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Novel Pedagogical Methods for Conditional-Probability Computations in Medical Disciplines

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Authors' contributions

This work was carried out in collaboration among the three authors. Author RAR envisioned and designed the study, performed the analysis, and solved the detailed running example. Author AMR introduced the tools of the Karnaugh map, normalized contingency table and SFG, and wrote the preliminary manuscript. Author FAT managed the literature search and drew the figures. All authors read and approved the final manuscript.

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ABSTRACT

There is a definite need for representations of and tools for conditional probability that enhance understanding, simplify calculations, foster insight, and facilitate reasoning. Such representations and tools are useful in a wide variety of disciplines, but their utility in medical contexts and applications are stressed herein, so as to address a clinical rather than a mathematical audience. We employ a plethora of time-tested pedagogical representations or tools of conditional probability including: (a) Visualization on Venn diagrams or Karnaugh maps, (b) Reformulation as natural frequencies, (c) Entity interrelations via Signal Flow Graphs, as (d) Specification of certain problem formats such as the format of Trinomial Graphs. The new representations or tools have well known histories of pedagogical advantages, but are still to be tested in the specific realm of conditional probability. Further assessment of the novel representations or tools proposed herein is needed. Each of these is to be taught to a group of students, and a control group of students is to be instructed *via* the conventional representation. Detailed statistical analysis of the

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outcomes is warranted. Similar investigations were performed earlier, but they were on a limited scale. Therefore, the need arises for an explorative study that exhausts all proposed representations or tools.

Keywords: Conditional probability; visualization; Karnaugh map; signal flow graph; trinomial graph; natural frequency.

1. INTRODUCTION

The notion of conditional probability is indispensable within many walks of life, and in diverse realms of scientific disciplines. In particular, this notion is of critical importance in many medical contexts, and constitutes an invaluable useful piece of knowledge for the physician and the patient alike. However, there are many contemporary complaints of collective probabilistic illiteracy, and even a widespread inability to merely understand the meaning of numbers [1]. Currently, there are many research efforts aiming at making the concepts of conditional probability more transparent and accessible to ordinary and professional people [1-37]. This paper is a serious attempt to review the aforementioned research topic *via* four avenues, to be depicted as representations or tools. Some of these avenues are novel methods and some have already appeared in the literature but are still subject to ongoing vigorous research. This research topic is of an obviously interdisciplinary nature as it combines elements from widely diverse areas such as mathematics, clinical medicine, epidemiological diagnostic testing, probability and statistics, problem solving, and educational psychology. We hope that this paper is of general interest to researchers in the aforementioned areas. However, we mainly target a clinical audience, in general, and medical researchers and educators, in particular. In addition, we hope that the paper might be of some benefit, at least partially, to practicing physicians as well as to medical students (perhaps with some graceful help from their competent educators).

Targeting a clinical audience, we strived to clarify our technical jargon, simplify our terminology, and illustrate the concepts being introduced *via* diversified means. We include a classic clinical example as a running computational example. We solve this example using the various proposed tools. Medical students and general physicians might be content to understand and master a single tool, and not necessarily all tools. However, medical researchers and educators might need (and are encouraged) to explore all tools. For them, further analytical and experimental comparisons between the proposed tools are definitely needed.

The organization of the rest of this paper reflects our choice of methods that facilitate the learning of concepts of conditional probability in medical disciplines. Section 2 summarizes some useful pertinent nomenclature. Section 3 proposes visualization via Venn diagrams, or, preferably, via Karnaugh maps. Section 4 reviews the concepts of natural frequencies and contingency tables. This section supplements its expository review with a detailed running computational example. This example reveals the connections and subtle differences among various representations. Section 5 suggests the utilization of signal flow graphs, and points out their utility in specified problem formats such as that known as the ternary problems of conditional probability, which are typically represented by trinomial graphs. Section 6 concludes the paper.

2. LIST OF NOMENCLATURE

2.1 Bayesian Reasoning

Bayesian reasoning denotes the issue of computing the conditional probability (or frequency) of a cause given an effect. Usually, Bayes' Theorem is employed to obtain this probability in terms of the conditional probability of the effect given the cause together with the absolute probability of the cause and that of the effect [36].

2.2 Natural Frequencies

Natural frequencies are integers counting the numbers of samples favorable to certain conjunctive events. These are the entries of a two-by-two contingency table that assesses a certain test i with respect to another j, which is a gold standard (the *status quo* or true (perfect) test). Both variables i and j are dichotomous such that [36,37]

$\{ j = +1 \}$ = {Disease is present}
$\{ j = -1 \}$ = {Disease is absent}

$\{ i = +1\}$ = {Test i indicates disease presence}
$\{ i = -1\}$ = {Test i indicates disease absence}

The natural frequencies are the True Positives (TP_{ij}), False Positives (FP_{ij}), False Negatives (FN_{ij}), and True Negatives (TN_{ij}), whose ratios to the total sample expresses probabilities of respective *conjunctive* events, namely [1, 14, 36]

$$TP_{ij} = N * P\big((i = +1) \cap (j = +1)\big) \quad (1)$$

$$FP_{ij} = N * P\big((i = +1) \cap (j = -1)\big) \quad (2)$$

$$FN_{ij} = N * P\big((i = -1) \cap (j = +1)\big) \quad (3)$$

$$TN_{ij} = N * P\big((i = -1) \cap (j = -1)\big) \quad (4)$$

2.3 Signal Flow Graphs

A linear signal flow graph (SFG), is a specialized directed graph in which nodes represent system variables, and branches or edges represent transmittances or functional connections between pairs of nodes. An edge emanating from a certain node and incident on a particular node brings to the latter node the value of the former node weighted (multiplied) by the transmittance carried by the edge. There are two main closely-related types of an SFG [37], namely

1. Mason SFG (employed herein) [38-39]: This is an SFG in which the value of a specified non-source node equals the weighted sum of nodes having arrows incident on the specified node (sum of the values of the nodes, each multiplied by the transmittance on its edge towards the specified node).
2. Coates SFG [40]: This is an SFG in which the aforementioned weighted sum of nodes with arrows incident on a specified non-source node is equal to zero.

2.4 Conditional-probability Problems

A conditional-probability problem is a probability problem that is formulated with at least one of the quantities explicitly mentioned (either as known quantity or as the unknown to be found) being interpreted as conditional probability [30,37].

2.5 Ternary Problems of Conditional Probability

A ternary problem of conditional probability is a conditional-probability problem formulated with exactly three known quantities and a single unknown quantity to be solved for [30]. Such a problem is represented by a trinomial graph [30], or by an SFG that mimics a trinomial graph [37].

3. VISUAL REPRESENTATION

The conditional probability of event *A* given event *B* is given by [37, 41]

$$P(A|B) = \frac{P(A \cap B)}{p(B)},\ P(B) \neq 0 \quad (5)$$

Equation (5) deliberately denies the existence of conditional probability when the conditioning event B has zero probability (such as when B is the impossible event $\emptyset$). If the event B is an extremely rare event (*i.e.,* of an ultra-small probability), the definition (1) is somewhat problematic and dubious, and might be associated with intriguing questions or even misconceptions.

There is a long history for employment of visual techniques in comprehending and manipulating probability [42-52]. We visually represent (5) by the Venn diagram in Fig. 1(a) and equivalently by the Karnaugh map in Fig. 1(b). We supplement each of these two figures by:

(a) A light red loop depicting the probability of the conditional (conditioned) event P(A).
(b) A bold blue loop representing the probability of the conditioning event P(B). This loop replaces the full rectangle in either figure as the entire sample space, or as the certain event.
(c) A bold black loop representing the intersection or overlapping of the two aforementioned loops or the probability $P(A \cap B)$ of the intersection of the two corresponding events. Hence the conditional probability $P(A|B)$ is given by the area of the black loop divided by that of the blue loop.

Fig. 2 makes the general notion of Fig. 1 more specific by employing concepts of medical diagnostic testing. In particular, event A is interpreted as $\{ j = -1\}$ or {disease absence} while event B is replaced by $\{ i = -1\}$ or {Test i says that disease is absent}. We call the complements $\{ j = +1\}$ and $\{i = +1\}$ of these two events the events of true prevalence and perceived (apparent) prevalence, respectively.

As pointed out earlier by Rushdi and Badawi [53] and Rushdi [54], the Karnaugh map has many advantages over the Venn diagram. An extra advantage, peculiar to our current study, is that the Karnaugh map can easily be interpreted as a contingency table or matrix [36,37]. As an offshoot of the beneficial use of Karnaugh maps, we use Figs. 3-5 to visualize the eight most prominent measures or indicators in medical diagnostic testing [36,37]. Fig. 3 depicts the eight possible conditional events, and is based on the use of three independent Boolean variables A_i, A_p and B_p defined as follows:

$A_i = B_j = \overline{A_j} = \overline{B_i}$ = {A is associated with an i value, and hence B is associated with a j value}.

$\overline{A_i} = B_i = A_j = \overline{B_j}$ = {A is associated with a j value, and hence B is associated with an i value}.

$A_p = \overline{A_n}$= {A is associated with a positive value}.

$\overline{A_p} = A_n$= {A is associated with a negative value}.

$B_p = \overline{B_n}$= {B is associated with a positive value}.

$\overline{\mathrm{B_p}} = \mathrm{B_n}$= {B is associated with a negative value}.

Note that despite the appearance of many variables, the three variables A_i, A_p and B_p suffice for full specification. For example, the cell $\overline{A_i} A_p \overline{B_p}$ in the Karnaugh map of Fig. 3 represents the conditional event $\{A|B\} = \{j = +1 | i = -1\}$.

Fig. 4 presents the probabilities of the events in Fig. 3 as conditional probabilities. Fig. 5 re-expresses these probabilities as quotients of natural frequencies. As stated earlier, symbols used in Figs. 4 and 5 express the eight most prominent measures or indicators used in diagnostic testing [36,37]. These are the Sensitivity or True Positive Rate (TPR_{ij}), the Specificity or True Negative Rate (TNR_{ij}), the Positive and Negative Predictive Values $(PPV_{ij}$ and $NPV_{ij})$, together with their respective complements, namely the False Negative Rate (FNR_{ij}), False Positive Rate (FPR_{ij}), False Discovery Rate (FDR_{ij}), and False Omission Rate (FOR_{ij}) [36, 37]. We stress that the first four among these measures could be viewed as basically independent (at first sight), while the remaining four are definitely dependent on the former four, being simply their complements (to 1). The solvability of a ternary problem (in which the known quantities are any three of the former four measures) means that only at most three of the eight measures could be independent.

4. REFORMULATION OF CONDITIONAL PROBABILITIES AS NATURAL FREQUENCIES

This section summarizes a really appealing thesis advocated by Gigerenzer, Hoffrage and coworkers [1,4,10,12-16,21] that representations of conditional probabilities as quotients of natural frequencies facilitate the computation of a cause's probability (or frequency) given that of an effect. This thesis is supported by many experimental studies conducted by these researchers and others, but it is sometimes confused with variations thereof that manifest different assumptions, and even fallacious misconceptions [14].

Hoffrage, et al. [14] start from the premise that "solving a problem simply means representing it so as to make the solution transparent," and then proceed to assert that "natural sampling is the way humans encountered human information during their history," and that "collecting data by means of natural sampling results in natural frequencies."

In addition to resulting from natural sampling, natural frequencies carry information about the base rates, and correspond to conjunctive events of the form $\{A \cap B\}$ or $\{i = \mp 1 \cap j = \mp 1\}$. They can be displayed in the form of natural-frequency trees, such as the one shown in Fig. 6. Such a tree is embedded on the 2-variable Karnaugh map of Fig. 7, which serves also as a 2×2 contingency table. We believe that the most prominent question in diagnostic testing is to compute the Positive Predictive Value

P {The disease is present | The available test says the disease is present}

$= P\{ j = +1 | i = +1\}.$ (6)

With natural frequencies, the probability is simply given by

$$TP_{ij} / (TP_{ij} + FP_{ij}). \quad (7)$$

With conditional probability format, this probability is computed via Bayes' rule as

$$P\{ j = +1 | i = +1\} = \frac{P(i=+1 \mid j=+1)\, P(j=+1)}{p(i=+1 \mid j=+1)\, P(j=+1) + P(i=+1 \mid j=-1)\, P(j=-1)} \quad (8)$$

Hoffrage, et al. [14] lamented the fact that several other authors confused the concept of

natural frequencies (frequency format) with that of normalized frequencies. These other authors "ran experiments with normalized frequencies, found that these did not improve Bayesian reasoning, and concluded that this result disproves the thesis that natural frequencies facilitate Bayesian reasoning" [14]. Fig. 8 pinpoints the trouble with the use of normalized frequencies, and explains why normalization defeats the purpose of employing frequencies rather than probabilities. The figure clearly shows that normalization is simply a retreat to the original realm of conditional probabilities. Hoffrage, et al. [14] indicate that, "normalized frequencies do not stem from the natural sampling of one population," and therefore, "require three different tress describing three different samples rather than a single tree." Fig. 8 uses symbolic notation to generalize the numerical values in Fig. 2 of [14], and clearly indicates that normalization restores conditional probabilities in place of conjunctive ones.

We now discuss a celebrated example of Gigerenzer et al. [1] using our present notation. This example is apparently the most cited example in the literature of diagnostic testing, and we are using it as a running example throughout the paper. The example has the conditional-probability formulation [1]:

"Assume you conduct breast cancer screening using mammography in a certain region. You know the following information about the women in this region:

- *(a) The probability that a woman has breast cancer is 1% (true prevalence)*
- *(b) If a woman has breast cancer, the probability that she truly tests positive is 90% (sensitivity)*
- *(c) If a woman does not have breast cancer, the probability that she nevertheless tests positive is 9% (false-positive rate)*

A woman tests positive. She wants to know from you whether that means that she has breast cancer for sure, or what the chances are. What is the best answer?"

In our notation, we are given the information:

(a) $P(j=+1)=0.01$ (9 a)

(b) $P(i=+1|j=+1)=0.90$ (9 b)

(c) $P(i=+1|j=-1)=0.09$ (9 c)

and it is desired to determine $P(j=+1|i=+1)$. First, we apply the Total Probability Theorem [36, 41] to obtain the *perceived* prevalence

$$\begin{aligned} P(i=+1) &= P(i=+1|j=+1)\,P(j=+1) + \\ &\quad P(i=+1|j=-1)\,P(j=-1) \\ &= (0.90)\,(0.01) + \\ &\quad (0.09)\,(1-0.01) \\ &= 0.0090 + 0.0891 \\ &= 0.0981 \end{aligned} \tag{10}$$

Then, we apply Bayes' Theorem [7,31,41] to obtain the required probability as

$$P(j=+1|i=+1)=\frac{P(i=+1|j=+1)P(j=+1)}{P(i=+1)}=\frac{0.0090}{0.098\ 1}=\frac{10}{109}=0.0917=9.17\ \% \tag{11}$$

An equivalent solution is to construct the *normalized* contingency table in Fig. 9. Initially, we enter the given true prevalence $P(j=+1)=0.01$, complement it to obtain $P(j=-1)=0.99$. The top two conjunctive probabilities in the table are given by

$$TP_{ij}/N = P(i=+1|j=+1)P(j=+1) = (0.90)(0.01) = 0.0090 \tag{12 a}$$

$$FP_{ij}/N = P(i=+1|j=-1)P(j=-1) = (0.09)(0.99) = 0.0891 \tag{12 b}$$

in agreement with our earlier calculations. The lower conjunctive probabilities are obtained via complementation as

$$\begin{aligned} FN_{ij}/N &= P(i=-1\cap j=+1) = P(j=+1) - \\ &\quad P(i=+1\cap j=+1) \\ &= 0.0100 - 0.0090 = 0.0010 \end{aligned} \tag{12 c}$$

$$\begin{aligned} TN_{ij}/N &= P(i=-1\cap j=-1) = P(j=-1) - \\ &\quad P(i=+1\cap j=-1) \\ &= 0.9900 - 0.0891 = 0.9009 \end{aligned} \tag{12 d}$$

Once the four conjunctive probabilities are obtained, pairs of them sharing the same row are added to obtain

$$\begin{aligned} P(i=+1) &= P(i=+1\cap j=+1) + P(i=+1\cap \\ &\quad j=-1 \\ &= 0.0090 + 0.0891 = 0.0981 \end{aligned} \tag{13}$$

$$P(i=-1) = P(i=-1 \cap j=+1) + P(i=-1 \cap j=-1) = 0.0010 + 0.9009 = 0.9019 \quad (14\text{ a})$$

Or alternatively

$$P(i=-1) = 1 - P(i=+1) = 1 - 0.0981 = 0.9019 \quad (14\text{ b})$$

The required probability is simply

$$P(j=+1|i=+1) = \frac{P(i=+1 \cap j=+1)}{P(i=+1)} = \frac{10}{109} = 0.0917 = 9.17\% \quad (15)$$

Based on the normalized contingency table of Fig. 9 the initial problem can be reformulated as follows [1]:

"Assume you conduct breast cancer screening using mammography in a certain region. You know the following information about the women in this region:

(a) One hundred out of every 10000 women have breast cancer
(b) Of these 100 women with breast cancer, 90 test positive
(c) Of the 9900 women without cancer, 891 nevertheless test positive."

The above formulation is the natural-frequency formulation. In a sense, this formulation presents the problem with half of the solution included. This is clear from our highlighting (in red) in Fig. 9 of the numbers given in the new formulation. In other words, the solution process is considerably simplified by representing the data in such a way that the solution becomes really obvious and less computationally demanding.

5. SIGNAL FLOW GRAPHS (SFGs)

Signal Flow Graphs are very useful in representing and manipulating linear relations. They find extensive uses in areas as diverse as microwave measurements [55], automatic control theory [56], DNA replication [57], two-dimensional recursive relations [58-65], and multidimensional recursive relations [66].

Following a proposal by Rushdi and Rushdi [36], Rushdi and Talmees [37] developed many SFGs for the diagnostic testing problem, which culminated with the somewhat sophisticated SFG presented in their Fig. 8. This figure is reproduced herein with several enhancements and improvements in Fig. 10. The SFG in this figure is used to relate the conditional, marginal and conjunctive probabilities of any contingency table. This SFG differs from a standard one, since in it a conjunctive probability should be understood to be expressed *via* one only of the two arrows incident on it. Another non-standard feature of this SFG is that each of the marginal probabilities makes its appearance thrice in the graph, and once computed in a certain location, it should be considered known at the two other locations. Nevertheless, the SFG has several particularly useful features. Each marginal probability is characterized with its related entities by a unique color. The SFG is supplied by an appropriate combination of three known probabilities and is then used to evaluate the remaining thirteen probabilities, and moreover to provide several checks on the correctness of the calculations. The SFG tool does not necessarily adopt the probability format, but might support the natural-frequency format as well. Fig. 11 is a replica of Fig. 10, with each of the conditional, marginal and conjunctive probabilities being replaced by a quotient of natural frequencies. Computations associated with the SFG might be *algebraic* in some cases such as the example solved in [37] in which all three known quantities are conditional probabilities. However, in most cases the SFG computations are *arithmetic* in nature. The running example in this paper (in which the known quantities are two conditional probabilities and one marginal probability) is amenable to arithmetic SFG computation as shown in Fig. 12. In fact, the detailed computations of this example in Sec. 4 can be followed and traced on the SFG of Fig. 12. The computations in Fig. 12 are accomplished in five stages (a)-(e) with stage (a) used simply for inserting the input data, and they go beyond obtaining the required unknown to achieving a complete characterization of the whole SFG, as well as checking correctness of the results. The results in Fig. 12 are the same as those in Equations (9)-(15) as well as those in Fig. 9.

Figs. 10-12 have striking similarity with trinomial graphs, which are special graphs designed by Pedro Huerta and coworkers [30] to represent a special kind of conditional-probability problems called ternary problems. The trinomial graphs are slightly enhanced with colors and arrows by Rushdi and Talmees [37] to stress their parallelism with signal flow graphs.

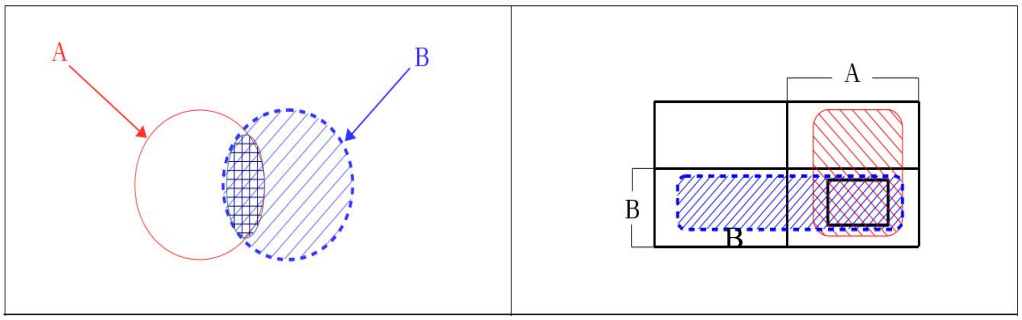

Fig. 1. Equivalence of the visualizations of conditional probability
$P(A|B) = P(A \cap B)/P(B), P(B) \neq 0$
by the Venn diagram (a) and the Karnaugh map (b)

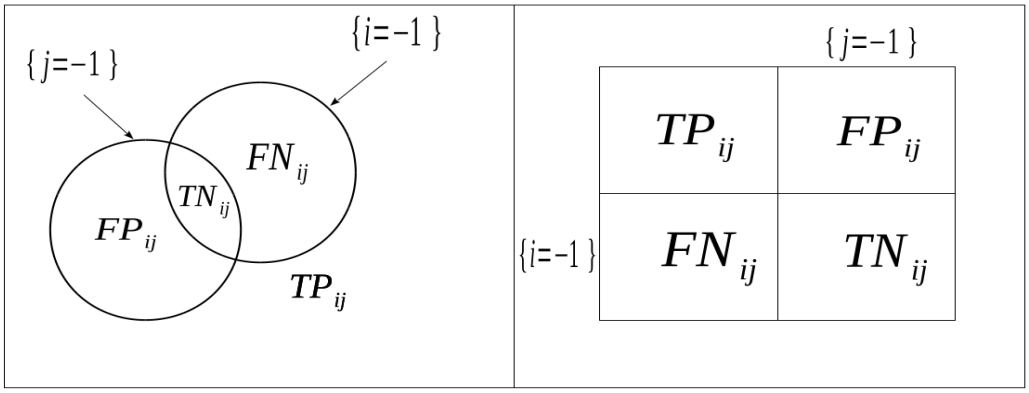

Fig. 2. The Venn diagram and Karnaugh map in Fig. 1 with A replaced by { $j = -1$} and B replaced by { $i = -1$}. Various areas are designated as natural frequencies. The Karnaugh map can be immediately viewed as a contingency table

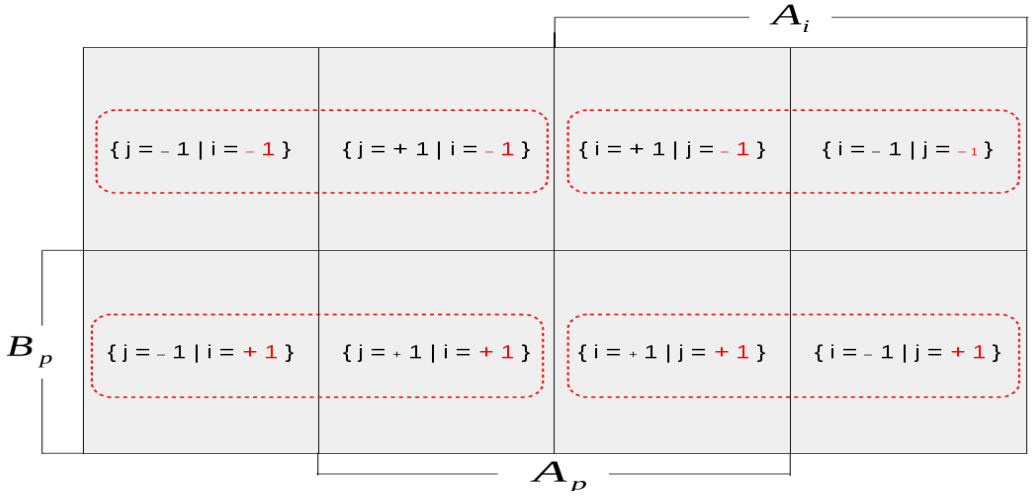

Fig. 3. A Karnaugh map depicting the eight possible conditional probability events {A|B}. complementary events are encircled together

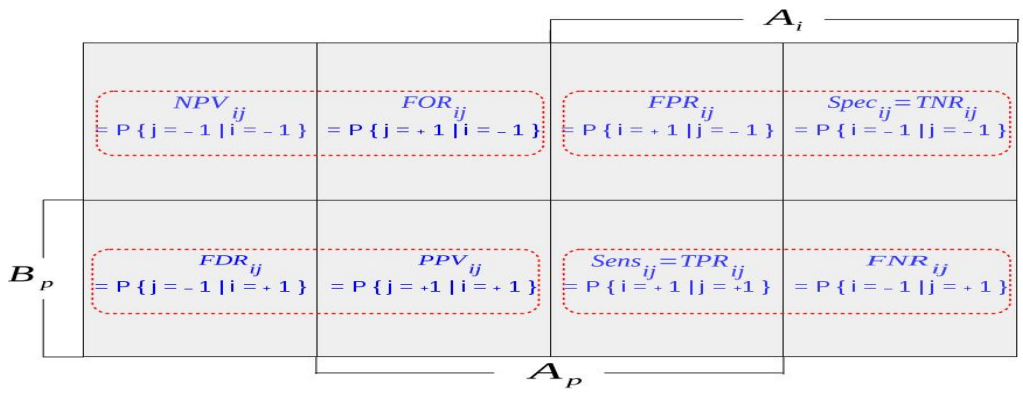

Fig. 4. The Karnaugh map in Fig. 3 redrawn to classify the probabilities of the corresponding conditional events. These are the eight most prominent indicators of diagnostic testing

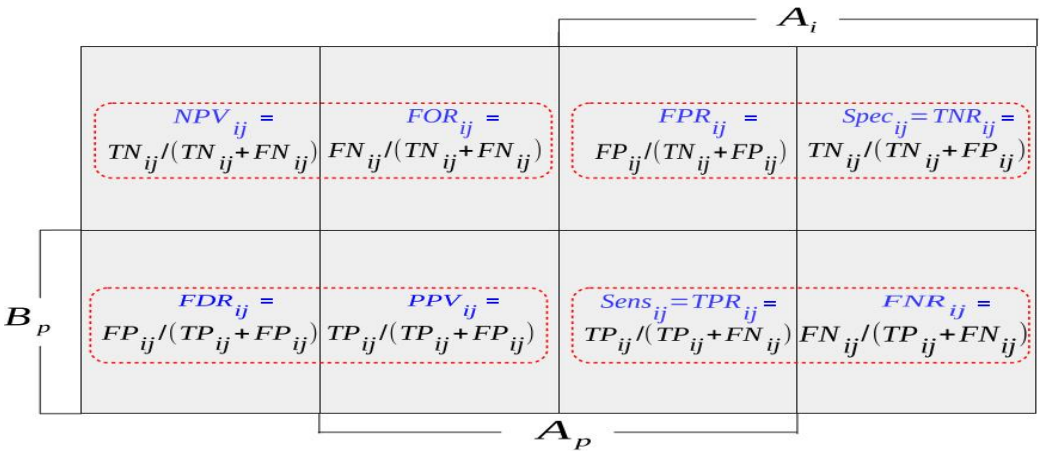

Fig. 5. The Karnaugh map in Fig. 4 with its entries of conditional probabilities being replaced by quotients of natural frequencies

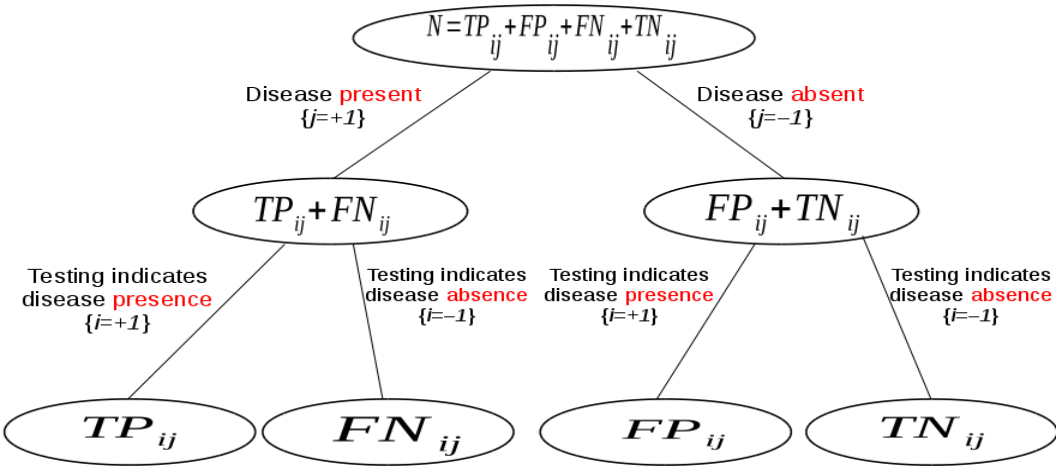

Fig. 6. A tree explanation of natural frequencies or a tree interpretation of the Karnaugh map in Fig. 2(b). which serves as a contingency table

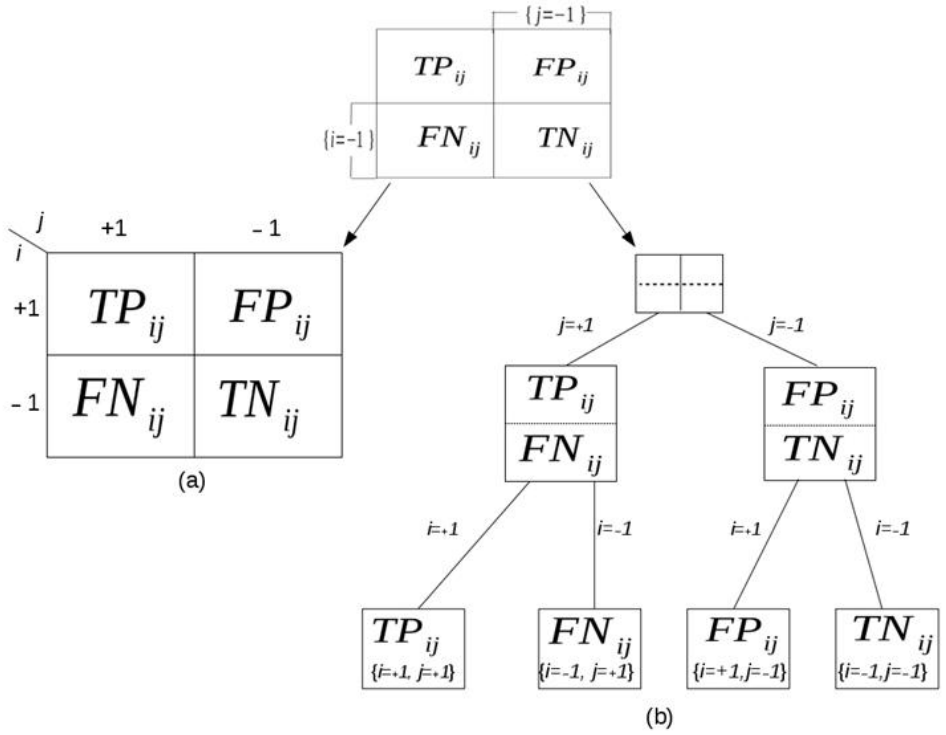

Fig. 7. The Karnaugh map plays an intermediary role or a liaison between a 2 by 2 contingency table in (a) and a natural frequency tree in (b)

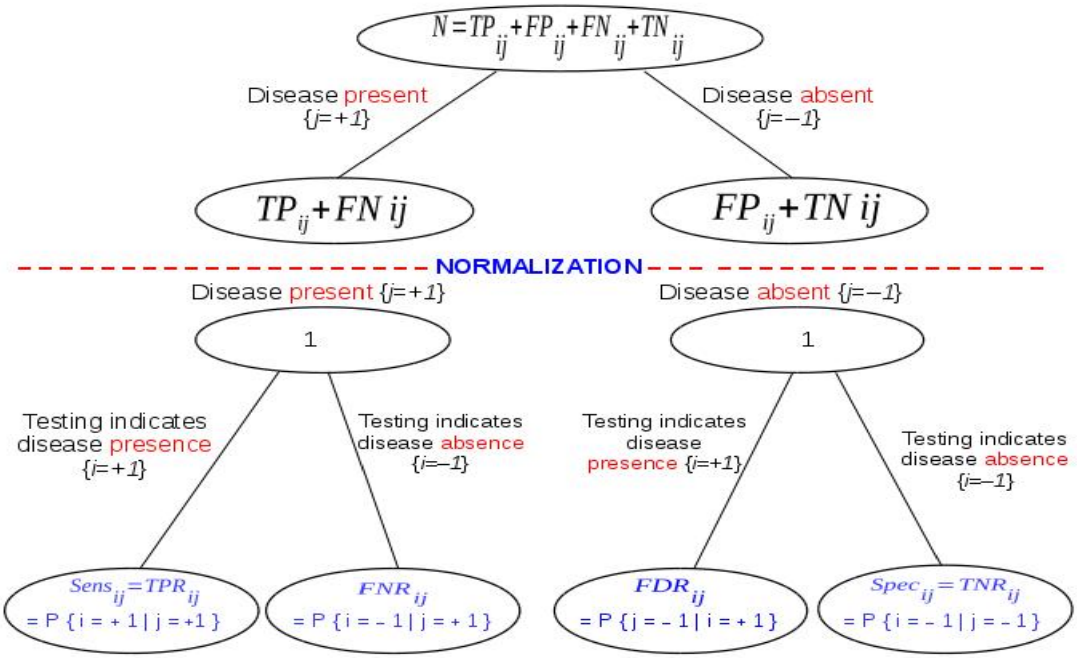

Fig. 8. A tree explanation of normalized frequencies. Obviously, normalization causes a loss of the advantage of using (natural) frequencies. This figure has three different trees rather than a single tree

$TP_{ij}/N=P(i=+1\cap j=+1)$	$FP_{ij}/N=P(i=+1\cap j=-1)$	$P(i=+1)$
$FN_{ij}/N=P(i=-1\cap j=+1)$	$TN_{ij}/N=P(i=-1\cap j=-1)$	$P(i=-1)$
$P(j=+1)$	$P(j=-1)$	1.0

(a)

0.0090	0.0891	0.0981
0.0010	0.9009	0.9019
0.01	0.99	1.0

(b)

Fig. 9. Normalized contingency table for use in the example problem. The table is essentially 2 by 2, but it is augmented by a third column that equals the sum of the two leftmost columns, and also augmented by a third row that equals the sum of the top two rows. Highlighted in red are the input numbers used in a natural-frequency formulation

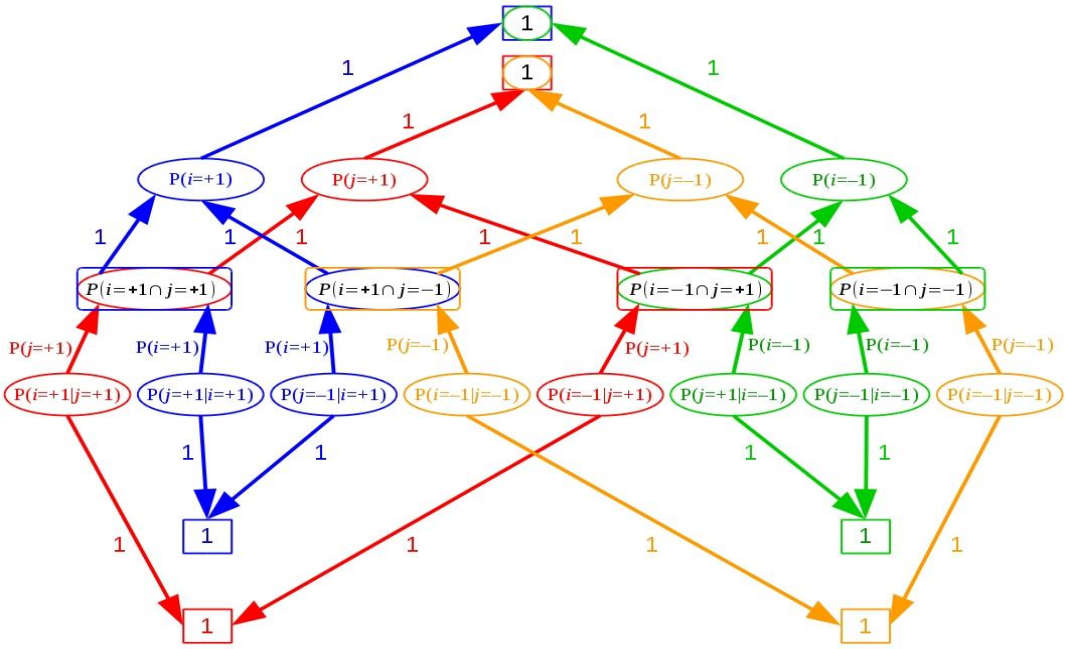

Fig. 10. Treatment of diagnostic testing via a Signal Flow Graph (in a fashion that mimics a trinomial graph) so as to relate the conditional, marginal and conjunctive probabilities of a contingency table. This SFG differs from a standard one, since a conjunctive probability is expressed *via* one only of the two arrows incident on it.

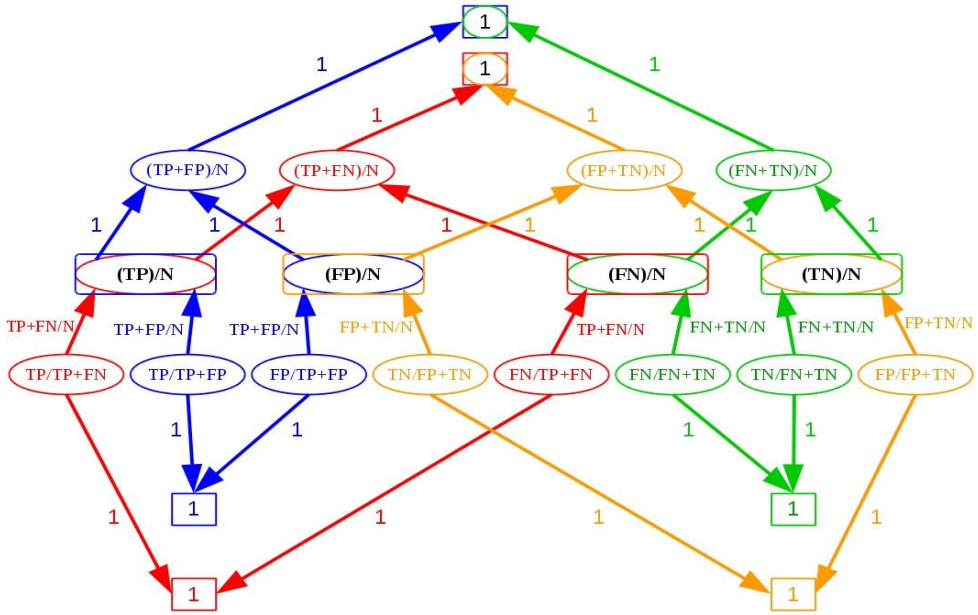

Fig. 11. The Signal Flow Graph in Fig. 10 with natural-frequency format. Each of the conditional, marginal and conjunctive probabilities in Fig. 10 is replaced by its expression as a quotient of natural frequencies

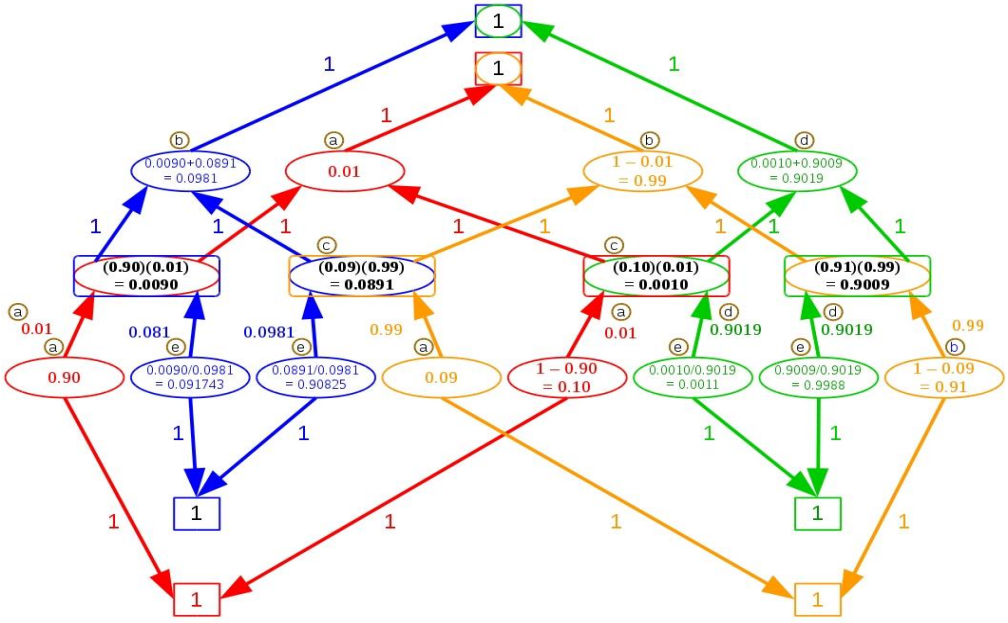

Fig. 12. Complete evaluation of all the conditional, marginal and conjunctive probabilities of the contingency table for the running example problem. The evaluation is accomplished in five stages (a)-(e) with stage (a) for simply inserting the input data

6. CONCLUSION

This paper is a tutorial review of novel representations or tools of conditional probabilities that enhance understanding, simplify calculations, foster insight, and facilitate reasoning. Such representations are of general utility, but their benefits to medical disciplines are stressed herein. One of the proposed representations, *viz.,* visualization *via* a Karnaugh map has many distinctive advantages. In particular, the Karnaugh map acts as a liaison or a link between the theoretically-rigorous concept of conditional probability and the pedagogically-popular concept of a contingency table (with the associated natural frequencies) [36]. Another representation *via* Signal Flow Graphs is quite promising and leads to obvious enhancements for specific problems such as the ternary problem of conditional probability. The bulk of this paper is devoted to understanding problem reformulation in terms of natural frequencies. Advantages of, and misconceptions about, this reformulation are highlighted. A detailed numerical example is also used to reveal the nature of such a reformulation, and to demonstrate other tools as well. The moral or significance of the example is that a good representation leads to a problem already half solved.

Though all the representations or tools discussed herein seem appealing and produce the same results for the same clinical example, they need to be tested in real-life situations with groups of physicians and medical students. Many research questions are still to be addressed in future investigations. These might include deciding the effect of employing one particular tool on how clinicians might interpret diagnostic test results, as well as the determination of the clinical instances where one tool is more appropriate than another.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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