CHAPTER 1

INTRODUCTION

1.1 Background

Tumour evolution is a very complex process involving many different phenomena, which occur at different scales. A scientist would probably describe the phenomena occurring during the evolution of tumours using three natural viewpoints: the sub-cellular level, the cellular level and the tissue level. From the modeling point of view, a connection can be approximately drawn between the description levels above and the microscopic, mesoscopic and macroscopic scales.

The microscopic scale refers to those phenomena that occur at the sub-cellular level and therefore to activities that take place within the cell at the cell membrane such as DNA synthesis and degradation and others. The mesoscopic scale refers to the cellular level and therefore to the main activities of the cell populations such as interaction among tumour cells and the other type of cells present in the body like endothelial cells, macrophages, lymphocytes and others. The macroscale refers to the tissue level and therefore to those phenomena which are typical to of continuum systems such as cell migration, convection and diffusion of nutrients.

Any event at a certain scale is strongly linked to other event at the other scales. Therefore it is impossible to completely describe a phenomenon without taking into

account others occurring at a smaller or larger scale. For instance, in the avascular phase tumour cells are packed in a multicellular spheroid not yet connected to the host's blood supply. Looking at this stage from the tissue level the evolution depends on the distribution of oxygen, glucose and other nutrients and on the production and reception of growth modulating chemical substances, phenomena involving the sub-cellular level. This phase can be described by mass balance equation and reaction-diffusion equations that can be derived not only on the basis of continuum mechanics but also on the basis of cell-based models. Going on with the evolutionary process, at a certain stage of maturation tumour cells start producing particular chemical factors switching on the process of angiogenesis. New blood vessels grow into a tissue from surrounding parent vessels. This crucial triggering mechanism is leading to the vascular growth phase regulated by phenomena occurring at the sub-cellular and cellular levels. Finally, the detachment of metastasis is regulated by the adhesion properties of the cells.

Research at each single level would certainly profit from the interactions among different branches of science. From the phenomenological observation of a certain phenomenon in real patients, biological scientists try to conceive a more convenient biological model. They can perform a series of experiments on that model. Mathematicians can generate mathematical model either directly from the phenomenological observation or through the biological model for describing the phenomenon of interest. The analysis of the properties of the mathematical solution will then give a qualitative description of the dynamics resulting in deeper insight into the problem. The model can then be implemented numerically. The quality of the modeling

process can be tested validating the results of the simulations with the experiments. If the comparison is considered satisfactory, then the modeling cycle closes successfully. Otherwise, one or more steps of the modeling process need to be refined and the cycle continues.

Approximate analytical schemes such as Adomian Decomposition Method (ADM) (Adomian, 1988) and Homotopy Perturbation Method (HPM) (He, 1999) have been the source of a lot of research activity. The schemes generate an infinite series of solutions to a wide class of linear and nonlinear differential equations and do not have the problem of rounding error (Wazwaz, 2005; He, 2008). However, only a few papers deal with the comparison of these methods (Sadighi et al, 2007; Biazar et al, 2008; Saghi & Ganji, 2008; Oziso & Yildirim, 2008; Siddiqui et al, 2010). In this thesis, we made a comparative study to examine the performance of the ADM and HPM when applied to various stage of tumour growth.

1.2 Research Objectives

This thesis is written in the belief that the use of mathematical modeling can help to advance cancer research. Progressive abstractions and simplification steps have helped this research to gain insight into the complex phenomena occurring during tumour evolution and growth. In this context, the objectives of this research are :

1) To seek the most effective method to be used in solving mathematical model of tumour growth.

2) To solve and produce analytical solution of tumour growth model using Adomian Decomposition Method (ADM) and Homotopy Perturbation Method (HPM).

3) To apply ADM and HPM to the linear and nonlinear tumour model.

4) To compare the performance of ADM and HPM when applied to various stages of tumour growth.

1.3 Thesis Organization

This thesis consists of eight chapters. Chapter 1 gives a brief introduction about the field of study, background of research and its research objectives. It also includes the layout of the thesis organization.

Chapter 2 gives the literature review of this research. This includes the history of research in tumour growth, type of stages in tumour growth (which are avascular, vascular, angiogenesis, metastasis), the models used in studying tumour growth and some of the latest advances achieved by other researchers in tumour model.

Chapter 3 focuses on the techniques to be used in solving the linear and nonlinear model of tumour growth. Two methods, Adomian Decomposition Method (ADM) and Homotopy Perturbation Method (HPM) have been identified as the most suitable method for this problem.

The next four chapters, Chapter 4, 5, 6, and 7, explains the detail of the tumour growth model in various stages. Chapter 4 explains the avascular model of spherical tumour with a necrotic core immerse into a nutrient bath. Chapter 5 looks more deeply into the multicell spheroid of avascular tumour growth. Chapter 6 deals with

mathematical model for tumour angiogenesis, while Chapter 7 explores with mathematical model for tumour invasion and metastasis.

Finally, conclusion and recommendations for future work are summed up and presented in Chapter 8.