Biomedical Applications of System Dynamics

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Abstract

Systems Biology is one of the most exciting areas of science. Research in this field aims at establishing a model-based description of the complex dynamic phenomena we observe in the living world. The perspective is that a better understanding of the mechanisms and processes underlying the regulation of the human body will improve the treatment of patients in the health care system, cut the development costs of new drugs, and reduce the need for animal experiments. The modeling problems we encounter in Systems Biology are similar in many respects to the problems addressed in managerial or macroeconomic modeling, and there is a significant potential for using System Dynamics in the biomedical field as well. The talk will present a particular example of work performed in collaboration with Novo Nordisk and the Danish Medicines Agency.

The absorption kinetics of subcutaneously injected soluble insulin is unusual in that clinical experiments show that a slow initial absorption after a couple of hours is replaced by a significantly faster absorption. Moreover, experiments with different injection volumes and insulin concentrations demonstrate that there is both a volume and a concentration effect. The slow initial phase disappears if either the injected volume or the concentration of the injected insulin is reduced. On the other hand, in the limits of very low concentrations or small volumes, a tail develops on the absorption curve, representing a new type of slow process.

A System Dynamics model of this absorption scenario was original developed in collaboration with the Steno Memorial Hospital in the mid 1980's [1]. In spite of the fact that the insulin concentrations in the mean time have increased by an order of magnitude, the model continues to correctly predict the absorption curves, and we are presently developing variants of the model that can explain the absorption curves for other insulin forms, some of which are bound to protein as they are injected or bind to protein as they enter the blood vessels while yet others are injected in crystalline form or precipitate immediately after the injection. A particularly interesting aspect is the sensitivity of the absorption rate to variations of the blood perfusion at the injection site.

[1] E. Mosekilde, K.S. Jensen, C. Binder, S. Pramming and B. Thorsteinsson: 'Modeling absorption kinetics of subcutaneously injected soluble insulin', J. Pharmacokin. Biopharm. 17, 67-87 (1989). (First presented at the Int. Systems Dynamics Conf., Oslo 1984).