THE BIHORMONAL INTRAPERITONEAL ARTIFICIAL PANCREAS ACHIEVES FULLY CLOSED LOOP CONTROL IN ANESTHETIZED ANIMALS.

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Background and Aims

Fully automated blood glucose (BG) control without meal announcement is a considerable challenge for artificial pancreas (AP) systems due to the slow subcutaneous (SC) insulin absorption and delayed effect on glucose homeostasis. Intraperitoneal (IP) insulin with a faster absorption rate is suggested. In addition, single hormone APs are shown to be conservative in dealing with exercises and sudden drops in the BG. Therefore, we use both insulin and glucagon infusions intraperitoneally to achieve a tight glycemic control without meal and exercise announcements.

Method

A combination of nonlinear model predictive control (NMPC) and Zone MPC algorithms is used to control the blood glucose level (BGL). The penalty used for different BGLs is shown in Fig.1.

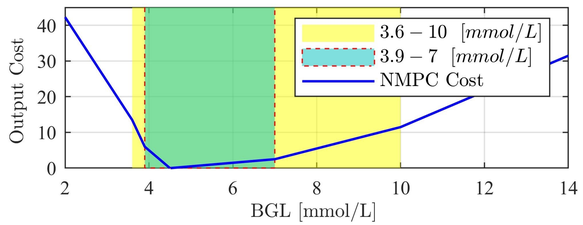

Fig. 1. Penalty used for different BGLs in the NMPC.

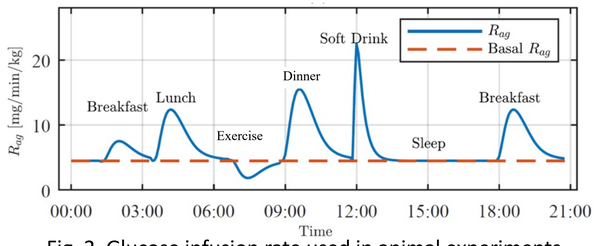

Fig. 2. Glucose infusion rate used in animal experiments.

Furthermore, a moving horizon estimator is used to estimate the states that are required for the predictions, such as the amount of insulin and glucagon in the peritoneum and the liver, as well as the glucose appearance rate in the blood. The controller uses a modified version of the model presented by Zazueta et al [1], in which the hepatic first-pass effect is included for insulin. Meals and exercise are simulated in the three anesthetized animals by manipulating the intravenous glucose infusion rates as shown in Fig. 2. The basal rate for intravenous glucose infusion is 4 mg/min/kg and the intestine model presented in [2] is used to generate the profile of the added glucose infusion rate during meals. In addition, the rate of glucose administration to the pig is reduced to simulate exercise.

Results

The designed AP kept the BGL in the target zone (3.9-10 mmol/l) at 87%, 93% and 94% of the time for the three experiments. This was achieved without informing the controller about the meals and exercise. The performance of the designed controller for the second experiment is shown in Fig. 3. It is important to note that the operator gave an insulin bolus instead of glucagon by mistake at 14:25. Therefore, two “rescue food” glucose infusions are given to prevent hypoglycemia at 14:45 and 15:05.

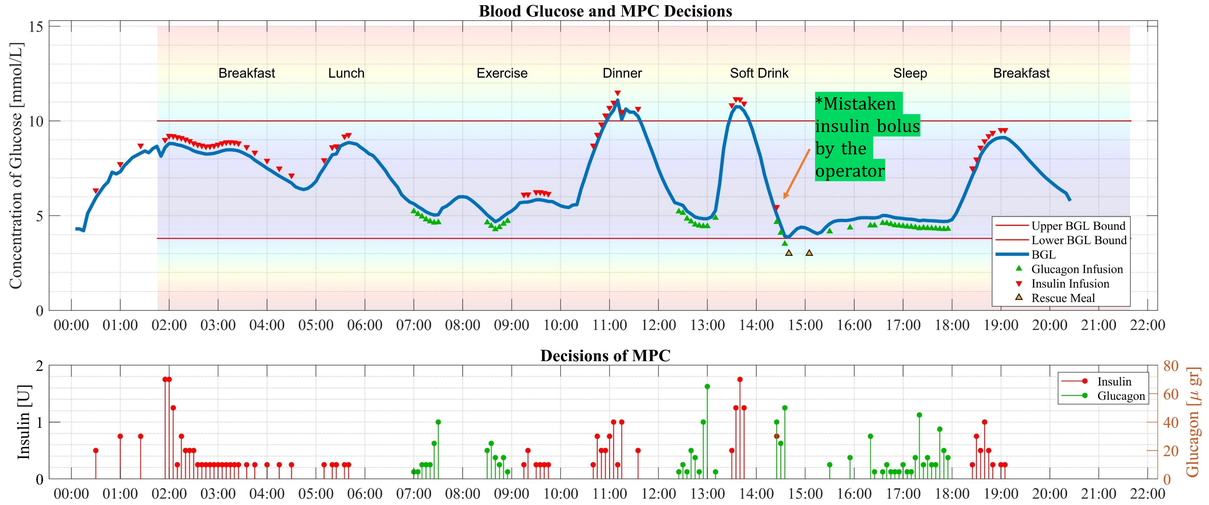

Fig. 3. The performance of the designed controller in controlling BGLs in the second animal experiment, which was carried out on a 36kg pig. It is worth noting that the controller began nearby 02:00, and the open-loop experiment prior to that was used to identify the parameters and initialize the controller.

Conclusion

The preliminary results in three animal experiments indicate that the fully automated bi-hormonal IP AP achieves satisfactory glycemic control. More realistic situations can be investigated in the future by conducting experiments on awake animals.

References

[1] Zazueta et al, 2021. DOI 10.1109/TBME.2021.3125839
[2] Dalla Man et al, 2007. DOI 10.1109/TBME.2007.893506.

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