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Modelling Insulin and Glucose Dynamics in Diabetes Mellitus Type 1: Intravenous, Subcutaneous and Intraperitoneal Approach

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HELSE MIDT-NORGE

apt ARTIFICIAL PANCREAS TRONDHEIM

Motivation

Diabetes mellitus type 1 (DM1)
- Normal glucose regulation by insulin
- Destructed insulin secretion in DM1
- Exogenous insulin infusions

State-of-the-art treatment
- Sensor-augmented insulin pumps
- Subcutaneous insulin delivery
- Subcutaneous glucose sensing
- Manual interventions required

Long-term aim
- Artificial Pancreas (AP)
- Fully automated insulin delivery

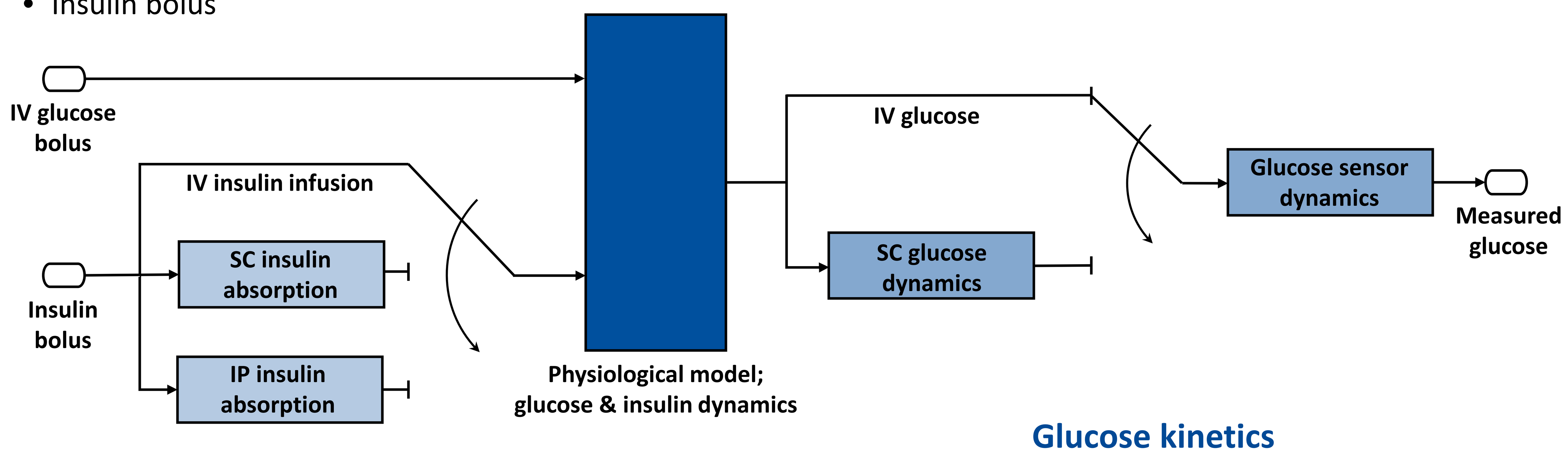
Strategy
- Easily extendable modular model
- Open- and closed-loop scenarios
- AP algorithm development based on simulation
- Validation by animal and clinical trials

Model

Input
- Intravenous glucose bolus
- Insulin bolus

Physiological glucose-insulin model [1]

Output
- Measured glucose concentration

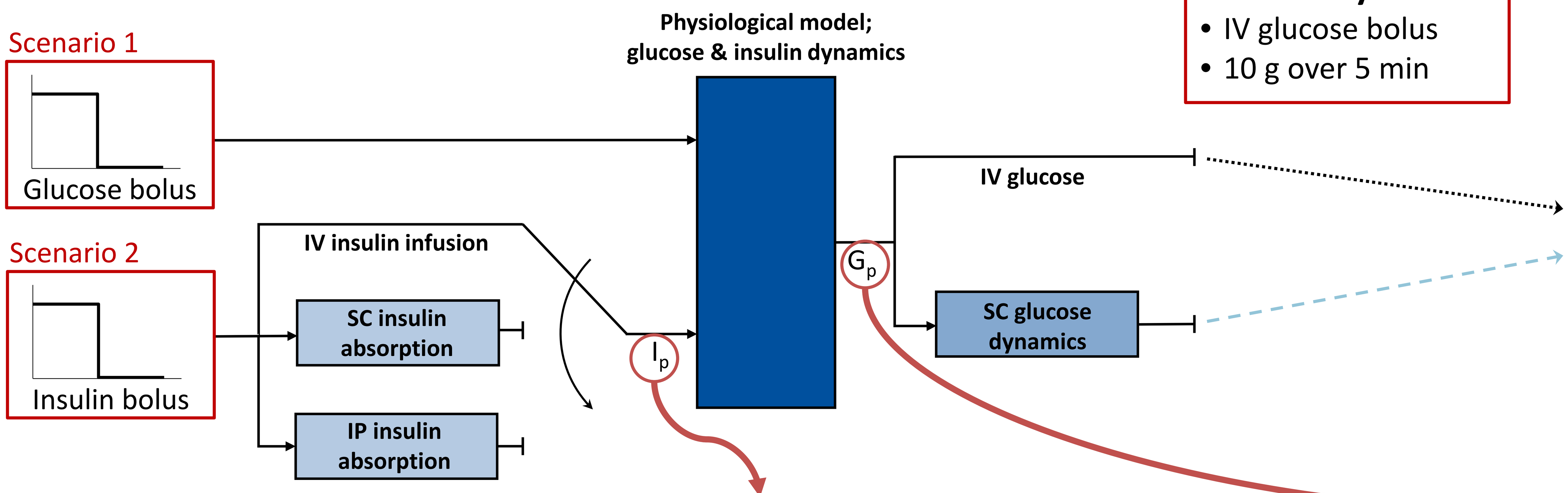


Insulin absorption kinetics
- Intravenous (IV) [1]
- Subcutaneous according to Wilinska at al. ($SC_{Wil.}$) [2]
- Subcutaneous according to Dalla Man et al. ($SC_{D.M.}$) [1]
- Intraperitoneal (IP) [3]

Glucose kinetics
- Intravenous (IV) [1]
- Subcutaneous (SC) [4]

- Sensor dynamics

Simulations



Scenario 1

Glucose Dynamics
- IV glucose bolus
- 10 g over 5 min

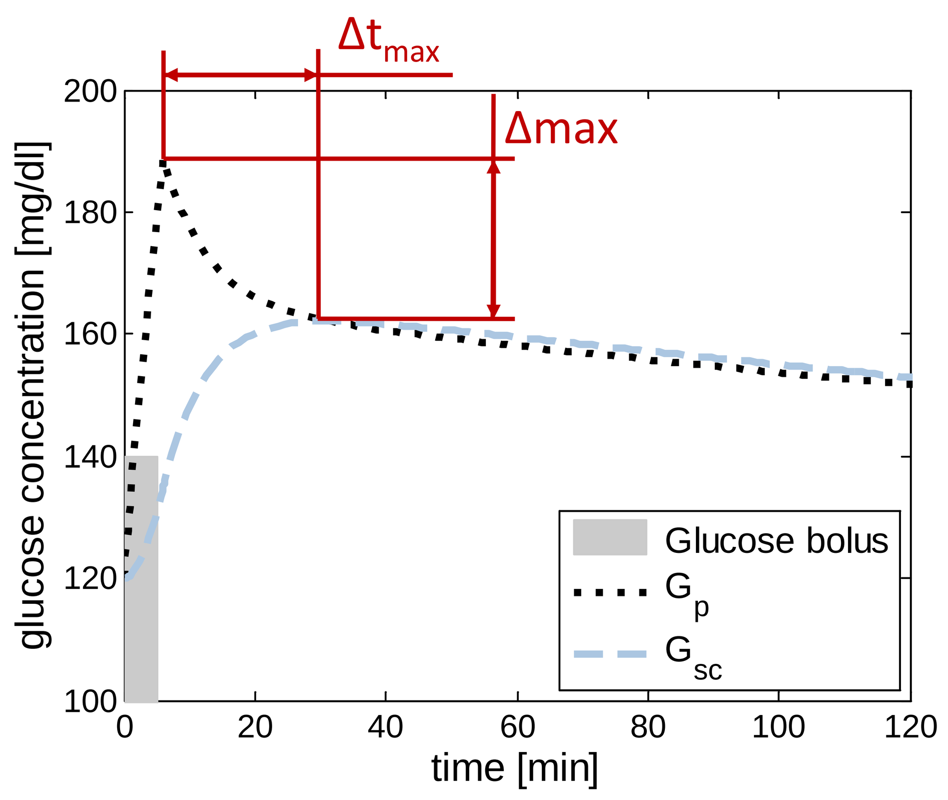


Fig. 1: Glucose response in plasma (G_p) and SC (G_{sc}) to IV glucose bolus.

Scenario 2

Insulin Dynamics
- Insulin bolus
- 5 IU over 4 min
- Injected IP, $SC_{Wil.}$, $SC_{D.M.}$

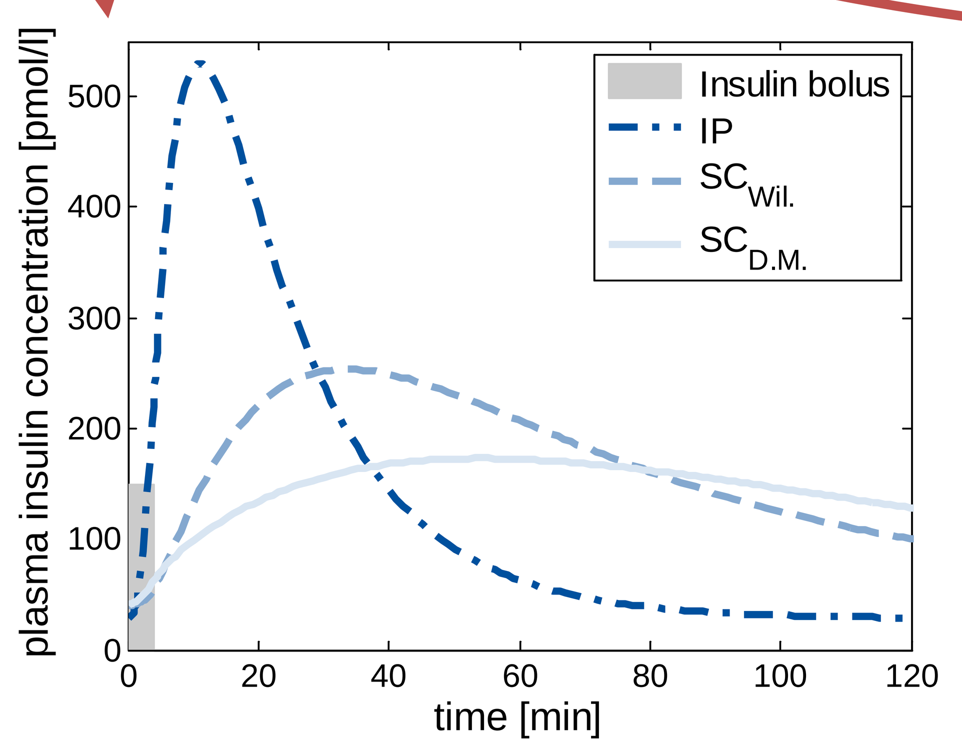


Fig. 2a: Plasma insulin responses (I_p) to insulin boli.

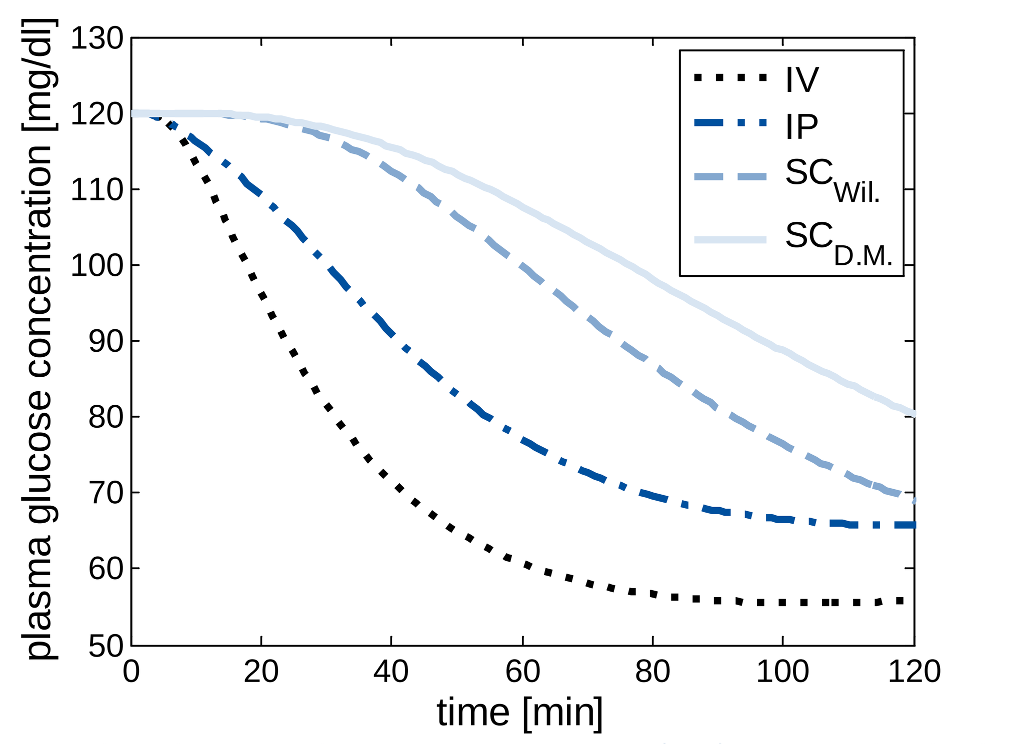


Fig. 2b: Plasma glucose responses (G_p) to insulin boli.

Conclusion

Insulin infusion
- SC: common but large time constants
- IV: fastest but not practical for safety reasons
- IP: promising

Glucose sensing
- SC: significant time delays/constants
- No other options available for outpatient use
- Faster sensing techniques highly desired

References

[1] Dalla Man C, Raimondo DM, Rizza RA, Cobelli C. GIM, Simulation software of meal glucose-insulin model. Journal of Diabetes Science and Technology. 2007;1(3):323-30.

[2] Wilinska ME, Chassin LJ, Schaller HC, Schaupp L, Pieber T, Hovorka R. Insulin Kinetics in Type-1 Diabetes continuous and bolus delivery of rapid acting insulin. IEEE Transactions on Biomedical Engineering. 2005;52(1):3-12.

[3] Matsuo Y, Shimoda S, Sakakida M, Nishida K, Sekigami T, Ichimori S, et al. Strict glycemic control in diabetic dogs with closed-loop intraperitoneal insulin infusion algorithm designed for an artificial endocrine pancreas. Journal of Artificial Organs. 2003;6(1):55-63.

[4] Burnett DR, Huyett LM, Zisser HC, Doyle FJ, 3rd, Mensh BD. Glucose sensing in the peritoneal space offers faster kinetics than sensing in the subcutaneous space. Diabetes. 2014;63(7):2498-505.