On the Sensitivity of Probabilistic Networks to Reliability Characteristics

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Abstract

Diagnostic reasoning in essence amounts to reasoning about an unobservable condition, based upon indirect observations from diagnostic tests. Probabilistic networks that are developed for diagnostic reasoning, take the reliability characteristics of the tests employed into consideration to avoid misdiagnosis. In this paper, we demonstrate the effects of inaccuracies in these characteristics by means of a sensitivity analysis of a real-life network in oncology.

Keywords: probabilistic networks, sensitivity analysis, diagnostic reasoning, reliability characteristics

1 Introduction

Since their introduction, probabilistic networks have become increasingly popular for reasoning with uncertainty in various domains of application. A probabilistic network in essence is a model of a joint probability distribution over a set of statistical variables. It is comprised of a graphical structure that captures the statistical variables concerned and the influential relationships between them, and an associated set of conditional probabilities that serve to describe the strengths of the represented relationships [4]. Since a probabilistic network uniquely defines a joint probability distribution, it allows for computing any probability of interest over its variables.

Probabilistic networks are often used for diagnostic reasoning, most notably in the medical domain. Diagnostic reasoning generally amounts to reasoning about an unobservable condition, based upon indirect observations from diagnostic tests. For diagnostic reasoning with a probabilistic network, the available observations are entered into the network; the posterior probability distribution given these observations then is computed and the most likely value for the main diagnostic variable is taken for the diagnosis.

In most application domains, the results of diagnostic tests are uncertain to at least some extent. In the medical domain, for example, a radiograph can be difficult to interpret: a physician may overlook a small tumour and state a negative result, or state a positive result based upon a phantom image. The uncertainty in the result of a test is captured by the test's *sensitivity* and *specificity*. The sensitivity is the probability of finding a positive result whenever the condition tested for is present; the specificity is the probability of finding a negative result in the absence of the condition.

The reliability characteristics of the various diagnostic tests in use should be taken into consideration in diagnostic reasoning to avoid misdiagnosis. From a study of a real-life probabilistic network in oncology, for example, we found that taking the uncertainties in the tests' results into account is essential to arrive at clinically acceptable behaviour [3]. For a probabilistic network, these characteristics are typically obtained, however, from literature, from statistical data, or from human experts, and inevitably are inaccurate. Since the characteristics are used in diagnostic reasoning with the network, the established diagnosis may be sensitive to the inaccuracies involved and, in fact, may be unreliable.

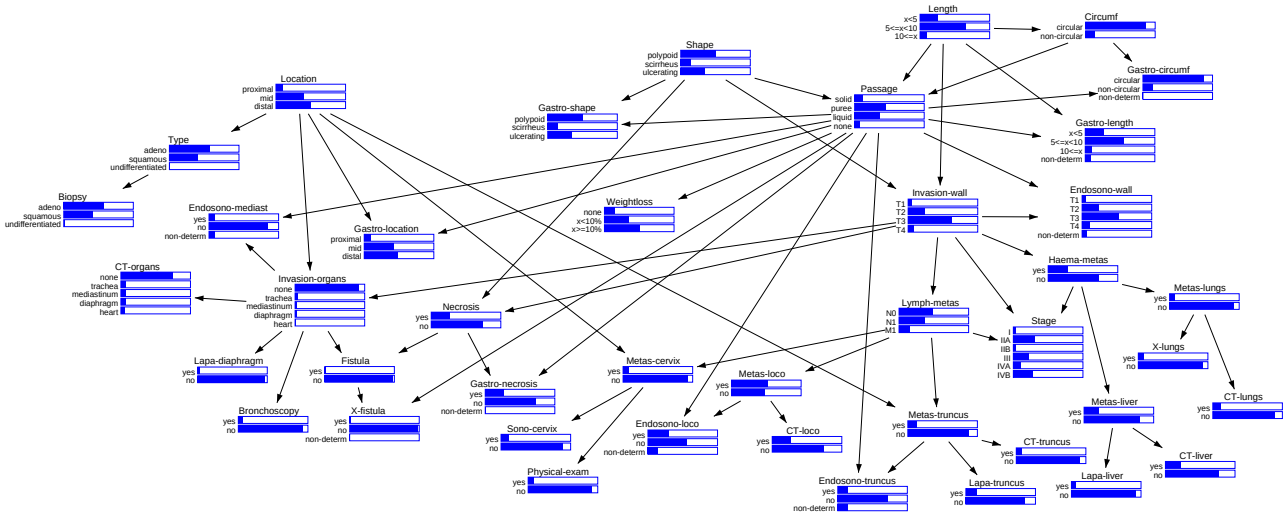


Figure 1: The oesophageal cancer network.

In this paper, we study the effects of inaccuracies in the reliability characteristics of diagnostic tests by means of a sensitivity analysis of a real-life probabilistic network in oncology. Sensitivity analysis is a general technique for studying the robustness of the output of a mathematical model to parameter variation. Within our network, we varied the sensitivity and specificity characteristics of the represented diagnostic tests, and studied whether or not this variation could change the diagnosis established from the network. From the analysis, some distinct patterns of sensitivity emerged that are dependent upon the actual test results entered.

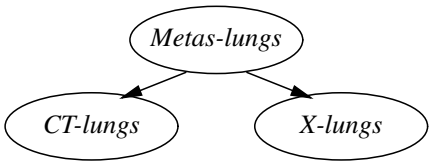
The paper is organised as follows. In Section 2, we introduce the oesophageal cancer network that we used for our study. In Section 3, we review sensitivity analysis of probabilistic networks in general. In Section 4, we present the results that we obtained from a sensitivity analysis of the oesophageal cancer network and provide some insights to explain them. The paper ends with our concluding observations in Section 5.

2 The oesophageal cancer network

The *oesophageal cancer network* was constructed with the help of two experts in gastrointestinal oncology from the Netherlands Cancer Institute, Antoni van Leeuwenhoekhuis [3]. The network describes the presentation characteristics of an oesophageal tumour, the processes underlying the tumour's invasion into the oesophageal wall and adjacent organs, and the process of its metastasis. The extent of a patient's cancer is summarised in a *stage*, which can be either I, IIA, IIB, III, IVA, or IVB, in the order of advanced disease. The network further models the diagnostic tests that are commonly used to establish the stage of cancer of the oesophagus; these tests range from a gastroscopic examination of the primary tumour to a CT scan of the patient's upper abdomen.

The oesophageal cancer network currently includes 42 statistical variables, for which almost 1000 parameter probabilities were specified by the experts. Of this total of 42 variables, 23 variables serve to represent test results. For these test variables, between 4 and 25 parameter probabilities are specified, with an average of 8 probabilities per variable. The network is depicted in Figure 1, which also shows the prior probabilities per variable.

To capture the uncertainties in the results of the diagnostic tests employed, the oesophageal cancer network explicitly models the tests' reliability characteristics. These characteristics are defined in terms of two variables. The disease variable D models the presence, indicated by d, or absence, indicated by $\bar{d}$, of the condition under consideration; the test variable T models the result of the test, where a positive result t suggests presence and a negative result $\bar{t}$ suggests absence of the condition. The sensitivity of the test to the condition now is the probability $\Pr(t \mid d)$ that a



		Metas-lungs	
		yes	*no*
X-lungs	*yes*	0.85	0.02
	no	0.15	0.98

Figure 2: A fragment of the oesophageal cancer network and some associated parameter probabilities.

positive test result is found in a patient who actually has the condition; the specificity of the test is the probability $\Pr(\bar{t} \mid \bar{d})$ that a negative result is found in a patient without the condition [5]. In the network, these characteristics are captured by the parameter probabilities specified for the test variables. As an example, Figure 2 shows the probabilities for a radiograph of a patient's thorax; these are the probabilities of a positive and of a negative test result, respectively, given the actual presence or absence of metastases in the lungs. The radiograph is stated, for example, to have a sensitivity of 0.85 and a specificity of 0.98.

With the oesophageal cancer network, we have available, from the Antoni van Leeuwenhoekhuis, the medical records of 185 patients diagnosed with cancer of the oesophagus. For each patient, between 6 and 21 test results are available, with an average of 14.8.

3 Sensitivity analysis

Sensitivity analysis is a general technique for studying the effects of inaccuracies in the parameters of a mathematical model on its output. In a sensitivity analysis of a probabilistic network, for each parameter probability x, a *sensitivity function* $f(x)$ is established, that expresses the output probability of interest in terms of x. If, upon varying x, the other parameters from the same conditional distribution are co-varied proportionally, such a sensitivity function is a quotient of two linear functions [1], that is,

$$f(x) = \frac{a \cdot x + b}{c \cdot x + d}$$

where the constants a, b, c, d are built from the parameter probabilities that are not being varied. These constants can be established by computing the output probability of interest from the network for a small number of values for the parameter probability under study and solving the resulting system of equations.

In general, a sensitivity function takes the shape of an orthogonal *hyperbola*

$$f(x) = \frac{r}{x - s} + t$$

where

$$r = \frac{b \cdot c - a \cdot d}{c^2}, \quad s = -\frac{d}{c}, \quad \text{and} \quad t = \frac{a}{c}$$

The hyperbola has two asymptotes parallel to the x- and y-axes; these asymptotes are $y = t$ and $x = s$, respectively. The hyperbola further has two branches; for ease of reference, Figure 3 depicts such a branch. The values of the four constants a, b, c, d of the sensitivity function now determine the actual shape of the hyperbola. For $r > 0$, for example, the hyperbola is composed of two decreasing branches in the first and third quadrants relative to the asymptotes; for $r < 0$, the two branches are increasing and located in the second and fourth quadrants.

Since the output probability of interest exists for any value of the parameter x under study, a sensitivity function $f(x)$ is well-defined on the interval $[0, 1]$. We therefore have that a sensitivity function is a fragment of just one of the branches of a hyperbola. We further have that the asymptote

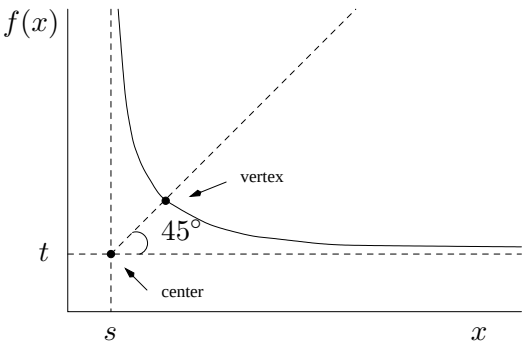


Figure 3: A branch of an orthogonal hyperbola, located in the first quadrant relative to the asymptotes.

$x = s$ cannot be located within the interval $[0, 1]$. We conclude that either $s < 0$, in which case the sensitivity function is a fragment of a branch in the first or fourth quadrant, or $s > 1$, in which case the sensitivity function is a fragment of a branch in the second or third quadrant.

A sensitivity function serves to express some output probability in terms of a parameter under consideration and therefore provides for studying the effect of varying this parameter on that particular probability of interest. In the oesophageal cancer network, however, we are not so much interested in the effect of parameter variation on a single output probability. Rather, we are interested in the effect on the most likely stage of a patient's cancer. To study this effect, we have to consider the sensitivity functions for the various possible stages of the cancer simultaneously and investigate whether or not parameter variation can change the most likely stage.

For the oesophageal cancer network, we study the six sensitivity functions $f_i(x)$, $i = \mathrm{I}, \ldots, \mathrm{IVB}$, that express the probability of a specific stage in terms of the parameter probability x. With the parameter's original value x_0, the most likely stage for a patient is a stage j for which $f_j(x_0) \geq f_i(x_0)$ for all $i \neq j$. Now, if the sensitivity function $f_j(x)$ intersects with the sensitivity function $f_i(x)$ for some stage i, then the most likely stage may change from j to i upon varying x. The intersections of the function $f_j(x)$ with the other sensitivity functions, therefore, reveal the effects of parameter variation on the most likely stage.

From the intersections of the various sensitivity functions for an output variable of interest, we compute a pair (α, β) that captures the deviation to smaller values and to larger values than the original value x_0 of the parameter under study, respectively, that are maximally possible without inducing a change in the most likely value of the output variable. Such a pair is called an *admissible deviation* [2]. We note that the admissible deviation (α, β) defines the range $[x_0 - \alpha, x_0 + \beta]$ within which the parameter can be varied without inducing a change in the most likely value. In the sequel, we will use the symbols $\leftarrow$ and $\rightarrow$ to denote that a parameter can be varied to the left and to the right boundary of the probability interval, respectively.

4 Experimental results

To study the effects of inaccuracies in the reliability characteristics of diagnostic tests, we conducted a sensitivity analysis of the oesophageal cancer network. In this analysis, we varied the parameter probabilities of all test variables discerned and studied the effects of their variation on the most likely stage computed from the network. Because the patterns of sensitivity exhibited by a network typically vary with evidence, we used in our study the data that we had available from 185 patients. The analysis revealed various distinct patterns of sensitivity. In this section, we discuss some of these patterns, focusing on the parameter probabilities of a small number of test variables.

4.1 Statistics on induced changes

We consider the four diagnostic tests that serve to give insight in the presence or absence of haematogenous metastases in a patient's liver or lungs. These tests are a CT scan of the upper abdomen and a laparoscopy of the liver, to establish the presence or absence of metastases in the liver, and a radiograph and a CT scan of the thorax, to establish the presence or absence of metastases in the patient's lungs. For each of the associated test variables, four parameter probabilities are specified that correspond with the test's sensitivity and specificity and their complements. Tables 1 and 2 summarise the results that we obtained from varying these parameter probabilities.

Table 1 describes, for each of the four test variables under consideration, the effects of varying its parameter probabilities on the most likely stage computed for patients for whom a negative result is available. For example, for 89 of the 91 patients for whom a negative result from a CT scan of the upper abdomen was found, varying the test's specificity resulted in a change in the most likely stage computed from the network; for just 3 patients, the complement of the test's sensitivity resulted in such a change. In general, we observe that, with the exception of a small number of patients, varying the specificities of the tests induces a change in the most likely stage computed for a patient under study; the complements of the sensitivities tend not to induce such a change.

Table 1: The number of induced changes in the most likely stage given negative test results: 91 patients have *CT-liver* = *no*; 15 patients have *Lapa-liver* = *no*; 127 patients have *X-lungs* = *no*; 109 patients have *CT-lungs* = *no*.

parameter	*induced changes*
p(*Lapa-liver* = *no* | *Metas-liver* = *yes*)	0 (0%)
p(*Lapa-liver* = *no* | *Metas-liver* = *no*)	15 (100%)
p(*CT-liver* = *no* | *Metas-liver* = *yes*)	3 (3%)
p(*CT-liver* = *no* | *Metas-liver* = *no*)	89 (98%)
p(*X-lungs* = *no* | *Metas-lungs* = *yes*)	2 (2%)
p(*X-lungs* = *no* | *Metas-lungs* = *no*)	122 (95%)
p(*CT-lungs* = *no* | *Metas-lungs* = *yes*)	1 (1%)
p(*CT-lungs* = *no* | *Metas-lungs* = *no*)	102 (94%)

Table 2: The number of induced changes in the most likely stage given positive test results; 4 patients have *Lapa-liver* = *yes*; 7 patients have *CT-liver* = *yes*; 9 patients have *X-lungs* = *yes*; 6 patients have *CT-lungs* = *yes*.

parameter	*induced changes*
p(*Lapa-liver* = *yes* | *Metas-liver* = *yes*)	3 (75%)
p(*Lapa-liver* = *yes* | *Metas-liver* = *no*)	3 (75%)
p(*CT-liver* = *yes* | *Metas-liver* = *yes*)	6 (86%)
p(*CT-liver* = *yes* | *Metas-liver* = *no*)	6 (86%)
p(*X-lungs* = *yes* | *Metas-lungs* = *yes*)	5 (56%)
p(*X-lungs* = *yes* | *Metas-lungs* = *no*)	6 (67%)
p(*CT-lungs* = *yes* | *Metas-lungs* = *yes*)	2 (33%)
p(*CT-lungs* = *yes* | *Metas-lungs* = *no*)	2 (33%)

The pattern of sensitivity that emerges from Table 1 can be explained by studying the predictive value of a negative test result. The *predictive value of a negative result* is defined as the probability of the condition under study indeed being absent in a negatively-tested patient [5]. For the four tests under consideration, these predictive values can be summarised by the abstractly stated probability $\Pr(\textit{Metas} = \textit{no} \mid \textit{Test} = \textit{no})$ of the absence of haematogenous metastases given a negative result from the test. This probability can be written as

$$\Pr(\textit{Metas} = \textit{no} \mid \textit{Test} = \textit{no}) = \frac{g \cdot (1-n)}{g \cdot (1-n) + h \cdot n}$$

where

$$\begin{aligned} g &= p(\textit{Test} = \textit{no} \mid \textit{Metas} = \textit{no}) \\ h &= p(\textit{Test} = \textit{no} \mid \textit{Metas} = \textit{yes}) \\ n &= \Pr(\textit{Metas} = \textit{yes}) \end{aligned}$$

For the sake of the argument, we note that since for oesophageal cancer, stage IVB is defined as a cancer with haematogenous metastases, the probability of *Metas* = *yes* roughly equals the probability of *Stage* = IVB.

From the predictive value of a negative test result, we observe that, if the probability n of the presence of haematogenous metastases is relatively small, then the term $h \cdot n$ will be small. Varying the complement h of the test's sensitivity will then have little effect on the predictive value: the most likely value of the main diagnostic variable is expected to remain unchanged. Variation of the test's specificity g then is expected to do result in a change in this most likely value. If n is extremely small, however, we have that the predictive value is almost 1: varying g will then show little effect.

In the oesophageal cancer network, the prior probability of stage IVB, and hence n, is relatively small; moreover, it will not increase unless there is some strong evidence of metastases in a patient's liver or lungs. From the above observations, we would therefore expect that varying the complement h of the sensitivity of a diagnostic test from which a negative result is available, will not induce a change in the most likely stage computed for a patient. The specificity g of the test is expected to do cause such a change upon variation. Figure 4 serves to corroborate these expectations by showing the effects of varying the two probabilities for a CT scan of the upper abdomen for a patient in whom all test results point to the absence of haematogenous metastases.

From Table 1, we observe that the expected pattern of sensitivity shows for most patients. For a small number of patients, however, the specificities of the four tests under study are not influential upon variation; for a small number of patients, moreover, the complements of the tests' sensitivities do induce a change in the most likely stage computed from the network. To explain these findings, we study once again the predictive value of a negative test result. We observe that, if the probability n of the presence of haematogenous

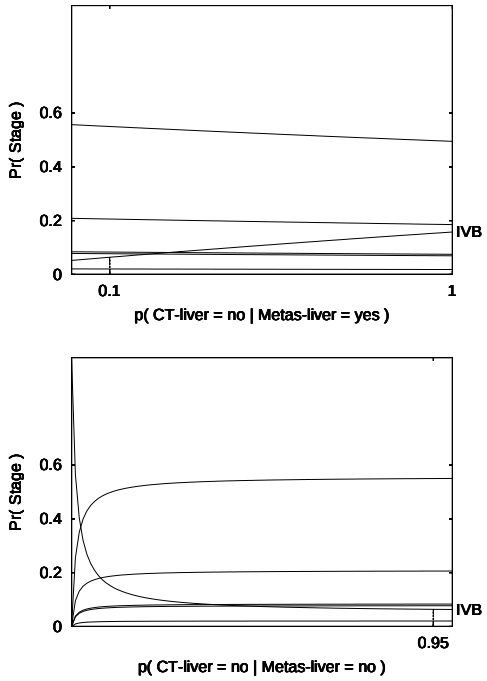


Figure 4: The effects of varying the probabilities for a CT scan of the upper abdomen for patient 94-2326, for whom all test results pertaining to haematogenous metastases are negative.

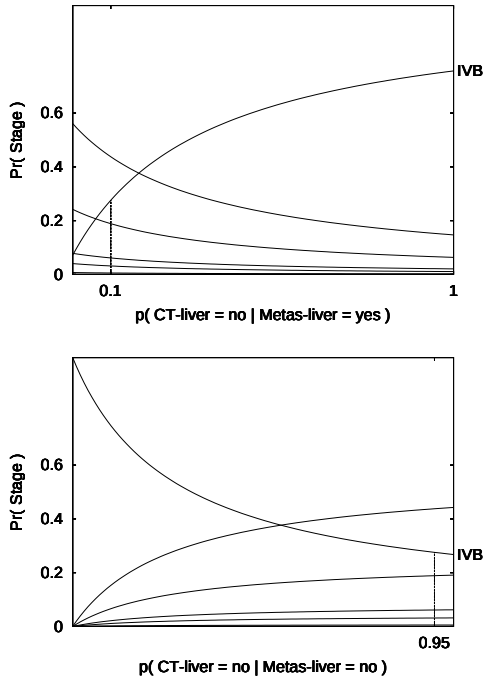


Figure 5: The effects of varying the probabilities for a CT scan of the upper abdomen for patient 95-1554, for whom a single positive test result pertaining to haematogenous metastases is available.

metastases increases, then the term $h \cdot n$ increases. Variation of the complement h of the sensitivity of a test can then affect the predictive value and thereby induce a change in the most likely value of the main diagnostic variable. The test's specificity g will have similar effects upon variation, unless the probability of haematogenous metastases being present has become very large: if n is quite large, we have that the term $g \cdot (1 - n)$ is quite small and varying g can no longer affect the predictive value.

As mentioned before, the prior probability of metastases in a patient's liver or lungs is rather small. The probability increases substantially, however, as soon as one or more positive results from the four tests under consideration are obtained. For patient 95-1554, for example, a positive result is available from a laparoscopic examination of the liver. From the above observations, we expect for this patient that varying the complement of the sensitivity of a CT scan of the upper abdomen will induce a change in the most likely stage computed from the network. Figure 5, showing the effects of varying the parameter probabilities for the CT scan for this patient, serves to corroborate this expectation.

For patient 94-1496, to conclude, positive results are available from two of the four tests under study. These results substantially increase the probability of the presence of haematogenous metastases. Figure 6 now shows that the large probability of stage IVB serves to suppress the effects of varying the probabilities for the radiograph of the thorax from which a negative result is available.

Where Table 1 pertains to negative test results, Table 2 describes the effects of varying the parameter probabilities for the tests from which a positive result is available. As the number of patients with positive test results is rather limited, the patterns of sensitivity observed are less clear. Roughly stated, upon variation both the sensitivities and the complements of the specificities of the four tests tend to induce a change in the most likely stage computed for a patient under study. This observation again is readily explained by studying the predictive value of a positive test result, that is, the probability $\Pr(\mathit{Metas} = \mathit{yes} \mid \mathit{Test} = \mathit{yes})$.

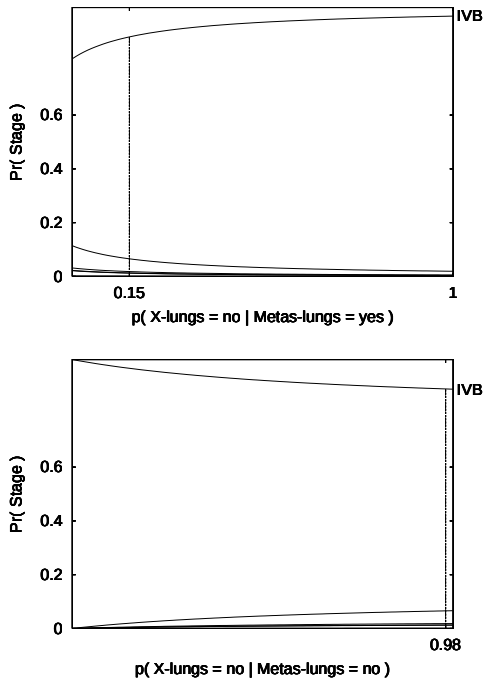


Figure 6: The effects of varying the probabilities for a radiograph of the thorax for patient 94-1496, for whom two positive test results pertaining to haematogenous metastases are available.

4.2 Statistics on admissible deviations

If varying a parameter probability induces a change in the most likely value of the main diagnostic variable of a network, then inaccuracies in this parameter are likely to affect the network's output. The extent to which inaccuracies can be influential, is expressed by the admissible deviation for the parameter. In this section, we discuss the admissible deviations that we found in the analysis of the oesophageal cancer network. In doing so, we focus once again on the reliability characteristics of the four diagnostic tests that serve to give insight in the presence or absence of haematogenous metastases. Tables 3 and 4 summarise the admissible deviations for the parameter probabilities of the associated test variables; the reported averages are computed over the admissible deviations that we found for the patients for whom varying the parameter under study induced a change in the most likely stage.

Table 3 reports the average admissible deviations for the parameter probabilities of the diagnostic tests from which a negative result is available. For

Table 3: The average admissible deviations given negative test results; in the order of presentation, the original values of the parameters are 0.75, 0.98, 0.10, 0.95, 0.15, 0.98, 0.10, and 0.95.

parameter	*admissible deviation*
$p(\textit{Lapa-liver} = \textit{no} \mid \textit{Metas-liver} = \textit{yes})$	–
$p(\textit{Lapa-liver} = \textit{no} \mid \textit{Metas-liver} = \textit{no})$	$(0.8610, \rightarrow)$
$p(\textit{CT-liver} = \textit{no} \mid \textit{Metas-liver} = \textit{yes})$	$(\leftarrow, 0.3043)$
$p(\textit{CT-liver} = \textit{no} \mid \textit{Metas-liver} = \textit{no})$	$(0.8992, \rightarrow)$
$p(\textit{X-lungs} = \textit{no} \mid \textit{Metas-lungs} = \textit{yes})$	$(\leftarrow, 0.8054)$
$p(\textit{X-lungs} = \textit{no} \mid \textit{Metas-lungs} = \textit{no})$	$(0.9683, \rightarrow)$
$p(\textit{CT-lungs} = \textit{no} \mid \textit{Metas-lungs} = \textit{yes})$	$(\leftarrow, 0.2009)$
$p(\textit{CT-lungs} = \textit{no} \mid \textit{Metas-lungs} = \textit{no})$	$(0.9456, \rightarrow)$

example, for the 89 patients for whom varying the specificity of a CT scan of the abdomen induced a change in the most likely stage, the specificity could be varied from 0.95 to 0.05 on average before the change occurred; for all these patients, moreover, the specificity could be varied to 1.00 without inducing any change in the stage computed from the network. We observe that, while originally close to 1.00, the specificities of all four tests can be varied to almost 0 before a change in the most likely stage is induced. Figure 7 shows, as an example, the distribution of the admissible deviations found for the specificity of a CT scan of the upper abdomen; similar distributions were found for the specificities of the other tests.

The distribution of admissible deviations from Figure 7 can be explained by studying the shapes of the sensitivity functions concerned. We re-

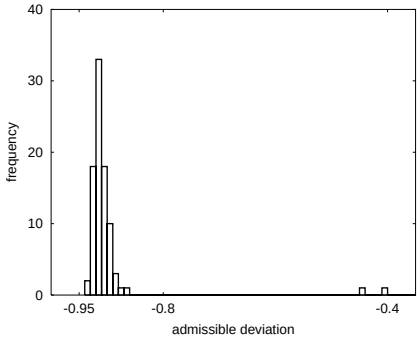


Figure 7: The distribution of admissible deviations for the parameter probability $p(\textit{CT-liver} = \textit{no} \mid \textit{Metas-liver} = \textit{no})$.

Table 4: The average admissible deviations given positive test results; in the order of presentation, the original values of the parameters are 0.25, 0.02, 0.90, 0.05, 0.85, 0.02, 0.90, and 0.05.

parameter	*admissible deviations*
$p(\textit{Lapa-liver} = \textit{yes} \mid \textit{Metas-liver} = \textit{yes})$	$(0.1875, \rightarrow)$
	$(\leftarrow, 0.2033)$
$p(\textit{Lapa-liver} = \textit{yes} \mid \textit{Metas-liver} = \textit{no})$	$(0.0090, \rightarrow)$
	$(\leftarrow, 0.0600)$
$p(\textit{CT-liver} = \textit{yes} \mid \textit{Metas-liver} = \textit{yes})$	$(0.7900, \rightarrow)$
$p(\textit{CT-liver} = \textit{yes} \mid \textit{Metas-liver} = \textit{no})$	$(\leftarrow, 0.4150)$
$p(\textit{X-lungs} = \textit{yes} \mid \textit{Metas-lungs} = \textit{yes})$	$(0.5658, \rightarrow)$
$p(\textit{X-lungs} = \textit{yes} \mid \textit{Metas-lungs} = \textit{no})$	$(0.0150, \rightarrow)$
	$(\leftarrow, 0.2017)$
$p(\textit{CT-lungs} = \textit{yes} \mid \textit{Metas-lungs} = \textit{yes})$	$(0.8839, \rightarrow)$
$p(\textit{CT-lungs} = \textit{yes} \mid \textit{Metas-lungs} = \textit{no})$	$(0.0461, \rightarrow)$
	$(\leftarrow, 0.0422)$

call from Section 3, that the sensitivity function yielded by varying a parameter probability x, in essence is a branch of an orthogonal hyperbola. We argued that, for the asymptote $x = s$ of this hyperbola, in general either $s < 0$ or $s > 1$ holds. Now, the denominator $c \cdot x + d$ of the sensitivity function in essence is a probability [1]. We thus have that $0 < c \cdot x + d \leq 1$. For the constant c more specifically, we find that $c > 0$. Informally speaking, upon varying the parameter x, a negative value for c can only arise from co-variation of the other parameters of the same distribution; since x is a probability associated with a test variable whose value has been observed, however, these other parameters do not partake in the sensitivity function. We further find that $d > 0$. From $s = -\frac{d}{c}$, we conclude that $s < 0$. The vertex of the sensitivity function thus lies to the left and is expected to have a relatively small x-coordinate. Figures 4, 5 and 6 support these observations.

From the locations of the vertices of the sensitivity functions under consideration, we have that the various functions are more likely to intersect for relatively small values of the parameter under study. Parameters that have a rather high original value thus are expected to have a large admissible deviation to smaller values. Parameters with a small original value are expected to have a much smaller admissible deviation. The results reported in the Tables 3 and 4 serve to corroborate these expectations.

5 Conclusions

To study the effects of inaccuracies in the reliability characteristics of diagnostic tests, we conducted a sensitivity analysis of a real-life probabilistic network. The patterns of sensitivity that emerged from the analysis, suggest that, while it is important to explicitly model the possibility of test results being erroneous, most of the reliability characteristics involved need not be very accurately specified. As we could explain the patterns of sensitivity found from fundamental insights independent of the network under study, similar patterns are expected also for other probabilistic networks for diagnostic applications.

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