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Systems Biology driven Pharmacokinetics and Pharmacodynamics

Pharmacokinetics is probably the most neglected field in the medically relevant biosimulations. It is a science about the drug fate in a living organism and embraces in broader sense four main domains: absorption, distribution, metabolism, and excretion, in short ADME. It is often combined and considered together with pharmacodynamics, a science branch dealing with the influence the drug has on its target and eventually on the whole body and disease progression. At the same time, the mechanism based but in most cases drugfree models and simulations are highly appreciated and developed in the Systems Biology community. There is no doubt that the full understanding of the underlying phenomena like physiological regulation and control, phenotypes, mutations and in general diseases is essential for the progress in medicine. However, much has been achieved in the last decades without sophisticated algorithms and supercomputers. Semimechanistic models or even simple phenomenological formulas and models are in use since beginning of the 20th century providing useful insights in e.g. physiology and pharmacokinetics related issues. We are convinced, that parallel application of these two seemingly unconnected approaches can eventually converge into more effective treatments methods now or in near future. We are making an attempt to introduce a new platform combining standard phenomenological models used in the PK/PD field with mechanistically based Systems Biology models and approaches. There are many examples of wellknown 1, 2 or more compartmental models providing valuable initial guesses and insights into the metabolism, and ADME processes in general, of a particular drug. However, their use is limited due to the non-mechanistic nature of such models. We consider Systems Biology driven models as complementary to their phenomenological counterparts. The ultimate goal of a wholebody full mechanistic model for the combined PKPDADME is doable on the scale of next few decades, but to support modern drug development now, we need the imperfect but useful phenomenological models in combination with mechanistic models under development.