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Research Article

A New Markov Model for Analysing Cancer Markers in Disease Adjacent States and in Disease Non-Adjacent States

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Abstract

The present paper is aimed at newly writing a Markov model for transient states which are also not adjacent, from chains with discretised time variable. The fundamental matrix of the Markov chain is spelled out; the choice of the representation of the probability matrix is analytically determined. No indicators are needed for the likeli-hood tests.

Keywords: Chains Markov Models, Hidden Markov State Models, Transition Probabilities Adjacent States into Non Adjacent States

1.Introduction

In a Markov model for transition between stages of disease with discretized time is looked for, in which transitions are described within adjacent states only [1]. In a time-continuous Markov model is looked for; nevertheless, the investigation of is founded on the assumption that the model be time-independent [2]. In the Markov state landscape in investigated, for models in which short time events are also taken into account [3]. In citeref4p, non-Markov processes are analysed; more in detail, the 'marginal transition intensities' are used.

In the present paper, the hypothesis are taken (i.e. as from) about the composition (of individuals) of the sample that the 'state occupation processes' are 'independent and identically distributed' [4]. This hypothesis is not only compliant with the aims of, but it also facilitates the comparison of the presented model with non-Markov features [1].

In the time evolution of the element of the sample can be represented as moving within a succession of states. Within a 'multivariate survival scheme. The items of bibliography from mainly deal with models in which the state $k + 1$ (death) is at least not avoidable [4]. The analysis of is based, nevertheless, on non-Markov models endowed with 'estimators' [4].

In a Homogeneous Markov model of states $S_i(t)$, $i01$, $n$is considered, where the fundamental matrix is chosen as representing passages between states adjacent to the diagonal only [5]. A probability matrix is chosen; nevertheless, its consistency is not tested: differently, a 'logistic model' is used in Eq. (1) ibidem, where 'explanatory variables' are used for the 'misclassification' of pairs of stages.

1.1 The Paper is Organized as Follows

In Section 2, the model developed in is revised; in particular, the aspects are recapitulated, which delineate the model for transitions between adjacent states only in a Markov model with discretized time [1].

In Section 3, the new Markov model with discretized time is presented, in which transitions between non-adjacent states are also accounted for; more in detail, the fundamental matrix of the chain is newly written. Furthermore, the choice of the representation of the probability matrix is newly spelled out. No use of estimators is made.

2. Introductory Material

From the description is based on the items of information about the disease state at various time, where the disease states are numbered. In Table page. 855 ibidem, the 'time to death' is discretised in '*days*' units The aim in is to construct a Markov model of transient states between 'adjacent states' only from one disease states to another disease state during the discretised time; the aim is less broad that one prepared for in Table pag. 855 ibidem [1].

The methods for the 'inference' of the parameters are there developed as follows. The transition are considered, between adjacent states only. The transition rate from the state i o the state j of the disease are named λ_{ij} at a given discretised time, as $i,j = 1,..., k, i 6= j$; the entries μ's are those on the rightmost column: the state $k + 1$ is death. The functions $F_i(t;i)$ are named the 'functions for survival times' and are defined as $F(t;i) = Pr(T \leq t \mid state\ i\ at\ the\ time\ t = 0)$,i.e.

$$F(t;i) \equiv Pr_{i,k+1}(t). \quad (1)$$

The fundamental matrix of the chain is chosen in [1] as $\hat{Q}_K$ from with *T* the survival time as

$$\hat{Q}_K = \begin{bmatrix} Q_{K\ 11} & Q_{K\ 12} & 0 & ... & 0 & Q_{K\ 1,k+1} \\ Q_{K\ 21} & Q_{K\ 22} & Q_{K\ 23} & 0 & ... & Q_{K\ 2,k+1} \\ 0 & Q_{K\ 32} & Q_{K\ 33} & 0 & ... & Q_{K\ 3,k+1} \\ ... & ... & ... & ... & ... & ... \\ 0 & 0 & 0 & 0 & ... & 0 \end{bmatrix} \quad (2)$$

The fundamental matrix $\hat{Q}_K$ is chosen and here spelled out as containing states adjacent to the diagonal entries only.

The representation of the probability matrix $\hat{P}_K$ is chosen as follows. The entries *PK ij* of the probability matrix $\hat{P}_K$ are calculated as

$$\frac{d}{dt}\hat{P}_K(t) = \hat{P}_K(t)\hat{Q}_K. \quad (3)$$

The hypothesis (1) pag. 860 of [1]is required as the homogeneity of the parameters *λ*'s and *μ*'s within a statistical sample.

The indicators x_i from the vector $\vec{x}$ from which the new parameters $\lambda_{ij}(\vec{x})$ and $\mu(\vec{x})$are obtained for the sake of likelihood tests.

2.1 The Markov Model of Adjacent States and of Non-Adjacent States

A Markov model of adjacent states and of non-adjacent states is here newly constructed as follows. Generalized fundamental matrix $\hat{Q}$

$$\hat{Q} = \begin{bmatrix} Q_{11} & Q_{12} & Q_{13} & Q_{14} & ... & Q_{1,k+1} \\ Q_{21} & q_{22} & Q_{23} & Q_{24} & ... & Q_{2,k+1} \\ Q_{31} & Q_{32} & Q_{33} & Q_{34} & ... & Q_{3,k+1} \\ ... & ... & ... & ... & ... & ... \\ Q_{k+1,1} & Q_{k+1,2} & Q_{k+1,3} & Q_{k+1,4} & ... & Q_{k+1,k+1} \end{bmatrix} \quad (4)$$

where the entries λ^{ij} are now generalised from their role in [1] as

$$\hat{Q} = \begin{bmatrix} Q_{11} & \lambda_{12} & \lambda_{13} & \lambda_{14} & ... & \lambda_{1,k+1} \\ \lambda_{21} & Q_{22} & \lambda_{23} & \lambda_{24} & ... & \lambda_{2,k+1} \\ \lambda_{31} & \lambda_{32} & Q_{33} & \lambda_{34} & ... & \lambda_{3,k+1} \\ ... & ... & ... & ... & ... & ... \\ \lambda_{k+1,1} & \lambda_{k+1,2} & \lambda_{k+1,3} & \lambda_{k+1,4} & ... & Q_{k+1,k+1} \end{bmatrix} \quad (5)$$

With the new definition of Q_{kk} as

$$-Q_{kk} \equiv \left(\sum_{1\neq k} \lambda_{ik}\right) + \lambda_{k,k+1} \quad (6)$$

The choice of the transition probability matrix $\hat{P}$ is as follows. The time variables t_j are here newly normalised as

$$t_j \equiv \frac{T_j}{T}, \quad (7)$$

being *T* the maximum value from Table pag. 855 in [1]. The new choice of the normalization is demanded for the choice of the representation of the probability matrix to be consistent with the Kolmogorov equations.

The representation of the probability matrix $\hat{P}$ is here chosen as follows.

The entries of the transition probability matrix p_{ij} are

$$p_{jj} \equiv 1 - q_{jj}t_j, \quad (8a)$$

$$p_{ij} \equiv o(\lambda_{ij}), \quad i \neq j, \quad i = 1, ..., k+1. \quad (8b)$$

As

$$\hat{P} = \begin{bmatrix} p_{11} & o(\lambda_{12}) & o(\lambda_{13}) & o(\lambda_{14}) & ... & o(\lambda_{1,k+1}) \\ o(\lambda_{21}) & p_{22} & o(\lambda_{23}) & o(\lambda_{24}) & ... & o(\lambda_{2,k+1}) \\ o(\lambda_{31} & o(\lambda_{32}) & p_{33} & o(\lambda_{34}) & ... & o(\lambda_{3,k+1}) \\ ... & ... & ... & ... & ... & ... \\ 0(\lambda_{k+1,1}) & o(\lambda_{k+1,2}) & o(\lambda_{k+1,3}) & o(\lambda_{k+1,4}) & ... & p_{k+1,k+1} \end{bmatrix} \quad (9)$$

3. Outlook

The present paper is aimed at writing a new Markov model of disease states with discretised time, in which transitions within non-adjacent states are also newly taken into account.

The hypothesis that 'state occupation processes' be 'independent and identically distributed'. The fundamental matrix of the chain is newly written. The representation of the probability matrix is newly chosen and spelled out. The mean sojourn times and the means passage time can be calculated accordingly.

The calculation of the time evolution of the eigenvalues allows one to define the errors. According to the variances, hidden Markov states models can be constructed (where some of the propositions of can be generalized) [5].

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