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Model-based and data-driven pharmacokinetic parameter estimation

Steady-state volume of distribution (Vdss) is a key pharmacokinetic parameter. Its estimation generally refers to data-driven non-compartmental analysis (NCA), historically based on the available plasma concentration date of linear pharmacokinetic models with central elimination. However, many drug compounds, such as granulocyte colony-stimulating factor (G-CSF), erythropoietin (EPO) and thrombopoietin (TPO) which are widely used during chemotherapy, often exhibit complex nonlinear mechanism, and their Vdss estimation has not been addressed to date. In this talk, two-compartmental pharmacokinetic models with simultaneous first-order and Michaelis-Menten elimination are studied, the corresponding model-based expressions of Vdss and their relationships to data-driven NCA estimation are derived. The impact of non-linearity and peripheral elimination is explicitly delineated in these formulas. Being concerned with the issues of model identifiability and indistinguishability, an interval estimate of Vdss is suggested. This is a joint work with Prof. Fahima Nekka and Jun Li at Universite de Montreal.