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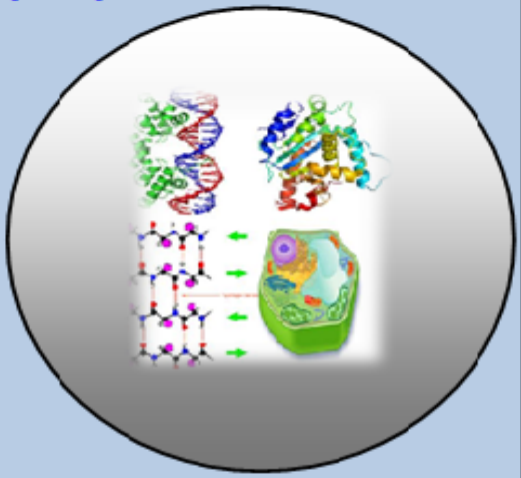

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Estimation of Information Matrix in the Dynamic Model of Patient's Conditions Influenced by the Applied Treatment

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ABSTRACT

The dynamic model of Model of Patient's Conditions Influenced by the applied treatment alternatives was introduced by Zaidi and Zaidi. This model categorized disease/patient properties into two parts. One is treatment independent, say patient age/gender, duration of disease etc. A database can be maintained for these properties and their interaction with drug qualities in the form of a matrix called information matrix. A suitable estimator for the information matrix can be obtained via generalized least squares method, which is a popular tool of mathematical statistics.
Keywords: Informaion Matrix, Dynamic Model, Disease and Mathematical Statistics.

INTRODUCTION

The dynamic model of Model of Patient's Conditions Influenced by the applied treatment alternatives was introduced by Zaidi and Zaidi [2016]. There developed a general user interfaced algorithm in the form of time dependent dynamic model with the help of concepts of vectors and matrices of mathematics and which includes various qualities/properties of drugs/treatment. The model comprises drug applicability with intensity of disease after integrating the patient data (medical history, family history, signs, and symptoms).

The basic feature of the dynamic model was to measure drug qualities subjectively with fuzzy scale with range 0 to 1, where 0 represents the worst and 1 represents the best.

Further the combination of all drug qualities of the drug α made the drug effect vector

$$M_{\alpha}\,(\alpha = 1, 2, \ldots, m) \qquad \ldots\ldots(1)$$

Where m (The number of available treatment alternatives) is depend on the particular disease.

Now, $M_\alpha = M_\alpha(X_1, X_2, \ldots)$ ……(2)

That is, all M_α's are the functions of drug effect variables X_1, X_2,…

Where X_1 is the variable associated with drug efficacy, X_2 is the variable associated with safety profile, and so on.

Therefore X_j (j = 1,2,…) represents the j^{th} quality of the drug.

Each drug property X_j (j=1,2,…) is a fuzzy variable having values in the range $\left[X_j^l, X_j^u\right]$ with some associated membership function x_j of the form

$$\left[X_j^l, X_j^u\right] \xrightarrow{x_j} [0,1] \quad \ldots\ldots(3)$$

If the variable X_j has the lowest value X_j^l in the range, it means that its membership function x_j has the value 0 (zero). On the other hand if the variable X_j has the highest value X_j^u in the range, it means that its membership function x_j has the value 1 (one). For all the other values of X_j the membership function x_j has a value between 0 and 1. The basic assumption for all the drug qualities is that it can be scaled into worst to best range. That is X_j has value X_j^l as 'worst' and value X_j^u as 'best' with corresponding value x_j between 0 and 1.

For example consider the variable X_1, the efficacy of the drug. It has the values in the range $\left[X_1^l, X_1^u\right]$ with associated (real valued) membership function x_1, where X_j^l means nil efficacy with x_1 = 0 and X_j^u means perfect efficacy with x_1 = 1.

All the above drug properties can be represented by a fuzzy vector

$$M_\alpha = \left[X_1 \;\; X_2 \;\ldots\; X_{14}\right]^{\mathrm{T}}$$

We called the vector $M_\alpha = \left[X_1 \;\; X_2 \;\ldots\; X_{14}\right]^{\mathrm{T}}$ the Effect Vector.

Further treatments effects are related with disease/patient properties say duration, intensity or complications. The disease properties are again fuzzy variables, and can have the values for example as High, Low, Normal, Very Low, Very High and so on.

Disease/Patient Properties versus Treatment Effects

On the basis of literature, disease/patient properties for a particular disease α may be categorize into two parts

a.) Disease/patient properties those are treatment independent, say patient age/gender, duration of disease, complications present, previous histories, family history etc. Let we denote it by $I_1, I_2, \ldots, I_p$.'s , the p fuzzy variables and can be modified using expert (doctor's) interventions, in the sense that experts can decide which variable are included for α.

An example is the study by Yuequan et. al [2010] on prognostic factors and family history for survival of esophageal squamous cell carcinoma patients after surgery suggested that Family history of esophageal cancer is an important prognostic factor that surgeons should take into consideration when selecting a treatment method.

Another example is the study of Ralevski et. al. [2010] on analgesic effects of ethanol. In this study they concluded that neuroticism and family history of alcoholism both influence the analgesic response of alcohol.

After finalizing $I_k^{'s};\ k=1,2,...,p$'s for a particular disease, the real condition of the disease in a particular patient is represented by the vector

$I = [I_1, I_2,..., I_p]^T$ ……(4)

With corresponding membership vector

$i = [i_1, i_2,..., i_p]^T$ ……(5)

$i_k \in [0,1];\ k=1,2,...,p$

Where we can say

$i_k \to 1,$ for a better condition

and

$i_k \to 0,$ for a worst condition

It should be noted that if i_k is some patient characteristics say age or gender then we called it 'worst' if it is a high risk group (having higher probability) for the disease say older age or 'male' (say for hemophilia).

These properties are essential to make initial steps to take decision about treatment. So we called *I* as Information Vector. For the information vector, there exists a one way relation between *I* and the treatment properties.

i.e. $I_k \to X_i$, for some *i*; *i* =1,2,…,14; *k* =1,2,...,*p*

Since both sides of the relations are the fuzzy variables, therefore these relations can be evaluated using fuzzy rules. One good technique is to show the relation between I_p and X_i by a matrix of the form

$$\begin{array}{c} \\ i_1 \\ i_2 \\ . \\ i_p \end{array} \begin{array}{c} \begin{array}{cccc} x_1 & x_2 & ... & x_{14} \end{array} \\ \begin{bmatrix} \alpha_{11} & \alpha_{12} & ... & \alpha_{1,14} \\ \alpha_{21} & \alpha_{22} & ... & \alpha_{2,14} \\ . & . & ... & . \\ \alpha_{p1} & \alpha_{p1} & ... & \alpha_{p,14} \end{bmatrix} \end{array}$$

We called it the Information Matrix $A_{p\times 14}$. The basic assumption here making for the information matrix is that the relationship between the information variable and the drug quality variable is a constant positive value for each combination of information-drug quality variables.

The fuzzy values of drug qualities will be changed on disease conditions or states of the disease. Assuming that old drug qualities and disease influenced drug quality changes are additive in nature, a new membership function for drug qualities is evaluated as discussed in [1] by the formula

$$\begin{bmatrix} x_1 \\ x_2 \\ . \\ x_{14} \end{bmatrix}_{\text{improved by } I} = \begin{bmatrix} x_1 \\ x_2 \\ . \\ x_{14} \end{bmatrix}_{\text{General}} + \begin{bmatrix} \alpha_{11} & \alpha_{12} & ... & \alpha_{1,14} \\ \alpha_{21} & \alpha_{22} & ... & \alpha_{2,14} \\ . & . & ... & . \\ \alpha_{p1} & \alpha_{p2} & ... & \alpha_{p,14} \end{bmatrix}^T \begin{bmatrix} i_1 - 0.5 \\ i_2 - 0.5 \\ . \\ i_p - 0.5 \end{bmatrix} \quad \text{.....(6)}$$

or in usual notations

$$X_{\text{improved by } I} = X_{\text{General}} + A^{\mathrm{T}} I - A^{\mathrm{T}} I_{0.5} \quad \text{.....(7)}$$

Where $I_{0.5}{}^{\mathrm{T}} = \begin{bmatrix} 0.5 & 0.5 & ... & 0.5 \end{bmatrix}$

subject to :

$x_j > 1 \Rightarrow x_j = 1$

and

$x_j < 0 \Rightarrow x_j = 0 \ ; \ j = 1,2,...,14$

It should be noted that

X_{General} are the observed qualities of the drug at $I = I_{0.5}$

b.) Disease properties those are treatment dependent, say intensity of disease, health recovery or complications initiated during treatment. For example Depression and anxiety are common in medical patients and are associated with diminished health status. We called these properties 'conditions'. Let we denote the 'conditions' by $D_1, D_2, ..., D_q$.

The estimation of information matrix is rather easy in comparison to the treatment dependent disease properties. Let us discuss tools of its estimation.

Estimation of Information Matrix

Usually the information, condition and improvement matrices will be unknown in practice and have to be estimated from the available data before the model can be used for forecasting and analysis purposes.

Consider the information matrix

$$A = \begin{array}{c} \\ i_1 \\ i_2 \\ . \\ i_p \end{array} \begin{array}{c} \begin{array}{cccc} x_1 & x_2 & ... & x_{14} \end{array} \\ \begin{bmatrix} \alpha_{11} & \alpha_{12} & ... & \alpha_{1,14} \\ \alpha_{21} & \alpha_{22} & ... & \alpha_{2,14} \\ . & . & ... & . \\ \alpha_{p1} & \alpha_{p1} & ... & \alpha_{p,14} \end{bmatrix} \end{array} \quad \text{.....(8)}$$

For the estimation of coefficients of matrix *A*, we will use the equation

$$X_{\text{improved by } I} = X_{\text{General}} + A^{\mathrm{T}} I - A^{\mathrm{T}} I_{0.5} \quad \text{.....(9)}$$

and using the assumption

X_{General} are the observed qualities of the drug at $I = I_{0.5}$,

We have $E\left(X_{\text{improved by } I}\right) = E\left(A^{\mathrm{T}} I\right)$ ……(10)

and for the j^{th} property of the drug, the equation has the shape

$$x_{j(improved)} = x_{j(General)} + \sum_{k=1}^{p} \alpha_{kj} \cdot \left(i_k - 0.5\right) \quad \text{……(11)}$$

Let for the different observation on i_k, (k=1,2,...,p), there comes out to be different observed values of x_j for random selection of different available treatments . So on different observations on x_j, we get a linear regression model of the form

$$\begin{bmatrix} x_{j(1)} \\ x_{j(2)} \\ . \\ x_{j(h)} \end{bmatrix}_{improved} = \begin{bmatrix} x_{j(1)} \\ x_{j(2)} \\ . \\ x_{j(h)} \end{bmatrix}_{general} + \begin{bmatrix} i_{1(1)} - 0.5 & i_{2(1)} - 0.5 & \ldots & i_{p(1)} - 0.5 \\ i_{1(2)} - 0.5 & i_{2(2)} - 0.5 & \ldots & i_{p(2)} - 0.5 \\ . & . & \ldots & . \\ i_{1(h)} - 0.5 & i_{2(h)} - 0.5 & \ldots & i_{p(h)} - 0.5 \end{bmatrix} \begin{bmatrix} \alpha_{1j} \\ \alpha_{2j} \\ . \\ \alpha_{pj} \end{bmatrix} + \begin{bmatrix} e_{j(1)} \\ e_{j(2)} \\ . \\ e_{j(h)} \end{bmatrix}$$

……(12)

This expression may be written compactly as,

$$X_{j(improved)} = X_{j(general)} + \left(I_j - \left[0.5\right]_{h \times p}\right) A_j + e_j \quad \text{……(13)}$$

Where X_j is a $(h \times 1)$ vector ($h \geq p$) of j^{th} drug quality, I_j is the information matrix of order $(h \times p)$ for the j^{th} drug property based on h observations, A_j is the $(p \times 1)$ coefficient vector, which is the j^{th} column of the information matrix $A_{p \times 14}$ and e_j is a random vector of order $(h \times 1)$. According to the basic assumption of linear regression model, e_j has a mean vector of 0 and a variance-covariance matrix of $\sigma^2 U$, where U is the unit matrix of order $(h \times h)$.

Now we can estimate the vector A_j. One good method to find the estimate is the generalized least squares rule.

Generalized least squares (GLS) is a technique for estimating the unknown parameters in a linear regression model. GLS can be used to perform linear regression when there is a certain degree of correlation between the residuals in a regression model. In these cases, ordinary least squares and weighted least squares can be statistically inefficient, or even give misleading inferences. GLS was first described by Alexander Aitken in 1934.

The generalized least squares estimate of A_j is given by

$$\hat{A}_j = \left(\left(I - \left[0.5\right]\right)_j^T \left(I - \left[0.5\right]\right)_j\right)^{-G} \left(I - \left[0.5\right]\right)_j^T X_{j(\text{improved})} \text{; } j = 1,2,\ldots,14 \quad \text{……(14)}$$

Where K^{-G} denotes the generalized inverse of the matrix K. Its details can be taken from Rao C. R et.al, 1971

So in this way we can find the information matrix A.

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