Working Notes on Glucose–Insulin Modeling

Based on the Dalla Man (2007) Meal Simulation Model

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Contents

1 Sensitivity Analysis Notebook

This section documents the sensitivity analysis experiments performed on the Dalla–Man glucose–insulin model. The purpose of this notebook is to track the methodology, numerical experiments, and observations in a chronological and reproducible manner.

All sensitivities reported here correspond to plasma glucose concentration as the observed output.

1.1 Sensitivity Analysis Setup

Local parametric sensitivity analysis was performed using finite-difference perturbations of model parameters. For a given parameter p_j, the normalized sensitivity of plasma glucose $G(t)$ was computed as

$$S_j(t) = \frac{p_j}{G(t)} \frac{\partial G(t)}{\partial p_j}, \tag{1}$$

where the partial derivative was approximated numerically using a small relative perturbation of the parameter.

The scalar sensitivity index used for ranking parameters was defined as

$$S_j^{\text{int}} = \int_0^T |S_j(t)|\, dt, \tag{2}$$

representing the time-integrated magnitude of sensitivity over the simulation horizon.

The following parameters were analyzed:

$$\{k_1, k_2, V_G, k_{\text{abs}}, k_{\text{gri}}, k_{p1}, k_{p2}, k_{p3}, k_i, k_{\max}, k_{\min}, k_{e1}\}.$$

1.2 Stage 1A: Sensitivity Correlation Analysis

To assess potential collinearity among parameters, sensitivity trajectories were collected for a representative post-prandial excitation and assembled into a sensitivity matrix.

Each sensitivity vector was normalized by its Euclidean norm, and a cosine-similarity correlation matrix was computed.

Figure 1 shows the resulting sensitivity correlation matrix.

Observations. Strong correlations are observed among groups of parameters associated with glucose absorption and insulin action (e.g. k_{abs}, k_{gri}, $k_{\max}$, k_{p3}, k_i). This suggests potential identifiability challenges when estimating these parameters simultaneously. Conversely, parameters such as V_G and k_1 exhibit more distinct sensitivity patterns.

1.3 Stage 1A: Basal (Fasting) Sensitivity Analysis

Sensitivity analysis was first conducted under fasting (basal) conditions, with no meal intake. The simulation horizon was extended to 600 minutes to capture slow glucose–insulin dynamics.

Table 1 reports the ranking of parameters based on the integrated sensitivity index.

Figure 2 shows the time evolution of the dominant basal sensitivities.

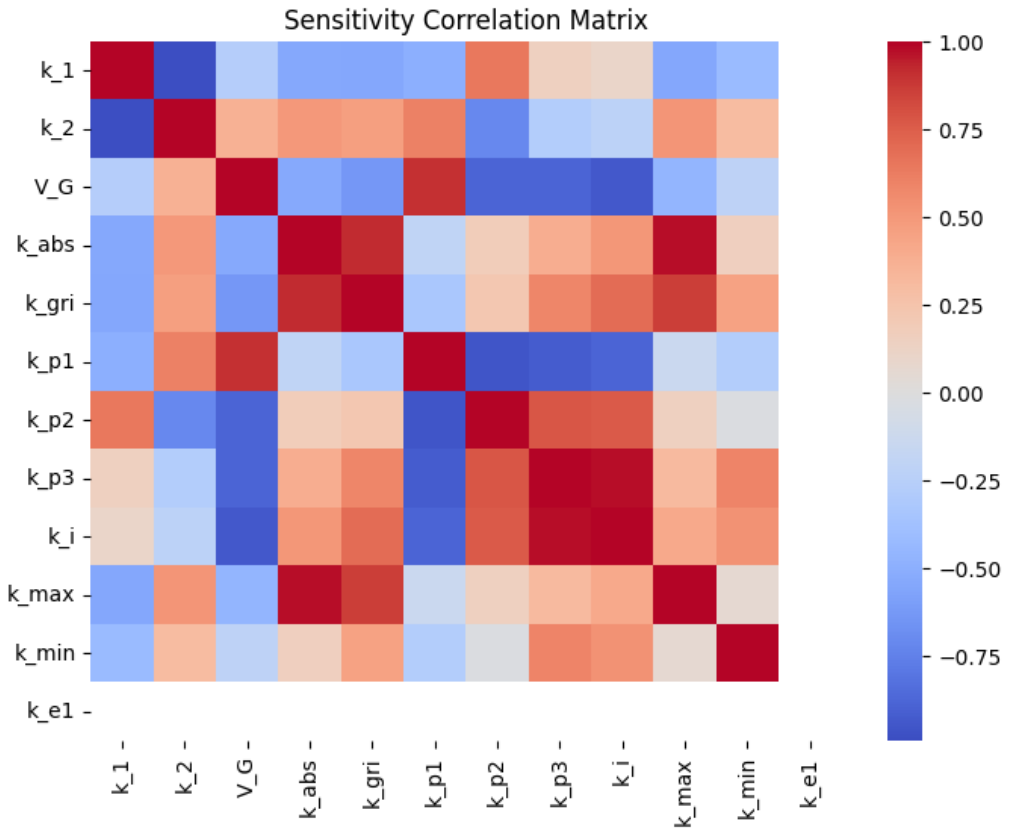

Figure 1: Sensitivity correlation matrix based on normalized sensitivity trajectories.

Table 1: Basal sensitivity ranking (fasting conditions).

Parameter	S_j^{int}
V_G	4.54×10^2
k_{p1}	2.50×10^2
k_1	6.84×10^1
k_2	6.35×10^1
k_{p2}	3.48×10^1
k_{p3}	2.40×10^1
k_i	1.88×10^0
Others	≈ 0

Observations. Under fasting conditions, plasma glucose is most sensitive to the glucose distribution volume V_G and the insulin action parameter k_{p1}. Sensitivity magnitudes are generally smooth and slowly varying, reflecting the dominance of basal glucose turnover mechanisms. Parameters related to gastrointestinal absorption exhibit negligible influence in the absence of a meal.

1.4 Stage 1A: Post-Prandial Sensitivity Analysis

Sensitivity analysis was repeated under post-prandial conditions, with a finite meal input introduced via the stomach compartment. The simulation horizon was set to 300 minutes.

Table 2 summarizes the sensitivity ranking in the meal condition.

Figure 3 shows the corresponding sensitivity trajectories.

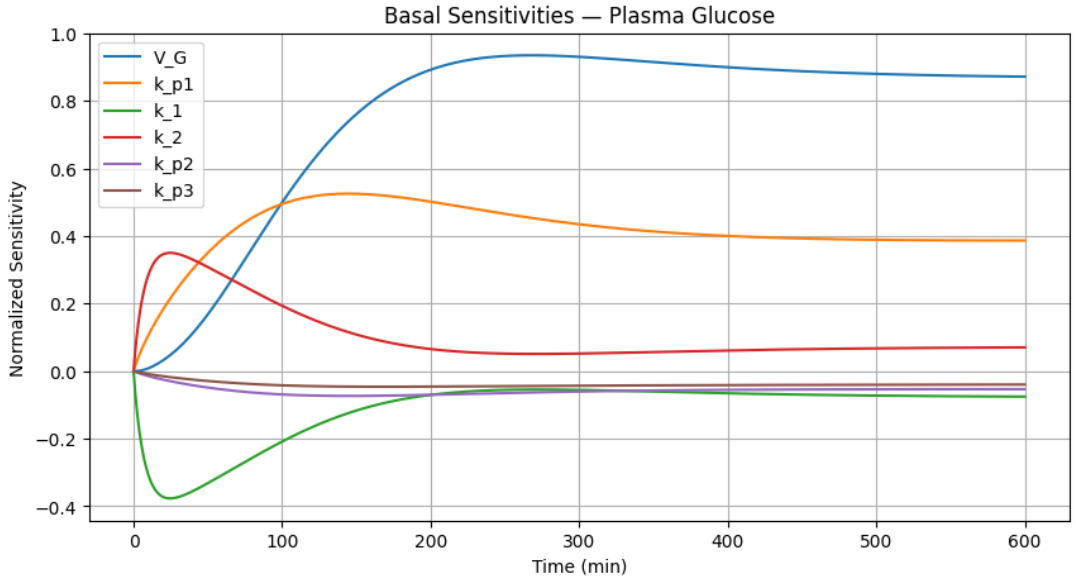

Figure 2: Basal sensitivity trajectories for dominant parameters.

Table 2: Post-prandial sensitivity ranking.

Parameter	S_j^{int}
V_G	2.48×10^2
k_{p1}	6.15×10^1
k_1	3.36×10^1
$k_{\min}$	3.03×10^1
k_2	3.02×10^1
k_{p3}	1.90×10^1
k_{abs}	1.77×10^1
k_{gri}	1.67×10^1

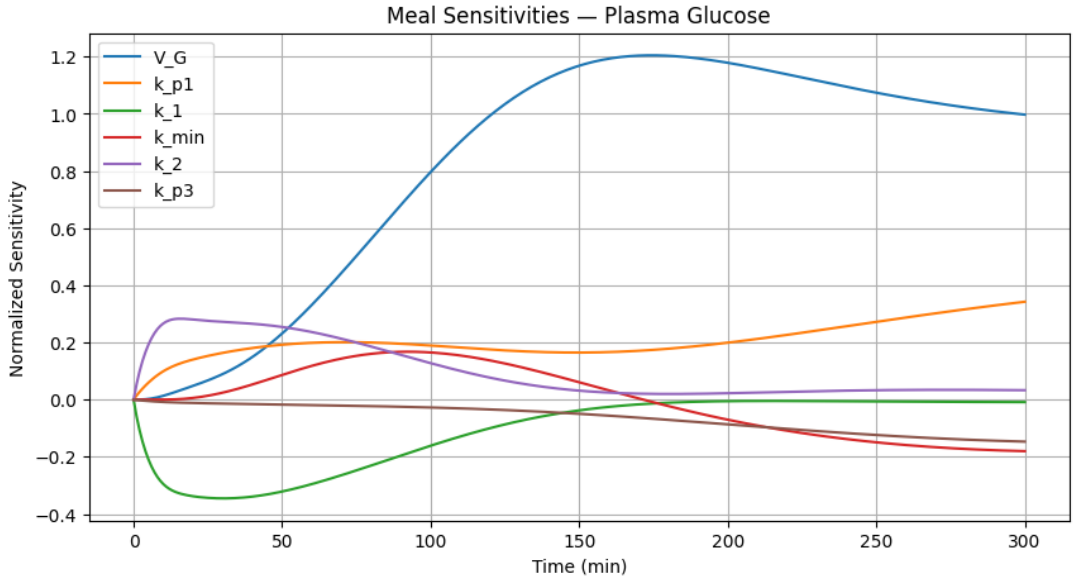

Figure 3: Post-prandial sensitivity trajectories for dominant parameters.

Observations. Following a meal, additional parameters associated with gastric emptying and insulin saturation dynamics become influential. While V_G remains the dominant parameter, the relative importance of $k_{\min}$, k_{abs}, and k_{gri} increases compared to the basal case. This indicates a clear regime dependence of sensitivity structure.

1.5 Stage 1A: Multi-Excitation Sensitivity and Robust Ranking

To assess robustness across physiologically distinct conditions, sensitivity analysis was performed for two meal sizes (small and large). A robust sensitivity score was defined as the mean of the integrated sensitivities across both excitations.

Table 3 reports the resulting rankings.

Table 3: Multi-excitation sensitivity and robust mean ranking.

Parameter	Small Meal	Large Meal	Robust Mean
V_G	217.35	252.59	234.97
k_{p1}	88.90	57.89	73.40
k_1	41.39	32.15	36.77
k_2	37.48	29.07	33.27
$k_{\min}$	14.94	33.54	24.24
k_{p3}	13.43	20.71	17.07

Observations. The robust ranking highlights parameters whose influence persists across excitation magnitudes. The glucose distribution volume V_G and insulin action parameter k_{p1} consistently dominate sensitivity rankings, indicating structural importance. Parameters such as $k_{\min}$ exhibit strong excitation dependence, suggesting their relevance is context-specific.

1.6 Stage 1A: Window-Length Sensitivity Analysis

Finally, sensitivity rankings were examined over multiple time windows (25, 60, and 120 minutes) to distinguish fast and slow dynamics.

Table 4: Window-length sensitivity rankings.

Parameter	25 min	60 min	120 min
V_G	0.66	7.19	50.09
k_1	6.77	18.26	29.58
k_2	5.82	14.71	23.49
k_{p1}	2.46	8.41	18.72
$k_{\min}$	0.08	2.47	12.21

Observations. Short time windows emphasize rapid insulin-mediated effects, whereas longer windows reveal the increasing dominance of glucose distribution and clearance parameters. This confirms that parameter importance is strongly time-scale dependent.

1.7 Interim Summary

The sensitivity experiments conducted in Stage 1A demonstrate that:

- V_G and k_{p1} consistently dominate plasma glucose sensitivity across regimes.
- Several parameters exhibit strong excitation and time-scale dependence.
- Correlated sensitivity patterns suggest potential identifiability challenges.

These results motivate subsequent analysis stages focused on identifiability assessment and parameter estimation.