Identifying model parameters from small data sets: Cell-viability model of melanoma under inhibition by MAZ-51

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Roumen Anguelov[1,4], Charlise Basson[2], Priyesh Bipath[2], Yvette N Hlophe[2], G Manjunath[1], Avulundiah E Phiri[1], June C Serem[3]

[1]Department of Mathematics and Applied Mathematics, University of Pretoria
{roumen.anguelov, manjunath.gandhi}@up.ac.za, edwin@aims.ac.za

[2]Department of Physiology, University of Pretoria
charlise.basson@gmail.com, {priyesh.bipath, yvette.hlophe}@up.ac.za

[3] Department of Anatomy, University of Pretoria
june.serem@up.ac.za

[4]Institute of Mathematics & Informatics, Bulgarian Academy of Sciences
roumen.anguelov@math.bas.bg

Constructing useful mathematical models is typically guided by the objectives of (a) representing adequately the biological processes of interest; (b) identifying the values of the involved parameters. These two objectives are often in competition. On the one hand, due to the complexity of the biological processes, objective (a) leads to models involving many unknown parameters. On the other hand, only a limited number of variables can be measured, and obtaining these measurements requires costly, time-consuming, and labor-intensive experiments. The challenge is not new, Quoting Einstein: "It can scarcely be denied that the supreme goal of all theory is to make the irreducible basic elements as simple and as few as possible without having to surrender the adequate representation of a single datum of experience."[3, page 384]

In this presentation we are confronting the competing objectives (a) and (b) in the setting of mathematical modeling of inhibition of melanoma. More precisely, we consider the treatment of the B16F10 melanoma cell line by MAZ-51. This work is part of a broader ongoing research project on inhibition of melanoma, with some results on other inhibitors already reported in [1, 2]. MAZ-51 is a synthetic molecule derived from indolinone, and it functions by suppressing the phosphorylation process of the tyrosine kinase receptor known as vascular endothelial growth factor receptor 3 (VEGFR-3). The cell viability of cancer cells is an important quantitative measure of efficacy of any treatment they are subjected to. Determining cell viability as a function of time and drug concentration is a crucial stage in the development of new cancer drugs and is our main goal for the stated treatment by MAZ-51.

Melanoma cells were exposed to MAZ-51 at concentrations of 11, 13, 14 and 16 micromolar (μM) for 24,48 and 72 hours. The cells are then tested for cell

viability using the crystal violet assay. Due to the inherent variability of the data obtained via this approach, [1], the experiments are repeated three times. The two essential steps in deriving the cell viability function are (i) deriving the model as a function of time and (ii) identifying the values of parameters as functions of the inhibitor concentration. The proposed methodology provides an approximation of the cell viability function, incorporating biologically meaningful parameters. It accurately represents all data and offers robust predictions that are not affected by small data perturbations.

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