The Influence of Noise in Cytoxicity Assessment

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Abstract

Industrial activity produces many chemicals that may be hazardous to human health or the environment. Traditionally, experiments can be carried out on live subjects (in vivo), but this is both expensive and raises significant ethical concerns. Rather than conducting these assays, we might try using mathematical or computational models to assess the effect of these toxicants (1).

With in vitro assays at the Alberta Centre of Toxicology using the xCelligence Real-Time Cell Analysis HT system, time-dependent response curves (TCRCs) were generated. These experimentally-derived curves reflect the response of human cells to these toxicants. The goal was to find a mathematical model that could accurately reproduce these curves (2).

Depending on the value of various parameters of the toxicant – such as its toxicity and how fast cells absorb it – there are generally two possible equilibria dependent on the toxicant's initial external concentration: a cell line may persevere and survive; or the concentration may be large enough to cause extinction of the cell population.

Data from the TCRCs were used to generate a deterministic model. That is, a given set of parameter values will always generate the same cell fate. However, there is inherently uncertainty in the value of these parameters.

To assess the influence of this noise on the external concentration of toxicant at which some population of cells would reach survival or extinction equilibria, a new model was created with additional variables for this uncertainty. Several simulations were run with this extended model. The information generated will be useful for planning further

experiments regarding cytotoxicity, and for numerically generating TCRCs for clustering and classification.

(1) T.G. Hallam, C.E. Clark, and G.S. Jordan. Effects of toxicants on populations: A qualitative approach II. First order kinetics. J. Math. Biology, 18:25–37, 1983.

(2) T. Pan, B. Huang, W. Zhang, S. Gabos, D.Y. Huang, and V. Devendran. Cytotoxicity assessment based on the AUC50 using multi-concentration time-dependent cellular response curves. Anal. Chim. Acta, 764:44–52, 2013.