Ideal Glycemic Control in Type 1 Diabetics

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CS 301: Ethical, Social, and Global Issues in Computing

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Mar 10, 2023

Abstract

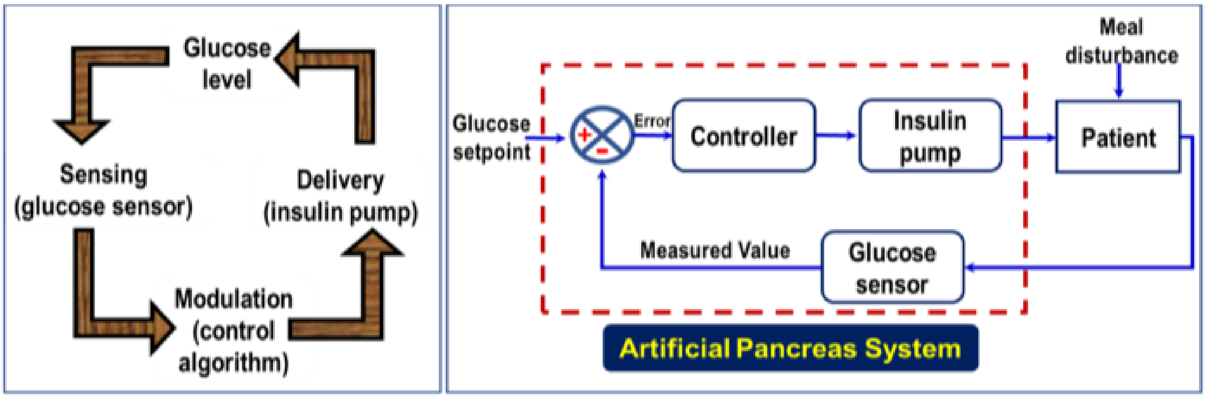
Patients with type 1 diabetes often suffer from a lack of glycemic control, which results in long-term health complications if left untreated. The use of a closed-loop insulin delivery system allows people with type 1 diabetes to have more control over their blood glucose levels, reducing the risk of complications later in life. Several types of control algorithms used in insulin pumps assist in maintaining target glucose ranges. Two popular control algorithms, model predictive control, and proportional integral derivative, maintain glycemic control using different methods; however, through multiple studies, model predictive control shows more promise in reaching the highest percentage of time in target ranges. Compared to the proportional integral derivative algorithm, model predictive control possesses greater predictive abilities which take meals, exercise, and future insulin doses into account. Further research and implementation of model predictive control in closed-loop insulin delivery systems have the potential to lessen the long-term difficulties associated with type 1 diabetes.

Ideal Glycemic Control in Type 1 Diabetics

Type 1 diabetes, an auto-immune disease resulting in the lack of insulin due to the destruction of beta cells in the pancreas, requires strenuous care and ongoing management. Ed Damiano, associate professor in biomedical engineering and co-founder of Beta Bionics, urges the importance of insulin as a “shuttle” for glucose from the bloodstream into fat and muscle cells for energy (TEDx, 2015, 4:05). Sohaib Mehmood, CEO of Infinite Scale Up and researcher at COMSATS Institute of Information and Technology, describes the dire consequences associated with poor glycemic control such as kidney failure, amputation, heart disease, and stroke (2020, p.1). Nicola Paoletti, lecturer at the Department of Computer Science at Royal Holloway, University of London, claims approximately one million type 1 diabetics globally wear an insulin pump, a subcutaneous insulin delivery device, which in certain cases comes paired with a continuous glucose monitor (CGM), providing glucose measurements to a control algorithm inside the pump (2020, p.1981). Two different algorithms primarily used in these closed-loop insulin delivery systems include model predictive control (MPC), and proportional integral derivative (PID); however, using the MPC algorithm rather than the PID algorithm has shown greater control in glucose levels in those using these insulin delivery systems. Shown below in Figure 1 are the components behind a closed-loop insulin delivery system that uses control algorithms such as MPC or PID (Mehmood, 2020, p.11).

Figure 1

Diagram of a closed-loop insulin delivery system using an artificial pancreas



(a) (b)

Note. (a) Overview of components in an artificial pancreas system, (b) Overview of artificial pancreas system

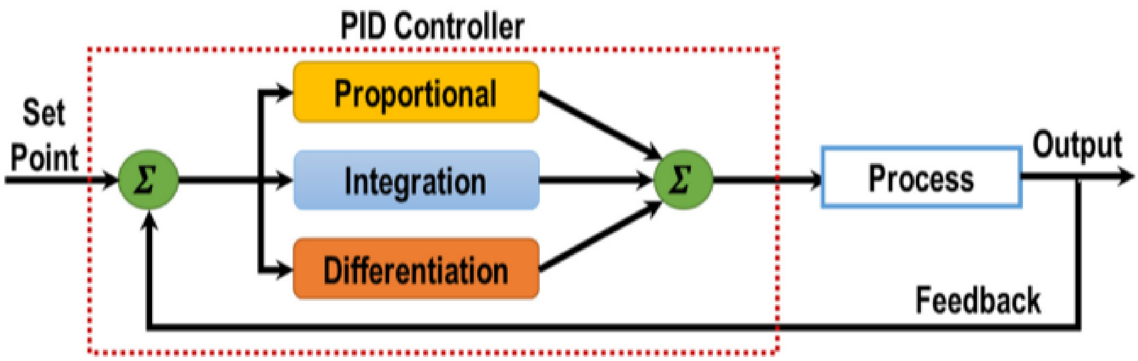
The MPC's algorithm's ability to predict future glucose levels leads to significantly greater stability in the range of such levels over extended periods, in comparison to the PID algorithm. Through higher percentages of glycemic control, MPC, compared to PID, shows more promise as the better algorithm in a closed-loop insulin delivery system due to a decreased risk of complications from type 1 diabetes.

Disadvantages of the Predictive Integral Derivative Algorithm

The predictive integral derivative algorithm works by imitating the function of beta cells' insulin secretion. In cases of high glucose levels, insulin releases in two phases, the first of which involves rapid delivery while the second implements slow delivery to stabilize glucose levels between meals. Insulin feedback ensures hypoglycemic episodes occur less frequently due to the over delivery of insulin (Mehmood, 2020, p.11). The functioning of PID controllers described in Figure 2 depicts a proportional, integration, and differentiation controller, which gain input from process output, and a deviation value is created (Mehmood, 2020, p.12).

Figure 2

Overview of the proportional integral derivative controller used to treat T1D patients



Maintaining blood glucose levels within an acceptable range (70 mg/dL - 200 mg/dL) remains crucial in preserving long-term health in type 1 diabetics. Checking blood glucose levels and delivering insulin manually makes such a task difficult; however, a closed-loop insulin delivery system makes target ranges much easier to sustain. Taking a closer look at the two most popular algorithms for insulin delivery, MPC displays higher percentages in the target range compared to PID. A study conducted by Su Lim Kang, a researcher in the Department of Medical Devices and Healthcare at Dongguk University in Seoul, found that MPC reduced time in the hypoglycemic range and maintained time in the target range more frequently than PID (2022, p.6). The main difference in the approach each algorithm takes to blood glucose levels shows how MPC achieves target numbers more than PID. PID shows promise when reacting to an ongoing situation, meaning the algorithm creates dosages based on current blood glucose readings coming from a CGM instead of predicting future glucose levels. Sara Trevitt, a Clinical Trial Coordinator at the Institute of Cancer and Genomic Sciences at the University of Birmingham, adds while PID responds to current measured glucose levels, MPC predicts such levels in the near future based on current readings from a CGM and delivers dosages based on how blood sugar levels trend; moreover, an MPC algorithm adapts and molds to the lifestyle of the user and better predict glucose levels with time (2016, p.715). In terms of the amount of time an insulin pump user maintains glycemic control, the MPC algorithm surpasses the PID algorithm.

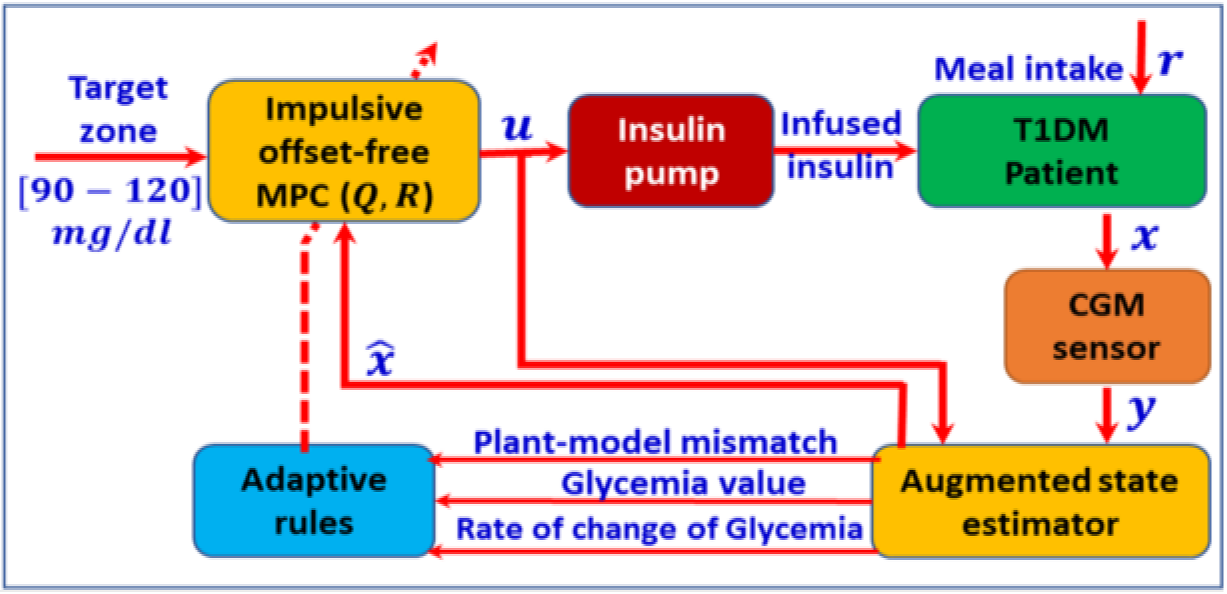
Description and Impact of Model Predictive Control

Introduction to the Model Predictive Control Algorithm

Predicting future glucose readings based on current levels creates a clear distinction between MPC and other control algorithms. Jordan Pinsker, the Senior Research Physician at Sansum Diabetes Research Institute and Vice President of Tandem Diabetes Care, describes MPC, not as a specific design, but as a “general control paradigm”, meaning there exists a set of sensors to provide information on the controlled system, a controller which processes information and makes decisions on how to adjust the system, and actuators that carry out the changes made by the controller (2016, p.1137). As such, MPC has the capability to take into account multiple factors that influence blood glucose levels such as insulin sensitivity, exercise, sleep, etc. MPC can divide the day into different periods, such as morning, afternoon, and evening, and give different objectives during each section of a 24-hour cycle. For example, an objective during the night may include avoiding hypoglycemia during sleep, while during the day tighter glycemic control after meals remains prioritized. Asymmetric costs, in the case of patients with type 1 diabetes, regard varying penalties associated with hypoglycemia and hyperglycemia. The methodology behind MPC as shown in Figure 3 below shows carbohydrates and blood glucose levels taken into account as well as consideration of target ranges between 90-120 mg/dl when creating a dose of insulin administered through a closed-loop insulin delivery system (Mehmood, 2020, p.19).

Figure 3

Overview of model predictive control strategy used in glycemic control for T1D patients



A patient susceptible to hypoglycemia requires a control algorithm that avoids low blood sugar, while a patient less sensitive to low blood glucose levels can accept a higher amount of hypoglycemic events in exchange for higher glycemic control (Pinsker, 2016, p.1138).

The use of Model Predictive Control algorithms in insulin pumps increases each year as predictive technology improves in quality. In a fixed interval of time, optimization problems are solved which produces the ideal control sequence and satisfies control objectives. This optimizes the performance of the control sequence and reduces cost functions (Mehmood, 2020, p.3). MPC contains unique characteristics which other control algorithms such as PID do not feature. Predictive control highlights MPC's capabilities by measuring insulin already in the body and anticipating future doses. The MPC algorithm compensates for delays associated with subcutaneous flow since insulin requires a certain time interval to take effect in the body. MPC takes into account dead time as well, or the difference in actual glucose concentration versus measured glucose concentration in a CGM, when adjusting blood glucose levels. Most importantly, the MPC can fine-tune control parameters to meet the specific requirements of each patient (Mehmood, 2020, p. 18-19). Using data from past inputs, outputs, and predictive future inputs, the MPC algorithm creates a predicted user output, optimizing blood glucose levels.

Studies Supporting Model Predictive Control

In a sample of 1,311 patients with type 1 diabetes, the use of the MPC algorithm compared to conventional insulin therapy showed that those who used the MPC-based artificial pancreas saw an increase of 12.57% in target glucose ranges (Kang, 2022, p.6). As previously mentioned, many factors contribute to fluctuations in blood glucose levels such as meals or exercise, with such activities resulting in the inability to maintain glycemic control. In a study conducted by Paoletti, 300-minute simulations ran which mimicked a type 1 diabetic eating a meal in three different scenarios: meals as expected, random meals, and delayed meals. Each scenario repeats 50 times, with results comparing the different controllers used in a closed-loop insulin delivery system. Overall, the robust controller (MPC) limited time spent in the hypoglycemic range below two percent and maintained target blood glucose ranges 8.5% to 21.23% more than other controllers (2020, p.1988). Physical activity was tested as well to measure a robust controller's response to decreasing blood glucose levels as opposed to increasing. In this study, a simulated scenario occurs where a virtual patient eats a meal, then performs an exercise consisting of moderate and light activity. Again, the robust controller outperformed the other controllers, maintaining target ranges 86% of the time, whereas the non-robust fails to predict exercise after the meal (Paoletti, 2020, p.1988-1989).

Model Predictive Control as the Ideal Algorithm in Insulin Pumps

Differences Between MPC and Other Control Algorithms

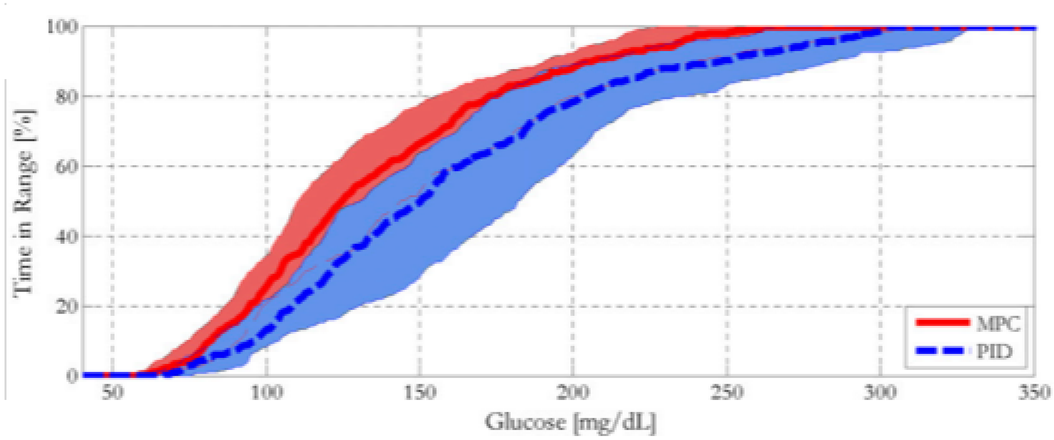
The PID algorithm works best when reading current blood glucose levels, however, lacks the ability to predict future readings, which MPC succeeds in; however, PID exceeds in maintaining glycemic control compared to other control algorithms other than MPC. For example, fuzzy logic control (FLC) takes into account variability in the human body and maps input signals based on a set of linguistic parameters such as “low” or “high” blood glucose levels. This algorithm works best when handling uncertainties and imprecise information, but PID provides faster and more accurate control when processing variables (Mehmood, 2020, p.18). MPC tops both algorithms in its ability to take into account uncertainties, meaning over time, it has the ability to reduce errors in its system and memorize specific habits of the wearer of the insulin pump. Due to distinctive features such as the ability to handle constraints, optimization of control signals, and the incorporation of multiple objectives, companies developing artificial pancreas systems use MPC over other control algorithms (Mehmood, 2020, p.18.

Glycemic Control Under Various Algorithms

Long-term hyperglycemia leads to severe health problems in the future, but hypoglycemia poses an immediate threat to the life of a type 1 diabetic, so an algorithm implemented in a closed-loop insulin delivery system should prioritize avoiding low blood glucose levels first. MPC and PID rank among the two most popular algorithms used in insulin pumps; however, there exist other, less popular, algorithms, for example, fuzzy logic control and state-dependent Riccati equation (SDRC). When comparing the percentage of time within target glucose ranges, PID spends less time in hypoglycemia than FLC and SDRC; even so, MPC lies on top with the most time in acceptable blood sugar ranges, with only 1.12% of the time below normal levels (Kang, 2022, p.6). As shown in Figure 4, MPC has a higher percentage of time spent in target ranges compared to PID, achieving higher levels of glycemic control (Pinsker, 2016, p.1138).

Figure 4

Glucose control performance characterized by cumulative % time in glucose ranges



Juxtaposing each algorithm's time spent in the hypoglycemic range allows researchers to determine which method poses the least short-term risk to a type 1 diabetic. Since MPC displays the least amount of time in low blood glucose levels, the use of the algorithm in insulin-delivery systems gains popularity every year.

Previously mentioned studies support the claim that MPC results in the highest percentages of stable blood glucose levels. Activities such as meals or exercise can lower or raise glucose levels outside of their normal ranges, and as such, algorithms must predict these changes before they occur to prevent extreme hypoglycemia or hyperglycemia. The robust MPC controller studied by Nicola Paoletti outperforms all other controllers simulating such actions listed above. Even in high carbohydrate meals, the robust controller maintains healthy blood glucose levels 81.02% of the time compared to 70.53% in non-robust controllers (2020, p.10). Glycemic control in type 1 diabetics remains essential in preserving long-term and short-term health. An algorithm that sustains stable glucose levels over extended periods of time will lead to longer, healthier lives in patients with type 1 diabetes, which gives MPC a clear advantage over other control algorithms used in closed-loop insulin delivery systems.

Conclusion

The effects of long-term blood glucose levels outside of target ranges cause a multitude of health complications in people with type 1 diabetes. Without a proper method of maintaining glycemic control, other facets of the body begin to shut down, creating many difficulties for patients with the condition. The use of a closed-loop insulin delivery system assists in the control of blood glucose levels and results in greater time in target ranges, allowing people with type 1 diabetes to suffer less from these complications. Two popular algorithms used in insulin pumps, model predictive control, and proportional integral derivative, show the most improvement in preventing hypoglycemia and hyperglycemia; however, the model predictive control algorithm exceeds in maintaining time in target ranges due to its predictive abilities. Under various activities which disrupt glycemic control such as exercise and eating, model predictive control excels at anticipating rises or drops in blood glucose levels and adjusting for them. As more research comes out and advancements in control algorithms used in closed-loop insulin delivery systems release, the ability of the model predictive control algorithm to maintain glycemic control will increase, reducing long-term health complications in people with type 1 diabetes.

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