

# A Computational Model of Hepatic Glucose Metabolism

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**Authors:**

REBECCA A. BAILLIE, RICHARD HO, PAUL BRAZHNIK, *Cupertino, CA*

**Results:**

Hepatic glucose uptake and release are critical factors in maintaining plasma glucose levels. Both hepatic overproduction of glucose or lack of glucose uptake can result in hyperglycemia and may contribute to the development of diabetes. We developed a simple mathematical model of human liver glucose metabolism to study the relationship between hepatic glucose uptake and release and plasma glucose. While previous models of hepatic glucose metabolism have focused on glycogen metabolism or specific metabolic pathways, this model was designed to explore the impact of hepatic glucose uptake or output on plasma glucose regulation. The model includes hepatic glucose uptake, use, production and release, peripheral tissue removal of plasma glucose, and insulin production and action. The model structure follows known physiology and model parameters have been extracted from peer-reviewed literature. In a basal state, the model reproduces normal subjects. Manipulation with parameters allows to force the model to mimic mild, moderate, and severe diabetics (with severity based on fasting plasma glucose levels), thus generating hypotheses about contributions of different factors to the disease. Such differentiation is often difficult or impossible to achieve experimentally. The model response was compared to literature data for fasting data, and oral glucose tolerance tests (OGTT) in normal and diabetic subjects. We have found that in mild to moderate diabetics, hepatic glucose output was a primary factor in fasting glucose levels, while glucose uptake had less impact. We found that in severe diabetes, hepatic glucose uptake had to be decreased in the fasting state. Decreased basal hepatic glucose uptake and increased hepatic insulin resistance resulted in an exaggerated peak glucose level and incremental area under the curve for glucose during an OGTT. Hepatic insulin resistance may limit glucose uptake into the liver in severe diabetics resulting in profound postprandial hyperglycemia. We conclude that our model can be a useful tool for further studies and explorations of complex interactions between hepatic glucose metabolism and plasma glucose homeostasis.

**Category:**

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