

Diabetes Phenotypes Quantified via a Physiofunctional Model Fitted to Raw CGM Time Series Data

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Objective:

The aim for this work is to establish a robust quantitative definition of diabetes phenotype—type 1 (T1D) vs. type 2 (T2D)—with the additional constraint that raw continuous glucose monitoring (CGM) data is the only input. Further, the phenotypic definition should incorporate the key physiological mechanism(s) underlying the observed glucose dynamics—in this case, glucagon and insulin.

Method:

A computational glucose model was developed to reproduce the glucose dynamics observed in CGM recordings (6–10 days long), which were obtained from a random sample of people with diabetes ($N_{T1D}=100$, $N_{T2D}=100$). The model parameters quantify the relative magnitude of the physiological mechanisms that could affect the observed (non-)linear fluctuations in glucose. For the model fitting procedure, models were instantiated in a paired fashion (per datum); next, a partial least-squares fit was computed, resulting in a best-fit inference solution. The fitted parameter vectors were then separated by diabetes type. Finally, the subpopulation-grouped parameters were compared via a 2-sample Kolmogorov-Smirnov (KS) test post-hoc.

Result:

KS tests revealed multiple statistically significant differences between the parameters for diabetes subpopulations (T1D vs. T2D). Of note were the parameters β and γ —the mean-centered and gradient-centered glucose sensitivity, respectively. Both were significantly higher for the T2D subpopulation ($p=0.006$, $p=0.002$).

Conclusion:

The statistically significant parameter differences reveal phenotypic differences in the physiological mechanisms underlying glucose dynamics in people with T1D and T2D. Moreover, this result illustrates an important use case for “physiofunctional” modeling techniques—namely that the functional importance of specific physiological mechanisms can be inferred by post-hoc analysis of the model parameters. Further, this work paves the way for future experiments to leverage physiofunctional models to produce counterfactual forecasts—e.g., for medication optimization/adherence algorithms.