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Modelling the Cervical Cancer Growth Process by Stochastic Delay Differential Equations

(Pemodelan Proses Pertumbuhan Kanser Serviks oleh Persamaan Pembezaan Stokastik Lengahan)

MAZMA SYAHIDATUL AYUNI MAZLAN, NORHAYATI ROSLI*, NINA SUHAITY AZMI & ARIFAH BAHAR

ABSTRACT

In this paper, the uncontrolled environmental factors are perturbed into the growth rate deceleration factor of the Gompertzian deterministic model. The growth process under Gompertz's law is considered, thus lead to stochastic differential equations of Gompertzian with time delay. The Gompertzian deterministic model has proven to fit well with the clinical data of cancerous growth, however the performance of stochastic model towards clinical data is yet to be confirmed. The prediction quality of stochastic model is evaluated by comparing the simulated results with the clinical data of cervical cancer growth. The parameter estimation of stochastic models is computed by using simulated maximum likelihood method. 4-stage stochastic Runge-Kutta is applied to simulate the solution of stochastic model. Low values of root mean-square error (RMSE) of Gompertzian model with random effect indicate good fits.

Keywords: Gompertzian model; simulated maximum likelihood; stochastic delay differential equation; 4-stage stochastic Runge Kutta

ABSTRAK

Kertas kerja ini mempertimbangkan faktor persekitaran tidak terkawal yang diganggu ke atas faktor penurunan kadar pertumbuhan model Gompertzian berketentuan. Proses pertumbuhan di bawah hukum Gompertz dipertimbangkan, seterusnya membawa kepada persamaan pembezaan stokastik Gompertzian dengan masa lengahan. Model Gompertzian berketentuan telah terbukti sesuai untuk data klinikal pertumbuhan kanser, walau bagaimanapun keberkesanan model stokastik terhadap data klinikal masih belum disahkan. Kualiti ramalan model stokastik dinilai dengan membandingkan keputusan simulasi dengan data klinikal pertumbuhan kanser pangkal rahim. Anggaran parameter model stokastik dikira dengan menggunakan kaedah simulasi kebolehjadian maksimum. Stokastik Runge-Kutta peringkat 4 diaplikasikan untuk mencari penyelesaian simulasi model stokastik. Nilai punca min ralat kuasa dua (RMSE) yang rendah bagi model Gompertzian dengan kesan rawak menunjukkan keputusan yang baik.

Kata kunci: Model Gompertzian; persamaan pembezaan stokastik dengan masa lengahan; simulasi kebolehjadian maksimum; stokastik Runge Kutta peringkat 4

INTRODUCTION

National Cancer Society Malaysia (NCSM) stated that an average of 1500 is diagnosed with cervical cancer every year, with the majority of cases presenting at the late stages of the diseases (Mohamed 2013). The National Cancer Institute (NCI) reported that cervical cancer growth usually develops slowly over time. Prior to the development of cervical cancer, the cells of the cervix go through the process that change the cervical cells. It is known as dysplasia or cervical intraepitherial neoplasia (CIN), in which cells on the surface of the cervix can appear abnormal in the cervical tissue. Later, cancer cells start to grow and spread into the deeper layers of the cervix and to the surrounding areas (American Cancer Society 2014).

Recently, many mathematical formulations offer a wide range of biological study that can be classified regarding to the precise tumor growth rate or the pattern of tumor growth in order to improve a better treatment strategies or at least to improve the patient's quality life. Many mathematical models of cancerous growth have ignored the presence of random variations. The uncontrolled factors cannot be neglected since cancerous growth are subjected to this effect. The presence of noise in mathematical model is therefore required. It reflects the actual behavior of cancerous growth and implies a cancer clone may regress prior reaching a detectable size. Moreover, noise is not completely understood in deterministic model, hence not feasible to model deterministically (Ferrante et al. 2000). To be realistic, mathematical models of a biological system should include noise or stochasticity. In fact, stochastic model has recently been used as an effective tool in understanding the dynamic behavior of cancer progression and metastasis formation. Most studies used a stochastic version that based on Gompertz law to account for random fluctuations of the model parameters. They assumed that the growth deceleration factors do not change and the variability of environmental conditions only induces fluctuations in the intrinsic growth rate (Ferrante et