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Mathematical modelling for CTCE-9908 (a CXCR4 inhibitor) on B16 F10 melanoma cell proliferation (Part II)

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The cell viability of tumour cells under treatment is an important quantitative measure of efficacy of that treatment. It is defined as the size of a treated population of cells expressed as a percentage of the size of a naturally growing population of the same cells. Hence, determining cell viability as a function of time is a crucial stage in the development of new cancer drugs. This function is frequently developed by interpolating the existing data using statistical techniques like regression. We use mechanistic modelling techniques rather than statistical tools to ensure that information on the dynamics of activation and inhibition is also included in the cell-viability function. We therefore derive a cell viability function in this presentation that is appropriate for experimental data collected from the inhibitory drug, CTCE-9980. Then, we use the experimental data to approximate the parameters at a 95% confidence interval. To validate the model, we use the bootstrapping technique to determine the stability of the estimated parameters at a 95% bootstrap confidence level.

The accuracy of predictions produced via interpolation, linear or nonlinear regression at any given value of an independent variable depends on the density of data points around this value. Predictions outside the domain adequately covered by data points can seldom be relied upon. Such predictions, often referred to as extrapolation, significantly depend on the type of functions used in the fitting process and, to a lesser extent, on the accuracy of the approximations of the data. To avoid the stated problem, the protocol followed here is focused on appropriately deriving a type of function to be used in the approximation/fitting process. More precisely, it consists of the following steps:

(i) A mathematical model of the processes tested in the experiment is constructed based on known quantitative relationships

(ii) The measured or observed variable is derived from the model in terms of its parameters.

(iii) The form of the theoretically derived observable determines the type of function to be fitted to the data. This is a function of the independent variable, which depends on a certain number of parameters.

(iv) The function in (iii) is fitted to the data to identify the values of the parameters.

This protocol follows the ideas in [1] and was applied in [2] to modelling and quantifying the inhibition of melanoma by L-Kynurenine. The specific advantage highlighted in this presentation is that the domain of validity of the approximation is determined by the domain of validity of the model and not the location of the data. Furthermore, we present the IC_{50} as a function of time. The practical value of the latter is that one can obtain cell viability at a specific concentration and at a given time.

References

[1] B. S. Hendriks, Functional pathway pharmacology: chemical tools, pathway knowledge and mechanistic model-based interpretation of experimental data, *Current Opinion in Chemical Biology*, 14(4):489-497, 2010.

[2] R. Anguelov, G. Manjunath, A. E. Phiri, T. T. Nyakudya, P. Bipath, J. C. Serem, Y. N. Hlophe, Quantifying assays: A modeling tale of variability in cancer therapeutics assessed on cancer cells, arXiv:2207.08449, 2022.