Titration algorithms based on feedback control and physiological insight

In this project, you will use feedback control (i.e., elements from PID control) to automatically determine a person's basal and meal bolus insulin requirements. First, you will address the tasks of estimating each quantity separately, and next, you will combine the solutions you have developed to estimate both simultaneously. Furthermore, you will address some real-life issues of automated titration. You can draw on the experiences reported by Ritschel et al. (2022). **It is important that each version of the controller you develop is in its own Matlab function such that you can easily compare them.**

Part 1 – estimate the basal rate

1. Create a PID controller which 1) administers the optimal bolus for each meal and 2) doesn't integrate for a number of hours after each meal. Experiment with different numbers of hours.
2. Perform a closed-loop simulation for 1 month – what should the controller gains be?
3. Implement meal superboluses in the controller, i.e., where the basal rate is set to zero for a number of hours after each meal (e.g., 2 h) and the amount of basal rate that would have been given is administered at the time of the meal.
4. Titrating people in too fast can cause nerve damage. Extend the controller with a time-dependent setpoint which slowly decreases over time. How should it decrease over time?
5. Repeat the closed-loop simulation – what should the controller gains be now?
6. Create a new simulation where the person fasts (doesn't eat) for the first two days – how much faster can we titrate people in?
7. Augment the MVP measurement model with a stochastic measurement model (add a zero-mean normal distributed measurement noise variable to each measurement)
8. Repeat the above closed-loop simulations.
9. Augment the MVP model with a stochastic diffusion term which will give rise to random variations in the dynamics of the virtual person. Assume that there are random variations in the blood glucose concentration, $G(t)$. (Ask Tobias, Sarah, or John for details.)
10. Implement the Euler-Maruyama method (see Section 4 in the paper by Higham (2001)).
11. Repeat the above closed-loop simulations with 1, 10, and 100 virtual people.

Part 2 – estimate the insulin-to-carb ratio

12. Copy the above versions of the controller and change them such that they administer the true basal rate and use the integrator to estimate the inverse insulin-to-carb ratio – you can remove the PD-terms, and you need to retune the gain of the integrator term as it now has a different meaning.
13. Repeat the above closed-loop simulations.

Part 3 – estimate both the basal rate and the insulin-to-carb ratio

14. Try to estimate both the basal rate and the insulin-to-carb ratio. You will need two separate integrators.
15. Is it easier to estimate both quantities simultaneously if the persons fasts for the first two days?

Contact: John Bagterp Jørgensen, jbjo@dtu.dk, DTU Compute

Ritschel, T.K.S., Reenberg, A.T., Lindkvist, E.B., Laugesen, C., Svensson, J., Ranjan, A.G., Nørgaard, K., Dammann, B., Jørgensen, J.B., 2022. A one-size-fits-all artificial pancreas for people with type 1 diabetes based on physiological insight and feedback control. In submission. arXiv: 2202.13338.

Higham, D.J., 2001. An algorithmic introduction to numerical simulation of stochastic differential equations. SIAM Review 43(3), pp. 525-546.