Background and Aims

Developing the model structure for the insulin-glucose regulatory system with an intraperitoneal route of insulin delivery, we encountered questions regarding the relationship between insulin action and clearance:

Q1. Does the body clear all insulin after it has affected the glucose level?
Q2. Does the liver clear some insulin before it can affect the system?
Q3. What mechanisms cause saturation in insulin clearance?
Q4. Does the saturation also affect the insulin action?

Method

In pursuit of answers, we have comprehensively reviewed relevant physiology and mathematical modeling literature.

Results

Despite a shared receptor binding step between insulin action and clearance, the destiny of insulin after binding (Fig. 1c) diverges from the signal it dispatches to impact glucose level (Figs. 1a and 1b). Upon binding, insulin and receptors internalize into cells before undergoing degradation, with subsequent receptors recycling to the cell surface (Fig. 1c).

Conclusion

The shared binding step suggests that saturation stemming from insufficient availability of receptors generally affects both insulin action and clearance (answers to Q3 and Q4). This should be taken into account when deciding about the model structure. Fig 2a and 2b show two different approaches for modeling saturation both in the insulin action and its clearance.

References