A Method Expanding 2 by 2 Contingency Table by Obtaining Tendencies of Boolean Operators: Boolean Monte Carlo Method

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Abstract: A medical test and accuracy of diagnosis are often discussed with contingency tables. However, it is difficult to apply a contingency table to multivariate cases because the number of possible categories increases exponentially. We hypothesize that randomly assigning Boolean operators and focusing on frequencies of Boolean operators could explain the outcome correctly, obtain the tendencies of operators, and overcome difficulties in analyzing large numbers of variables and categories. The aims

of this paper are introducing a method to obtain tendencies of Boolean operators and expanding 2 by 2 contingency tables to multivariate cases. To test this method, we construct two types of data: 1) when variables and outcome were randomly determined and 2) when the outcome depends on one variable. Analysis of the first type of data by this method showed that there was no significant result. Analysis of the second type of data reflected the bias of the data. As far as we know, this is the first attempt to use a frequentist approach to randomly assigned Boolean operators.

Key words: Boolean operator; Monte Carlo method; frequentist approach; contingency table

1 Introduction

Boolean algebra for Boolean parameters (often represented by binomial variables 0, 1) is a field of mathematics ([Givant and Halmos, 2009](#)) and has been applied to other fields, e.g., circuit of computer science, cryptography, and medicine ([Wu and Feng, 2016](#)). In these applications, Boolean function $f : \{0, 1\}^n \rightarrow \{0, 1\}$ is constructed by *not*, *and*, *or*, and parentheses. In medicine, 0 and 1 are used to represent medical test results and whether a patient has a disease or a symptom. One of the most useful applications of binominal variables in medicine is a contingency table. Contingency tables enable us to discuss the usefulness of a medical test and diagnostic performance. However, it is difficult to apply a contingency table to a situation with multivariables. When we use N binomial variables, the number of categories is 2^N . The number of possible categories increases exponentially, making it difficult to model interactions

of variables. Moreover, taking the interaction of variables into consideration, we cannot get a large enough sample size for each category. We hypothesize that randomly assigning Boolean operators and focusing on frequencies of Boolean operators could explain the outcome correctly, obtain the tendencies of operators, and overcome difficulties in analyzing large numbers of variables and categories. The aims of this paper are introducing a method called the Boolean Monte Carlo Method (BMCM) to obtain tendencies of Boolean operators and expanding 2 by 2 contingency tables for use in multivariate situations.

2 Method

This method was composed of three steps. In the first step, we defined 4 kinds of null data as follows: 1) all explanatory variables were 1 and the objective variable was 1, 2) all explanatory variables were 0 and the objective variable was 0, 3) all explanatory variables were 1 and the objective variable was 0 and 4) all explanatory variables were 0 and the objective variable was 1. Then we created data that only contained null data and performed a chi-square test (Fishers exact test). This was done because results from a Boolean operation for null data are trivial (Figure 1). For example, when all explanatory variables were 0, the result was 0 whether *and* or *or* was used for each operation. When performing a chi-square test for a 2 by 2 contingency table that includes null data with trivial results, we might underestimate the trends of data (Figure 1). Meanwhile, we could use null data to see a rough trend. When explanatory variables are all 0 (1), objective variables should tend to be 0 (1). If there was no such trend, this method would make no sense, and we

should change the variables or hypothesis. In the second step, we constructed a model and analyzed the operator trends. We constructed a model and randomly allocated operators between explanatory variables. In constructing the model, we adjusted orders of explanatory variables with parentheses. We performed operations and checked whether the randomly assigned operators could explain an objective variable. If the operator cannot explain the objective variable, we call this type of operator unfaithful. After we examined all data, we analyzed each operator that was grouped as faithful with a chi-square binomial test. As operators were assigned by the same probability, $1/2$, we could detect a tendency by examining the frequency of *and* or *or*. After the second step, we determined proper operators. In the third step, proper operators from the second step were used. We applied these operators to the original data and made a 2 by 2 contingency table. Finally, we performed a chi-square test. In Figure 2, the summary of these steps is shown. In this paper, we call this the Boolean Monte Carlo Method (BMCM).

$$\begin{aligned}
 & x_1 \square x_2 \square \cdots \square x_{n-1} \square x_n = x_O \\
 & 1) \ 1 \square 1 \square \cdots \square 1 \square 1 = 1 \\
 & 2) \ 0 \square 0 \square \cdots \square 0 \square 0 = 0 \\
 & 3) \ 1 \square 1 \square \cdots \square 1 \square 1 = 0 \\
 & 4) \ 0 \square 0 \square \cdots \square 0 \square 0 = 1
 \end{aligned}$$

Figure 1: Null data such as 1) and 2) were satisfied whether we used *and* or *or* for each operation. Each combination of operators was obtained by probability $1/2^n$ and trend might be hidden. Null data such as 3) and 4) were not satisfied whether we used *and* or *or* for each operation.

Figure 2: Three steps of boolean monte calro method. 1st step, null data was analyzed. 2nd step, data excluded null data was analyzed. 3rd step, analysis for original data was performed.

Table 1: Categorization of Boolean function calculation and outcome. When the Boolean function calculation was equal with outcome, we categorized it as "faithful". When the Boolean function calculation was not equal with outcome, we categorized it as "unfaithful".

	$x_O = 1$	$x_O = 0$
$f(x_1, \dots, x_n) = 1$	faithful	unfaithful
$f(x_1, \dots, x_n) = 0$	unfaithful	faithful

3 Example

In this section, we applied the BMCM to a sample data set. The data contained 1,000 observations for three variables x_1, x_2, x_3 and outcome x_O . In this data, x_1 determined x_O , and x_2 and x_3 were determined randomly, i.e., if $x_1 = 1$ then $x_O = 1$ and if $x_1 = 0$ then $x_O = 0$. The half of x_1 and half of x_O were 1 (Figure 3).

	x_1	x_2	x_3	x_O
1,000 data prepared	1	Variables in this area are determined randomly (0 or 1).		1
	$\vdots$			$\vdots$
	1			1
	0			0
	$\vdots$			$\vdots$
	0			0

Figure 3: x_1 determined x_O , and x_2 and x_3 were determined randomly.

Null data analysis

Table 2 shows the contingency table for null data. Fisher's exact test showed that there was a significant difference in the proportions of x_O between $x_1 = x_2 = x_3 = 1$ and $x_1 = x_2 = x_3 = 0$ ($\chi^2 = 2.4 \times 10^2, p = 1.1 \times 10^{-53}$).

Model: $x_1 x_2 x_3 = x_O$

A chi square binomial test for faithful data showed that in operator 1 *or* had a higher probability than *and* ($\chi^2 = 41, p = 1.6 \times 10^{-10}$) and in operator 2 *and* had a higher

Table 2: Null data analysis for data in which x_1 associated with x_O .

	$x_O = 1$	$x_O = 0$
all 1	120	0
all 0	0	122

probability than *or* ($\chi^2 = 42, p = 8.5 \times 10^{-11}$). Similarly, a chi-square binomial test for unfaithful data showed that in operator 1 *and* had a higher probability than *or* ($\chi^2 = 55, p = 1.0 \times 10^{-13}$) and in operator 2 *or* had a higher probability than *and* ($\chi^2 = 57, p = 4.4 \times 10^{-14}$).

Model: $x_1 x_3 x_2 = x_O$

A chi square binomial test for faithful data showed that in operator 1 *or* had a higher probability than *and* ($\chi^2 = 34, p = 6.4 \times 10^{-9}$) and in operator 2 *and* had a higher probability than *or* ($\chi^2 = 35, p = 3.6 \times 10^{-9}$). Similarly, a chi-square binomial test for unfaithful data showed that in operator 1 *and* had a higher probability than *or* ($\chi^2 = 47, p = 7.0 \times 10^{-12}$) and in operator 2 *or* had a higher probability than *and* ($\chi^2 = 49, p = 3.2 \times 10^{-12}$).

For the third step, we analyzed the original data when the operator in 1 is *or* and the operator in 2 is *and*. Table 3 shows the result of the analysis of the original dataset, including null data and other data. Fisher's exact test showed that there was a significant difference in the proportions of x_O between $f(x_1, x_2, x_3) = 1$ and $f(x_1, x_2, x_3) = 0$ ($\chi^2 = 5.8 \times 10^2, p = 1.7 \times 10^{-128}$).

Table 3: Contingency table for 3rd step.

	$x_O = 1$	$x_O = 0$
$f(x_1, x_2, x_3) = 1$	500	131
$f(x_1, x_2, x_3) = 0$	0	369

4 Discussion

In this study, we proposed a new method (BMCM) to model interactions of binomial variables by assigning Boolean operators, and to expand the 2 by 2 contingency table to handle multivariate cases. We applied the BMCM to data of which variables and outcome were randomly determined. This analysis showed that there was no significant result (Appendix). We applied the BMCM to data that was dependent on one variable. This data had null data, which was significant, and some operators could be determined. In the model $x_1x_2x_3 = x_O$, 1 tended to be *or* and 2 tended to be *and*. When 1 was *or* and 2 was *and*, the calculation between x_2 and x_3 was performed first, and then the calculation between x_1 and the result of x_2x_3 was performed. This model with operators (1= *or*, 2= *and*) might reflect the fact that x_1 determined x_O , and x_2 and x_3 were assigned randomly. We could interpret the model $x_1x_3x_2 = x_O$, in the same way because there was symmetry between x_2 and x_3 . Applications of Boolean functions have been attempted in medicine. Previous studies applied this method mainly for the gene regulatory network (GRN). In these studies, to construct GRN models, operators between variables should be determined using methods such as the Bayesian approach (Lin and Khatri, 2014; Zhou et al., 2004), Markov chain approach (Xiao, 2009), and satisfiability problem solver (SAT solver) approach (Moskewicz et al.; Lin and Khatri, 2012). These studies construct

models of mutual interaction of genes by operators. These mutual interactions often can be interpreted as a GRN. A hypothesis of constructing a GRN randomly was also reported. [Kauffman \(1969\)](#) studied an approach for a GRN that is randomly connected. [Pal et al. \(2005\)](#) discussed a method to construct random attractors to examine GNR. To our knowledge, the combination of random assignment of operators and the frequentist approach to operators have not been reported. We consider this method can be applied not only to genes, but also to medical tests because the BMCM can expand the 2 by 2 contingency table. This expansion enables us to discuss the odds ratio in multivariate cases. A logistic regression model is also used to estimate the odds ratio in multivariate cases. Using a logistic regression model, we can calculate additive interactions of variables ([Hosmer et al., 2013](#)). However, when we assume explanatory variables are independent of each other, we cannot consider non-additive interactions. [Pepe \(2004\)](#) pointed out that there was a pitfall in using the logistic regression model for medical markers. They argued that strong associations are required for meaningful classification accuracy in using the logistic regression model. The BMCM has a disadvantage in weighting variables, similar to the logistic regression model, whereas it has an advantage in modeling interactions. Thus, the BMCM can be an option to evaluate medical markers. This study has some limitations. First, this method can be applied only to binomial data. Second, an interpretation of results can be complex (Appendix), as the number and order of variables and positions of parentheses increase exponentially. Moreover, variables can be incommutable. Third, when a contingency table is written, we can use different functions. For example, we can choose a function to maximize sensitivity and choose another function to maximize specificity. There can be many cross tables and there may be a person who does not belong to any faithful categories. In this case, we

should index the number of stateless persons. To clarify properties of this method, further study should be done.

5 Conclusion

We introduced a method, BMCM, to determine operators between binomial variables using a frequentist approach. This method can expand a 2 by 2 contingency table.

Appendix

In this paper, we examined some models that did not have any significant results. These results are summarized in the appendix.

Randomly determined variables and outcome

This data contained 1,000 observations to three variables x_1 , x_2 , x_3 and outcome x_O . In this data 0, 1 is randomly assigned to x_1 , x_2 , x_3 , and x_O (Figure 4). There was no significant result because this data had no tendency.

Null data analysis

Table 4 shows the contingency table for null data. Fisher's exact test showed that there was no difference in the proportions of x_O between $x_1 = x_2 = x_3 = 1$ and $x_1 = x_2 = x_3 = 0$ ($\chi^2 = 0.0036, p = 0.95$).

Model: $x_1 x_2 x_3 = x_O$

	x_1	x_2	x_3	x_O
1,000 data prepared	Values were determined randomly (0 or 1).			

Figure 4: x_1 , x_2 , x_3 and x_O were determined randomly.

Table 4: Null data analysis for random data.

	$x_O = 1$	$x_O = 0$
all 1	58	59
all 0	65	65

A chi-square binomial test for faithful data showed that there was no bias in 1 ($\chi^2 = 0.0027, p = 0.96$) and in 2 ($\chi^2 = 0.53, p = 0.47$). Similarly, a chi square binomial test for unfaithful data showed that there was no bias in 1 ($\chi^2 = 0.0026, p = 0.96$) and in 2 ($\chi^2 = 0.51, p = 0.47$).

Model: $x_1x_3x_2 = x_O$

A chi square binomial test for faithful data showed that there was no bias in 1 ($\chi^2 = 0.15, p = 0.70$) and in 2 ($\chi^2 = 0.081, p = 0.78$). Similarly, a chi square binomial test for unfaithful data showed that there was no bias in 1 ($\chi^2 = 0.15, p = 0.70$) and in 2 ($\chi^2 = 0.080, p = 0.78$).

Model: $x_2x_1x_3 = x_O$

A chi square binomial test for faithful data showed that there was no bias in 1 ($\chi^2 = 0.011, p = 0.92$) and in 2 ($\chi^2 = 0.61, p = 0.44$). Similarly, a chi square binomial test for unfaithful data showed that there was no bias in 1 ($\chi^2 = 0.010, p = 0.92$) and in 2 ($\chi^2 = 0.59, p = 0.44$).

Model: $(x_1x_2)x_3 = x_O$

A chi square binomial test for faithful data showed that there was no bias in 1 ($\chi^2 = 0.033, p = 0.86$) and in 2 ($\chi^2 = 0.73, p = 0.39$). Similarly, a chi square binomial test for unfaithful data showed that there was no bias in 1 ($\chi^2 = 0.032, p = 0.86$) and in 2 ($\chi^2 = 0.72, p = 0.40$).

Model: $(x_3x_1)x_2 = x_O$

A chi square binomial test for faithful data showed that there was no bias in 1 ($\chi^2 =$

0.69, $p = 0.41$) and in 2 ($\chi^2 = 0.024, p = 0.88$). Similarly, a chi square binomial test for unfaithful data showed that there was no bias in 1 ($\chi^2 = 0.67, p = 0.41$) and in 2 ($\chi^2 = 0.023, p = 0.88$).

Model: $(x_2 1 x_3) 2 x_1 = x_O$

A chi square binomial test for faithful data showed that there was no bias in 1 ($\chi^2 = 0.00066, p = 0.98$) and in 2 ($\chi^2 = 0.41, p = 0.52$). Similarly, a chi square binomial test for unfaithful data showed that there was no bias in 1 ($\chi^2 = 0.00067, p = 0.98$) and in 2 ($\chi^2 = 0.42, p = 0.52$).

Data of which outcome depends on a variable

This data was the same data used in section 3.

Model: $x_2 1 x_1 2 x_3 = x_O$

A chi square binomial test for faithful data showed that there was no bias in 1 ($\chi^2 = 0.29, p = 0.59$) and in 2 ($\chi^2 = 0.42, p = 0.52$). Similarly, a chi square binomial test for unfaithful data showed that there was no bias in 1 ($\chi^2 = 0.29, p = 0.59$) and in 2 ($\chi^2 = 0.41, p = 0.52$). In this model, the tendency of x_1 might be absorbed in the first calculation ($x_1 1 x_2$) because x_2 was randomly determined.

Model: $(x_1 1 x_2) 2 x_3 = x_O$

A chi square binomial test for faithful data showed that there was no bias in 1 ($\chi^2 = 0.19, p = 0.66$) and in 2 ($\chi^2 = 0.30, p = 0.59$). Similarly, a chi square binomial test for unfaithful data showed that there was no bias in 1 ($\chi^2 = 0.19, p = 0.66$) and in 2 ($\chi^2 = 0.29, p = 0.59$). In this model, the tendency of x_1 might be absorbed in the

first calculation $(x_1 1 x_2)$ because x_2 was randomly determined.

Model: $(x_3 1 x_1) 2 x_2 = x_O$

A chi square binomial test for faithful data showed that there was no bias in 1 ($\chi^2 = 0.19, p = 0.66$) and in 2 ($\chi^2 = 0.11, p = 0.74$). Similarly, a chi square binomial test for unfaithful data showed that there was no bias in 1 ($\chi^2 = 0.19, p = 0.66$) and in 2 ($\chi^2 = 0.11, p = 0.74$). This model can be interpreted in the same way as $(x_1 1 x_2) 2 x_3 = x_O$.

Model: $(x_2 1 x_3) 2 x_1 = x_O$

A chi square binomial test for faithful data showed that there was no bias in 1 ($\chi^2 = 0.0080, p = 0.93$) and in 2 ($\chi^2 = 0.0, p = 1.0$). Similarly, a chi square binomial test for unfaithful data showed that there was no bias in 1 ($\chi^2 = 0.016, p = 0.90$) and in 2 ($\chi^2 = 0.0, p = 1.0$). In this model, the tendency of 2 might be canceled out when $x_1 = 1$, 2=or satisfied $x_O = 1$, and when $x_1 = 0$, 2=and satisfied $x_O = 0$.

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