Koch, Gilbert. 2012. Modeling of Pharmacokinetic and Pharmacodynamics of Cancer and Arthritis. PhD Dissertation. 118 pp.

See <u>http://www.math.uni-konstanz.de/numerik/personen/koch/papers/Diss\_Koch\_Final.pdf</u>. Accessed 28 March 2023.

Abstract: Mathematical modeling of pharmacokinetics / pharmacodynamics (PKPD) is an important and growing field in drug development. In this work we develop preclinical PKPD models based on fundamental biological and pharmacological principles. Equipped with a PKPD model, different dosing schedules could be simulated and therefore, a valuable contribution to first in human dose selection could be achieved.

We consider different mathematical model figures and discuss the properties and biological basis. Such tools serve as modules for a final PKPD model. We apply ordinary and delay differential equations and especially focus on modeling of delays and lifespans in populations. We show a fundamental relationship between transit compartments and lifespan models. Moreover, we investigate the weighted least squares estimator and derive statistical characteristics of model parameter.

We present a PKPD model to describe tumor growth and anticancer effects for mono- and combination therapy. Further, we construct a PKPD model for arthritis development and antibody effects.

Summarizing, we develop (semi)-mechanistic mathematical PKPD models based on pharmacological assumptions and apply our models to measured data from preclinical phase.

Keywords: model, differential equation, system, pharmacokinetics