High sensitivity is likely to be a property of the expert-rating approach across many domains. In a typical consulting session, an expert is hypersensitive to errors in diagnosis, whether such errors matter to a decision maker or not, because the integrity of the expert is on the line. It is likely that this hypersensitivity will carry over into expert-rating ratings of diagnostic performance. This advantage of using an expert-rating metric is not absolute. Considerations of integrity or liability, for example, can always be incorporated into the diagnostic utilities. Indeed, the fact that components of preference can be made explicit and are under the direct control of the expert is one advantage of the decision-theoretic approach.

Another advantage of the expert-rating metric is that it is less time-consuming to implement. It took the expert approximately 20 hours, working with two people trained in decision analytic techniques, to develop the utility model used in this evaluation. It took the expert less than 1 minute per case to rate the distributions produced by the three inference methods.

Overall, the two approaches are complementary. The expert-rating approach is useful for identifying differences in performance that may be important in *some* domain. The decision-theoretic metric reveals the degree of importance of such differences for a particular domain of interest. It should be mentioned that information-theoretic metrics exist for measuring differences between probability distributions, such as relative entropy and the Brier score [**?**] [**?**]. The advantages and disadvantages of the information-theoretic and expert-rating methods are similar with respect to the decision-theoretic approach, except that the information-theoretic methods require probabilistic interpretations for the distributions to be compared.

Given these considerations about the evaluation metrics, differences in performance among the inference methods can now be discussed. In this experimental comparison, the method for selecting an optimal diagnosis with the highest decision-theoretic rank is simple Bayes-MEU. The difference between the rank of this method and the gold standard is 811 micromorts. With the caveats described previously, this value can be seen to represent the maximum room for improvement in the knowledge base. Such improvements may include more careful assessments of probabilities in the knowledge base, and the representation of dependencies among features.

The difference in ratings between simple Bayes-MEU

| Decision-theoretic ratings (micromorts) | | | |
| | | Differences | |
	Absolute mean	mean	sd
Informed gold standard	205,804	–	–
Simple Bayes-MEU	206,615	811	4079
Simple Bayes	206,635	831	4078
Odds–likelihood	206,635	831	4078
Naive Dempster–Shafer	216,371	10,587	19,101

Table 1: Decision-theoretic ratings of the inference methods.

| | Expert ratings | |
	mean	sd
Simple Bayes	8.52	1.17
Odds–likelihood	7.33	1.95
Naive Dempster–Shafer	0.03	0.17

Table 2: Expert ratings of the inference methods.

and simple Bayes is only 20 micromorts and is not significant. This result suggests that, in the lymph-node domain, little is gained by using the more sophisticated decision rule. Three factors of this domain appear to be responsible for this observation. First, the resident pathologist recorded all salient features observed under the microscope for each case. Second, the lymph-node domain appears to be structured such that, when all salient features are entered, most of the probability mass will fall on one disease hypothesis or a set of disease hypotheses within the same utility equivalence class. In 20 of the 24 cases, 95 percent of the probability mass fall on a set of diseases within the same equivalence class. Third, the structure of diagnostic utilities in the domain is such that a disease with small probability will rarely be chosen as the optimal diagnosis using the principle of maximum expected utility. In light of these factors, the relative value of decision rules should not be extrapolated to other domains without explicit justification.

Several interesting observations can be made about the relative performances of the simple Bayes and odds–likelihood inference methods. First, the expert-rating metric shows a significant difference between these methods, whereas the decision-theoretic metric shows no difference between them. This result is a clear example of the decreased sensitivity of the decision-theoretic approach to evaluation.

Second, the theoretical difference between the simple Bayes and odds–likelihood inference methods is that the former assumes evidence to be conditionally independent on the hypotheses, as shown in Equation **??**, whereas the latter assumes evidence to be conditionally independent on both the hypotheses and on the negation of the hypotheses, as reflected in Equations **??** and **??**. Thus, the decision-theoretic and expert-rating results show that, although the additional assumption of conditional indepen-

dence on the negation of hypotheses is inconsequential in the lymph-node domain, it may lead to significant degradation in performance in other domains.

Third, there is a regularity in the differences between the distributions produced by the two methods. Specifically, the simple Bayes distributions produced in this study are, with only one exception, more peaked. That is, the variance of these distributions are smaller than are those produced using the odds–likelihood approach. This difference can be traced to the additional assumption of conditional independence on the negation of hypotheses, Equation **??**. To see this connection, consider a hypothetical example in which there are three mutually exclusive and exhaustive hypotheses—H_1, H_2, and H_3—that have equal prior probabilities. Suppose there are many pieces of evidence relevant to these hypotheses such that each piece of evidence E_j has the same probability of occurrence for a given hypothesis. That is, $p(E_j|H_i) = p(E|H_i)$ for all E_j, and $i = 1, 2, 3$. Also suppose that the likelihoods have values such that:

$$p(E|H_1) > p(E|H_2) > p(E|H_3)$$

and

$$\frac{p(E|H_1)}{p(E|\overline{H_1})} = \frac{2p(E|H_1)}{p(E|H_2)+p(E|H_3)} > 1$$

$$\frac{p(E|H_2)}{p(E|\overline{H_2})} = \frac{2p(E|H_2)}{p(E|H_1)+p(E|H_3)} > 1$$

$$\frac{p(E|H_3)}{p(E|\overline{H_3})} = \frac{2p(E|H_3)}{p(E|H_1)+p(E|H_2)} < 1$$

These constraints are satisfied easily (for example, $p(E|H_1) = 0.8$, $p(E|H_2) = 0.6$, and $p(E|H_3) = 0.2$). Under these conditions, evidence E is confirmatory for H_1, confirmatory to a lesser degree for H_2, and disconfirmatory for H_3. Using the simple Bayes inference procedure (Equation **??**) it can be shown that, as the number of pieces of evidence grows, the posterior probability of H_1 tends

| | Decision-theoretic ratings (micromorts) | | |
| | | Differences | |
	Absolute mean	mean	sd
Informed Gold Standard	205,804	–	–
Descriptive Gold Standard	205,888	84	1273

Table 3: Decision-theoretic ratings of expert distributions.

to one whereas the posterior probability of both H_2 and H_3 tends to zero. However, using the odds–likelihood approach (Equation **??**) where evidence is conditionally independent given the negation of hypotheses, a different result is obtained. In particular, as the number of pieces of evidence grows, it can be shown that the posterior probabilities of both H_1 and H_2 tend to one, whereas the posterior probability of H_3 tends to zero. In the odds–likelihood approach, these probabilities are renormalized, so the probabilities of H_1 and H_2 each approach one-half. Thus, in this example, the odds–likelihood distribution is less peaked than is the simple Bayes distribution. In general, simple Bayes distributions will be more peaked, because this method tends to amplify differences in likelihoods, whereas the odds–likelihood method tends to washout differences.

Unlike previous observations, this one does not appear to be tied to the lymph-node domain. Provided a large body of evidence is reported such that the simple Bayes approach produces a sharp distribution, the odds–likelihood inference method should, in general, produce distributions that are less peaked. An important consequence of this phenomenon is that degradation in performance due to the incorrect assumption of conditional independence on the negation of hypotheses is likely to occur in other domains.

A final observation about the simple Bayes and odds–likelihood inference methods is that there is a regularity among the exceptional cases (5 of 24) in which distributions produced by odds–likelihood were preferred to the those produced by simple Bayes. Although obvious dependencies among features were captured by a clustering technique, subtle ones remained unrepresented in the lymph-node knowledge base. It seems that the failure to represent the more subtle dependencies led to decreased performance of the simple Bayes method relative to the odds–likelihood method. In particular, the incorrect assumption of conditional independence in the simple Bayes approach led to overcounting of evidential support. This overcounting, in turn, produced distributions that were overly peaked. In the odds–likelihood approach, the impact of evidence was also overcounted. However, it appears that such overcounting was partially compensated by the washout effect described.

The performances of the odds–likelihood and naive Dempster–Shafer approaches are also interesting to compare. Both evaluation metrics revealed a significant difference between the two methods. There are two major theoretical differences between the inference procedures,

one or both of which may be responsible for the differences in performance. First, from Equation **??**, it is clear that each mass assignment in the inference method contains a component proportional to the prior probability of diseases. Thus, when the masses for many different observations are combined, the prior probability components will be overcounted. Priors are not overcounted in the odds–likelihood approach. Second, due to the way mass is assigned in the naive Dempster–Shafer approach, disconfirmatory observations for disease hypotheses are not recognized. For example, if some observation completely rules out a disease hypothesis in the odds–likelihood method, the Dempster–Shafer mass for the disease–observation pair is zero. In the naive Dempster–Shafer inference method, a zero mass leaves the score of a hypothesis unchanged. Therefore, a hypothesis ruledout by an observation in the odds–likelihood approach is left with its degree of belief unchanged in the naive Dempster–Shafer approach. It is suspected that this difference is more significant than is the overcounting of priors.

IX.   Future Work

The combination of the decision-theoretic and expert-rating approaches to performance evaluation provides useful insights about various components of the inference process within the lymph node domain and about the inference process in general. This same approach to evaluation can be used to probe many different aspects of the construction of an expert system. For example, the Pathfinder research team has developed a set of procedures that recommends additional features for observation to the pathologist-user. The methods discussed in this paper should prove useful in evaluating the merits of these procedures. In addition, the Pathfinder group is currently exploring different techniques for constructing consensus knowledge bases that combine the beliefs of two or more experts. Again, the evaluation methods can be used to quantify the value of each approach. In yet another study, sensitivity to assessment errors in the knowledge base could be examined.

It is hoped that the presentation of these evaluation methods will encourage other researchers to evaluate a wide variety of issues surrounding the building of real-world expert systems.

X.   Acknowledgements