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Physiological-based model of the incretin effect on the insulin production related to intestinal glucose absorption

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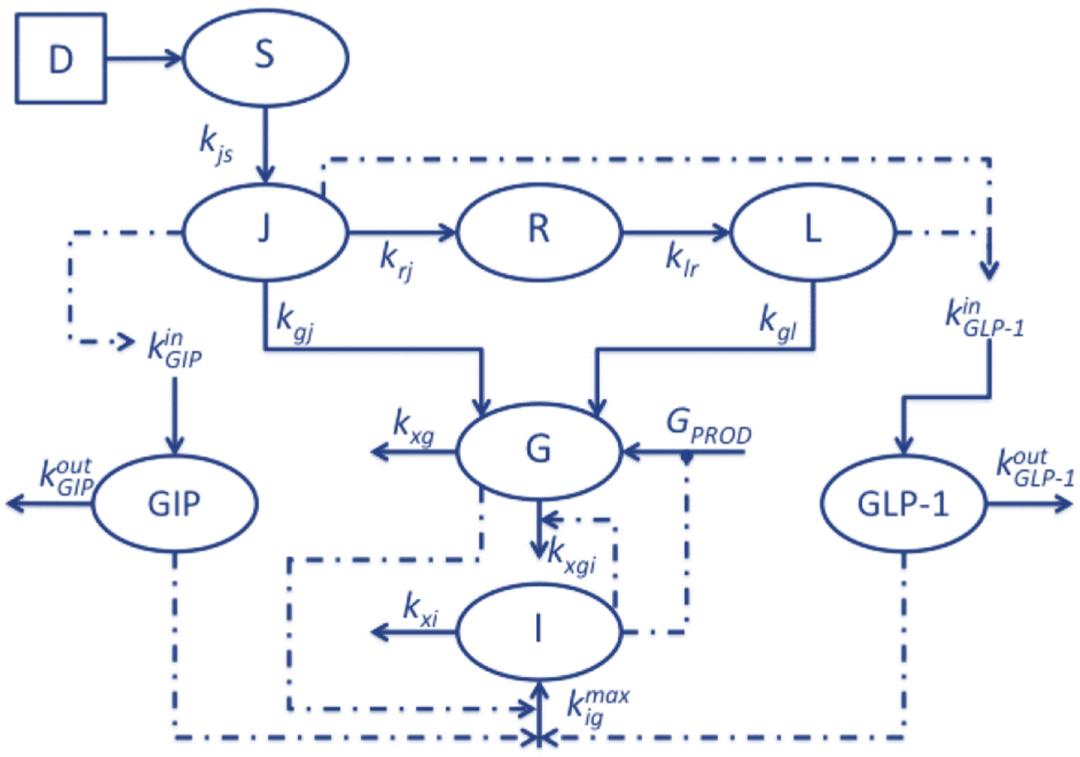
INTRODUCTION & AIM

- The prevalence of diabetes, especially of Type 2, is increasing rapidly, particularly in low and middle-income countries. This is due to factors such as overweight, obesity, and hypertension [1].
- The Oral Glucose Tolerance Test (OGTT) and the Intravenous Glucose Tolerance Test (IVGTT) are commonly used experimental procedures to measure blood glucose concentrations over time after glucose administration [2].
- The objective of this study is to develop a mathematical model for the representation of OGTT data, with the aim of describing the dynamics of incretins and identifying insulin sensitivity.

METHODS



The model consists of 8 ordinary differential equations, including a total of 19 parameters:

1. **Glucose mass balance in the stomach S**

$$\frac{dS}{dt} = -k_{js}S$$

2. **Glucose mass balance in the jejunum J**

$$\frac{dJ}{dt} = k_{js}S - k_{gj}J - k_{rj}J$$

3. **Glucose mass balance in a delay compartment R**

$$\frac{dR}{dt} = k_{rj}J - k_{lr}R$$

4. **Glucose mass balance in the ileum L**

$$\frac{dL}{dt} = k_{lr}R - k_{gl}L$$

5. **Plasma glucose dynamics G**

$$\frac{dG}{dt} = -k_{xg}G - k_{xgi}I \cdot G + G_{prod} + f\frac{k_{gj}J + k_{gl}L}{V \cdot BW}$$

6. **Plasma insulin dynamics I**

$$\frac{dI}{dt} = -k_{xi}I + k^{max}_{ig}\frac{G^{\gamma}}{G^{\gamma}_{50} + G^{\gamma}} \cdot \left[(1-\beta) + \beta\frac{G^{inc}}{G^{inc}_{50} + G^{inc}}\right]$$

7. **Glucose-dependent Insulinotropic Peptide dynamics GIP**

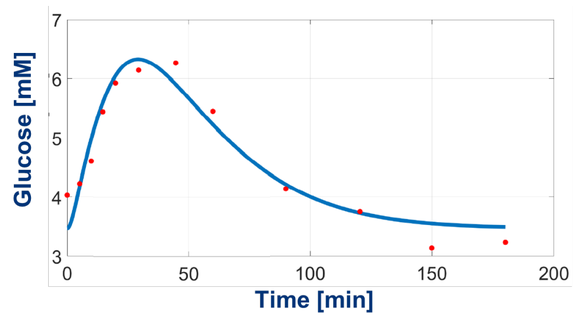
$$\frac{dGIP}{dt} = -k_{out,GIP}GIP + k_{in,GIP}\left(1 + \alpha_{GIP}\frac{J^{\sigma}}{G^{\sigma}_{50,GIP} + J^{\sigma}}\right)$$

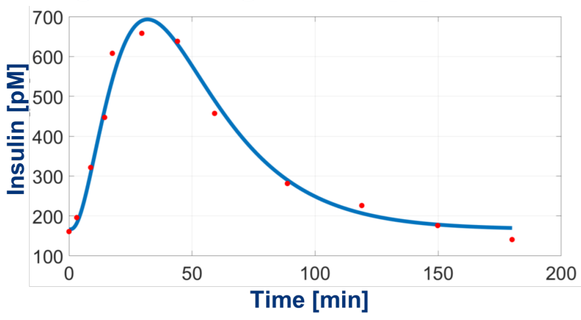
8. **Glucagon-Like Peptide-1 dynamics GLP**

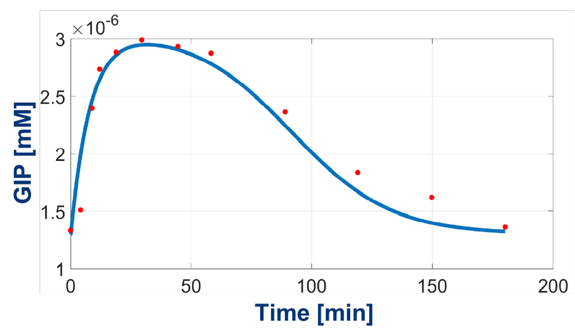
$$\frac{dGLP}{dt} = -k_{out,GLP}GLP + k_{in,GLP}\left(1 + \alpha_{1,GLP}L + \alpha_{2,GLP}J\right)$$

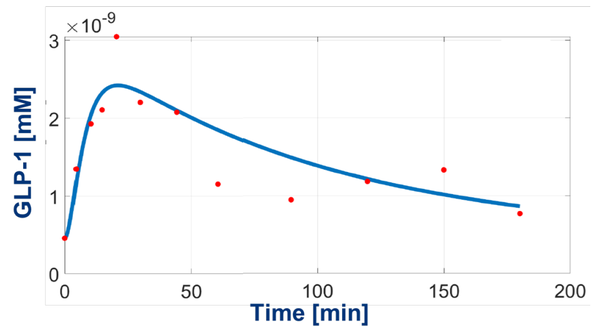
RESULTS & DISCUSSION

The parameters were estimated based on experimental data obtained from the administration of 50 grams of glucose [3]:

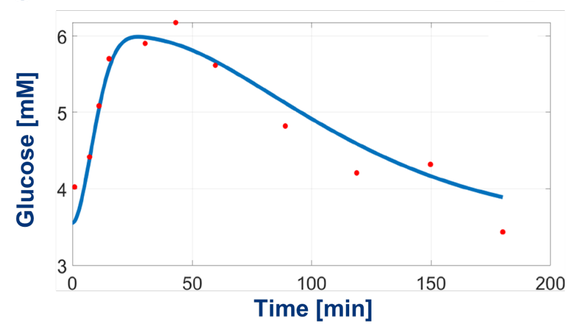


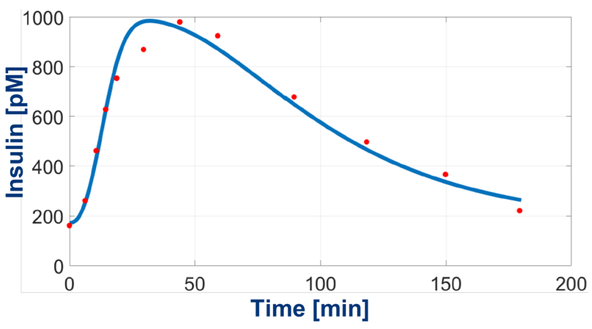


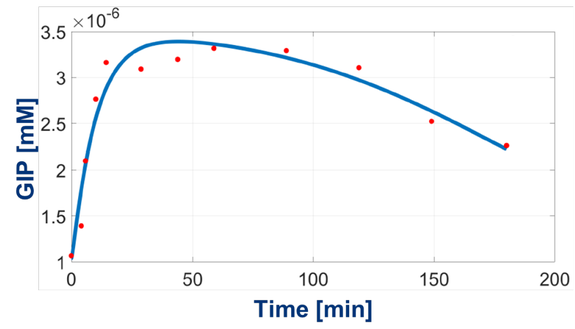


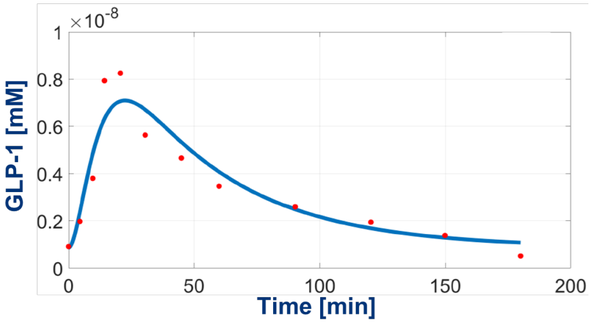


A second data set was also considered, in which 100 grams of glucose were administered [3]:









CONCLUSIONS

The developed model demonstrates satisfactory results, particularly in terms of reproduction of trends identified in the literature. Furthermore, there is consistency between estimated parameters and physiological values from previous studies.

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