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# Propositions to the thesis “Mechanistic modelling of drug target binding kinetics as determinant of the time course of drug action *in vivo*”

1. The role of drug-target binding kinetics cannot be understood without taking into account the kinetics of the full pharmacokinetic and pharmacodynamic context. *This thesis*
2. The concept of the rate-limiting step is essential to understand the behavior of pharmacokinetic-pharmacodynamic models. *This thesis*
3. The terminal plasma half-life is not directly informative about the rate of elimination of a drug. *This thesis*
4. Only an unsuccessful attempt to describe a pharmacokinetic-pharmacodynamic dataset with a mechanism-based model can be used as evidence for the mechanism of hysteresis. *This thesis*
5. The application value of a model is determined by the extent to which it reduces uncertainty and the general relevance of the described mechanism.
6. Since “the goal of science is theory”, hypothesis generation should be considered as valuable as hypothesis testing. (*L. B. Sheiner, Clin. Pharmacol. Ther., 1989.*)
7. A mathematical model describing a biological system “enables explicit communication of assumptions” and does not directly represent understanding of the system’s behaviour. (*N. Benson et al., CPT pharmacometrics Syst. Pharmacol., 2014.*)
8. Everything can be modeled.
9. Science aims to generate knowledge, rather than opinions. The practice of excluding valuable information to improve the readability of a scientific publication should therefore be discouraged.
10. The assumption that sufficient knowledge or understanding has been obtained decreases the chance to learn and increases the chance to be wrong.
11. The current practice of budget allocation to Dutch universities on the basis of market share and number of graduations leads to a disparity between the goals and objectives of university management teams and their academic staff.
12. The inherent subjectivity of morality leads inevitably to Wittgenstein’s “Ethik und Ästhetik sind Eins”. L. Wittgenstein, *Tractatus Logico-Philosophicus*, 6.421.

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