Simulation techniques for parameter estimation in tumor related stochastic processes

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Introduction

Purpose of the paper:

- Represent tumor related processes in a computer-based simulation

- Analyize simulation data as compared to population data

Hypothesis

1. For each patient, each tumor originates froma single cell, and grows exponentially at a rate of α.

2. The probability of systematic occurrence of a tumor in $(t, t+\Delta)$ equals $\lambda\Delta+o(\Delta)$ independent of the prior history of the patient.

3. The probability that a tumor, not previously detected, will be detected and removed in $(t, t+\Delta)$ is $bY_j(t)\Delta + o(\Delta)$

4. Until the removal of the primary tumor, the probabilty of a metastatis in $(t, t+\Delta)$ is $\beta Y_0(t)(\Delta) + o(\Delta)$. Here $Y_0(t), Y_1(t), \cdots$ denote the sizes of the primary and secondary tumors at t, the subscript representing the order in which they originated.

Input Parameters

α = tumor growth rate

λ = systemic rate

b = detection rate

β = metastic rate

Random Variables

P_D = time of detection of primary tumor

M_T = time of origin of first metastatis

S_T = time of origin of first systemic tumor

R_T = time of origin of first recurrence

R_d^* = time from R_T to detection of first recurrence

R_D = time from P_D to detection of first recurrence

Generation of Random Variables

$$
\begin{aligned}
F_{P_D}(t) &= 1 - exp(\frac{bc}{\alpha}[1 - e^{\alpha t}]) \\
F_{M_T}(t) &= 1 - exp(\frac{\beta c}{\alpha}[1 - e^{\alpha t}]) \\
F_{S_T}(t) &= 1 - e^{\lambda t} \\
F_{R_d^*}(t) &= 1 - exp(\frac{bc}{\alpha}[1 - e^{\alpha t}])
\end{aligned}
$$

where c is the volume of one cell (10^{-9}cc).

Note: These formulas in the paper were incorrect.

Algorithm

Input: $\alpha.\lambda, b, \beta$

Repeat until $R_D > 0$

Generate P_D, M_T

If $(M_T > P_D)$ then $M_T \leftarrow \infty$

Generate S_T

$R_T \leftarrow \min\{M_T, S_T\}$

Generate R_d^*

$R_D \leftarrow R_T + R_d^* - P_D$

End Repeat

Return R_D