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Application of Discrete-Time Markov Model Models In Medical Prognosis

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ABSTRACT

The paper probes into the applications of Discrete-time Markov Models in the fields of Medical Prognosis and disease prediction.

Markov Models are quite popular and extensively deployed in fields like Medicine and Engineering to model phenomena owing to their relative simplicity yet remarkable accuracy. Medical Prognosis using Markov Models involves classifying specific health states based on clinical measures and modelling subsequent transitions between them. The transition matrix thus obtained is solved by Gauss Jordan elimination to get the average number of cycles a patient stays in a particular state. The salient feature that differentiates Markov models from existing methods is the fact the future state depends exclusively on the present state only, irrespective of patient's history. This helps researchers get past vast multitude of computations, while delivering reliable results. Here we utilise the absorbing Markov Model to map out the likely course of a patient's health status, where the initial state influences the final state.

INTRODUCTION

Estimation of prognosis under a definite clinical treatment is crucial in therapeutic decision making. Any treatment administered aims to alleviate the impact and eliminate any underlying morbidity. Thus, having knowledge of the probable outcomes a priori can significantly enhance the treatment being administered and plan for any future interventions required beforehand. Current methods used for predictions are computationally intensive involving numerous variables and are not of any help when the sequence of the patient's condition can reverse to a previous state as well. Diseases where one may attain a particular health status more than once, Markov Model fares well since we solely consider the present conditions as a means to predict the future, without any reference to the patient's medical history. Thus, providing better and more accurate results and predictions.
Markov Models are described in terms of the clinical conditions of patients i.e. "Health states" and the entailing transition probabilities between these states in a fixed cycle period. Our model involves categorisation into 3 states of well-being, namely: 'Well', 'Ill' and 'Dead' and modelling the subsequent transition probabilities. These probabilities are calculated based on numerous parameters (which we haven't discussed in our paper owing to certain limitations) and previous datasets. So, well-defined, and more robust states and probabilities accounting for maximum parameters will ensure more accurate and reliable results.
Henceforth, we computed the expected time period a patient is likely to spend in a particular state and the overall life expectancy of the patient. We utilized Gauss Jordan elimination for finding inverses and developed codes for multiplying multiple matrices simultaneously, replicating the results in the original paper.

BACKGROUND INFORMATION

1) Markov Property / Memoryless Property –

On a given probability space (Ω,F,P), let X be a random variable, $X: \Omega \rightarrow \mathbb{R}$. We define the conditional probability here such that if the probability $P(X > t + s \mid X > s) = P(X > t)$ satisfies, then, this random variable X is said to satisfy the Markov property/ Memoryless property.

Let a sequence of random variables $(X_n) = (X_0, X_1, X_2, \ldots)$ be a stochastic process in discrete time $(n = 0,1,2,..)$ and discrete space S, then this process is called **Discrete Time Markov Process** if it satisfies the condition $P(X_{n+1} = i_{n+1} \mid X_n = i_n, X_{n-1} = i_{n-1}, \ldots, X_0 = i_0) = P(X_{n+1} = i_{n+1} \mid X_n = i_n)$.

So, this property suggests that the probability that we go to the state X_{n+1} depends only on the previous state X_n. In simpler words, given the present, the future doesn't depend on the past.

For a Discrete Time Markov chain, we define $p_{ij}^{(m)} = P(X_{n+m} = j \mid X_n = i)$ which gives the probability that starting from state i in nth trial, we end up in state j in (m+n)th trial. This means we took m steps here. Define m-step transition matrix $P^{(m)} = [p_{ij}^{(m)}]_{i,j \in S}$.

For m = 1, probabilities $p_{ij} = P(X_{n+1} = j \mid X_n = i)$ are known as transition probabilities or one step probabilities which are independent of n. The matrix P is then called as transition matrix. Always, $p_{ij} >= 0$ and $\sum_{j \in S} p_{ij} = 1$.

Thus, for some initial probability distribution defined as π (vector): $\pi_i = P(X_0 = i)$, for a Discrete Time Markov process, if we know the probability function of transitions we can measure the probability of going from a state i ($\in$ S) to state j ($\in$ S) in m ($\in$ N) steps .

2) Definitions –

1) **Absorbing state** – A state j (€ S) is called absorbing state if pjj = 1.
2) **Recurrent state** – If the return to a state j is certain then state j is called recurrent.
3) **Transient state** – Any state which is not recurrent is called transient.

The transition matrix P can be rewritten in the canonical form,

$$P = \begin{pmatrix} R & 0 \\ A & B \end{pmatrix}$$

where,

i) Submatrix R is of transition probabilities between recurrent states.
ii) Submatrix A is of transition probabilities from transient to recurrent states
iii) Submatrix B is of transition probabilities between transient states.
iv) Submatrix 0 is zero matrix.

Definitions (contd.)

4) Fundamental matrix M –

It is defined as $M = (I - B)^{-1}$ where I is the identity matrix and B is given above.
The entry m_{ij} of matrix M gives the expected number of visits in transient state j (€ S) if process initiates in the transient state i (€ S) before absorption occurs.

5) Absorption probability matrix G -

It is defined as G = MA where M and A are given above.
The entry g_{ij} of matrix G gives the probability that the process reaches the recurrent state j (€ S) if the process initiates in the transient state i (€ S).

We can thus get the probability that a process starting in the transient state i (€ S), absorbs in the state j (€ S) since absorbing states are recurrent.

PROBLEM FORMULATION

A patient's current year medical state can be used to predict his/her life expectancy by modelling the situation into the Markov model.

Let X be the random variable which gives the health state of an individual. The collection $(X_t) = (X_0, X_1, \dots, X_n)$ is a stochastic process which satisfies the Markov property that given the present health state, the future health condition depends only on the present and not on the past years health state. The index set here are years t = 0, 1, 2,… . This means that this model uses a yearly cycle length.

We will here define the health of an individual in three states that are Well, ill, and Dead. Let well state be described by 1, ill state by 2, and dead state by 3. At any time (year), t, a patient resides in one of these three states. The state space is given by S: S = {1,2,3}.

Hence, the above is a Discrete Time Markov Process.

Considering the example from the study by Beck, Robert, and Stephen in medical prognosis. The study estimates an individual's prognosis and research come up with the following transition probabilities.

From state 1, in one transition it is possible to move to state 2 or remain in state 1 or go to state 3.

From state 2, in one transition it is possible to remain in state 2 or move to state 3.

In state 3, since it is the dead state, we can't get back to states 1 and 2. Once the process reach state 3, it remains in state 3. Thus, it is an absorbing state.

They came up with the transition probability matrix P for an individual in different clinical states given by,

$$\begin{array}{cc} & \begin{array}{ccc} \text{Well} & \text{ill} & \text{Dead} \end{array} \\ P = & \begin{bmatrix} 0.3 & 0.5 & 0.2 \\ 0 & 0.5 & 0.5 \\ 0 & 0 & 1 \end{bmatrix} \end{array}$$

According to the above matrix, the probability of going from state 2 to state 3 in one step is 0.5 represented by $p_{23} = 0.5$. And since once we go to state 3, the probabilities $p_{31} = p_{32} = 0$ and $p_{33} = 1$. Thus, state 3 is absorbing state.

NUMERICAL APPROACH

Since the state3 is absorbing state, we can intuitively see that after a period of time every process would end up in the absorbing state 3.

Generating matrix $P^{(4)}$ and $P^{(10)}$ from the code 'matrixmult.cpp'.

$$P^{(4)} = \begin{bmatrix} 0.0081 & 0.136 & 0.8559 \\ 0 & 0.0625 & 0.9375 \\ 0 & 0 & 1 \end{bmatrix}$$

$$P^{(10)} = \begin{bmatrix} 5.9049e-06 & 0.00242664 & 0.997567 \\ 0 & 0.000976562 & 0.999023 \\ 0 & 0 & 1 \end{bmatrix}$$

It can be seen by above matrices that as the process goes forward (P is raised), the process will end up in absorbing state. This means that a patient will eventually die.

We want to know how much time a patient spent in well and ill states before dying. For this, we can use the fundamental matrix M.

The matrix P can be rearranged into the canonical form as –

$$P_c = \begin{bmatrix} 1 & 0 & 0 \\ 0.2 & 0.3 & 0.5 \\ 0.5 & 0 & 0.5 \end{bmatrix}$$

Here,

$R = [1]$ (Recurrent to Recurrent)

$A = \begin{bmatrix} 0.2 \\ 0.5 \end{bmatrix}$ (Transient to Recurrent)

$B = \begin{bmatrix} 0.3 & 0.5 \\ 0 & 0.5 \end{bmatrix}$ (Transient to Transient)

$O = [\, 0 \;\; 0 \,]$ (Zero Matrix)

$M = (I - B)^{-1}$ where I is an identity matrix of same order as B.

Generating matrix M from the code 'gaussJordan.cpp'

$$M = \begin{bmatrix} 1.42857 & 1.42857 \\ 0 & 2 \end{bmatrix}$$

RESULTS AND DISCUSSIONS

Above matrix says that expected time of stay in state 1 is 1.43 and expected time of stay in state 2 is also 1.43 given we start in state 1.

This means, that a **well person** will be expected to remain in **well** state for 1.43 cycles and he will be expected to remain in **ill** state for 1.43 cycles before dying. **Total life expectancy = 1.43 + 1.43 = 2.86 cycles.**

If a person starts in **ill** state, he will be expected to stay for 2 cycles in **ill** state before dying. **Total life expectancy = 2 cycles.**

This result is same as was obtained by the authors Beck, Robert and Stephen in their paper published on Medical Prognosis. [2]

ABSORPTION PROBABILITY (LEVEL 2)

What if there were more absorbing states?

If there more absorbing states, then we can calculate the probability of a process starting in the transient state i gets absorbed in state j using the matrix G.

$G = MA$

Let a experiment define the mind state into 4 states i.e. 1(suicidal); 2(severe depression); 3(mild depression); 4(seeking for psychiatric help).

We will model these states into a DTMC (X_n, n = 0,1,2,...).

Let one step transition probability matrix P,

$$P = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0.5 & 0 & 0.25 & 0.25 \\ 0.25 & 0.5 & 0 & 0.25 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

Rearranging the matrix P into canonical form gives,

$$P_c = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0.5 & 0.25 & 0 & 0.25 \\ 0.25 & 0.25 & 0.5 & 0 \end{bmatrix}$$

Here,

$R = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$

$A = \begin{bmatrix} 0.5 & 0.25 \\ 0.25 & 0.25 \end{bmatrix}$

$B = \begin{bmatrix} 0 & 0.25 \\ 0.5 & 0 \end{bmatrix}$

$O = \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix}$

States 1 and 4 are recurrent while states 2 and 3 are transient.

The fundamental matrix M is given by $M = (I - B)^{-1}$

Generating matrix M from the code 'gaussJordon.cpp' –

$M = \begin{bmatrix} 1.14286 & 0.285714 \\ 0.571429 & 1.14286 \end{bmatrix}$ having states 2 and 3.

This means that if we start the process in state 2, expected time of stay in state 2 before getting absorbed is 1.14286 and expected time of stay in state 3 before getting absorbed is 0.285714. Expected number of changes of state of mind before getting absorbed if we start in state 2 is (1.14286 + 0.285714) = 1.428574.

Similarly, if we start in state 3, Expected number of changes of state of mind before getting absorbed is (0.571429 + 1.14286) = 1.714289.

Now we want to know that if a student is currently in mild depression state i.e. state 3, what is the probability that he will seek professional psychiatric help?

We can get that using the matrix G = MA.

Generating matrix G using the code 'absorption_prob.cpp' ,

$$G = \begin{bmatrix} 0.642859 & 0.357144 \\ 0.571429 & 0.428572 \end{bmatrix}$$

This means that if we start in state 2, the probability that the process will get absorbed in state 1 is equal to 0.642859, the probability that it will get absorbed in state 4 is 0.357144.

Similarly, if we start in state 3, the probability that the process will get absorbed in state 1 is equal to 0.571429, the probability that it will get absorbed in state 4 is 0.428572.

Hence, if a student is currently in mild depression state i.e. state 3, the probability that he will seek professional psychiatric help i.e. state 4 is 0.428572.

CONCLUSION

We can model the real-world problems into Markov process so that predicting the future is comparatively easier than using statistical models for prediction because they are very complex. The important and making life easier property of Markov Chains is that we need not worry about the past if we know to present to predict the future.

Modelling medical prognosis into a Markov Chain resulted in us being capable of predicting the future health states of individuals and their life expectancy.

Level 2: We also concluded from a example modelled by Markov process that it is possible to calculate the probability of absorbing in a particular recurrent state (since there can be multiple absorbing states) if we start from a transient state.

SELF ASSESMENT

In our paper, we came up with a mathematical model for Disease Prognosis using Discrete-time Markov Model and utilized various numerical methods studied by us to deploy the same and reproduce the results in the original paper.

We learned about Markov Models and their extensive usage in making prediction models across a vast range of domains. Their sole reliance on the present conditions and relative simplicity make them a powerful tool in the decision making process. We scraped through a good number of real life case studies to comprehend and appreciate the same.

We developed C++ algorithms for Gauss Jordan Elimination to find the inverse of a matrix as well as developed on original code for multiplying multiple matrices simultaneously, drawing upon the knowledge imparted to us in the lectures. Our codes are attached herewith for your reference.

The entire paper was dedicated to describe the application of the Markov Models in the field of medical prognosis and showed that if transition probabilities are properly computed, we can obtain the expected time period a patient is likely to spend in a specific clinical state he was initially in, as well as get a fairly good estimate of the life expectancy of a patient.

Infact, we went beyond the original paper to compute the probability of getting absorbed in a particular state.

Our team has genuinely put sincere efforts to replicate the results in the original research paper, learning a lot of new concepts in the process. The paper gave us a platform to brainstorm upon both existing and new ideas, to come up with novel applications of the concepts taught and how real-world problems are modelled and solved. To conclude, this term paper was a great learning experience for each one of us.

REFERENCES

1) MTL106 DTMC Notes

2) (PDF) the Markov process in medical prognosis – researchgate https://www.researchgate.net/publication/16527320_The_Markov_Process_in_Medical_Prognosis

3) MTL106 University of Leeds Notes https://mpaldridge.github.io/math2750/S01-stochastic-processes.html