# ANALYSIS AND SIMULATION OF MATHEMATICAL MODELS FOR TUMOR THERAPY

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**Thesis Submitted in Fulfillment of the Requirement for the Degree of Master of Science in the Faculty of Science and Technology Universiti Malaysia Terengganu**

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## DEDICATION

Specially dedicated to the best peoples for me:

My mother Erlina and my father Supadi

To peoples who inspires me:

Witono, S.Pd.

Muhammad Findi Alexandi, Ph.D.

drg. Hj. Haryanti

Abstract of thesis presented to the Senate of Universiti Malaysia Terengganu in fulfillment of the requirement for the degree of Master of Science

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**August 2012**

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There are many possible approaches to tumor treatment. The most common of tumor treatments today are immunotherapy, chemotherapy and biochemotherapy. The goal of these treatments does strengthen the body's own natural ability to combat cancer by enhancing the effectiveness of the immune system. There are still many unanswered questions about how does the immune system interact with a tumor and what does component of the immune system play significant roles in responding to these treatments? Mathematical model is a tool that helps us to understand not only the interaction between immune and tumor cells but also effect of these treatments.

In this research, mathematical model of tumor therapy is proposed in the form of couple system of ordinary differential equations (ODEs). This model described tumor growth on a cell population in the absence of therapy. This model also described the effect of tumor infiltrating lymphocytes (TIL), interleukin-2 (IL-2), interferon alpha (INF-$\alpha$) and chemotherapy drug on dynamics of tumor cells under the influence of therapy.

Analysis and characterization of mathematical model in the absence of treatments is presented by locating equilibrium points and determining stability properties. Numerical simulations that describe the stability of analysis are also presented. The analysis system is useful to understand the parameter that plays important role in our ODEs system and also helps to guide development of the best strategy tumor therapy.

Then, there are two main parts of the numerical results in this study. Firstly, the numerical simulation for tumor-immune interaction without therapy is presented. In this simulation is very important, in order to determine initial values for the simulation model with therapy. Secondly, numerical simulations for several of tumor treatments in the presence of therapy are also presented. These results showed that biochemotherapy is more effective than immunotherapy alone or chemotherapy alone to treat tumor with large size. In addition, we create a graphic user interface that can be used to guide clinicians performed a simulation of tumor therapy, so that clinicians can design the best strategy of tumor therapy.

Abstrak thesis yang dikemukakan kepada Senat Universiti Malaysia Terengganu sebagai memenuhi keperluan untuk ijazah Sarjana Sains

# ANALISIS DAN SIMULASI MODEL-MODEL MATEMATIK BAGI TERAPI TUMOR

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**Ogos 2012**

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Terdapat banyak pendekatan yang mungkin untuk rawatan tumor. Rawatan tumor yang paling biasa pada hari ini adalah imunoterapi, kemoterapi dan biochemotherapy. Matlamat rawatan ini adalah untuk mengukuhkan keupayaan semulajadi badan sendiri untuk memerangi kanser dengan meningkatkan keberkesanan sistem imun. Masih terdapat banyak soalan yang tidak dijawab tentang bagaimana sistem imun berinteraksi dengan tumor dan komponen sistem imun apa yang memainkan peranan penting dalam bertindak balas kepada rawatan ini? Model matematik adalah alat yang membantu kita memahami bukan sahaja interaksi antara sel-sel imun dan tumor tetapi juga kesan rawatan ini.

Dalam kajian ini, model matematik terapi tumor yang dicadangkan dalam bentuk sistem Persamaan Pembezaan Biasa (PPB). Model ini menggambarkan pertumbuhan tumor pada kumpulan sel dalam ketiadaan terapi. Model ini juga menggambarkan kesan daripada *tumor infiltrating lymphocytes* (TIL), *interleukin-2* (IL-2), *interferon alfa* (INF-$\alpha$) dan ubat kemoterapi pada dinamik sel-sel tumor di bawah pengaruh terapi.

Analisis dan ciri-ciri model matematik dalam ketiadaan rawatan yang dibentangkan dengan mencari titik keseimbangan, dan menentukan ciri-ciri kestabilan. Simulasi berangka yang menggambarkan analisis kestabilan juga dibentangkan. Sistem analisis ini berguna untuk memahami parameter yang memainkan peranan penting dalam sistem ODE kami dan juga membantu untuk membimbing pembangunan strategi terapi tumor terbaik.

Kemudian, terdapat dua bahagian keputusan berangka dalam kajian ini. Pertama, simulasi berangka untuk interaksi tumor-imun tanpa terapi telah dibentangkan. Simulasi ini sangat penting, untuk menentukan nilai awal daripada model simulasi dengan terapi. Kedua, simulasi berangka untuk beberapa rawatan tumor dalam kehadiran terapi telah dibentangkan. Keputusan ini menunjukkan biokemotherapi yang lebih berkesan daripada imunoterapi sahaja atau kemoterapi sahaja untuk merawat tumor yang bersaiz besar. Di samping itu, kita mewujudkan satu antar muka pengguna grafik yang boleh digunakan untuk memberi petunjuk klinikal melakukan simulasi terapi tumor, supaya klinikal mampu untuk mereka bentuk strategi terapi tumor terbaik.