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ORIGINAL ARTICLES

# Coordinated Basal–Bolus Infusion for Tighter Postprandial Glucose Control in Insulin Pump Therapy

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## Abstract

***Background:***

Basal and bolus insulin determination in intensive insulin therapy for type 1 diabetes mellitus (T1DM) are currently considered independently of each other. A new strategy that coordinates basal and bolus insulin infusion to cope with postprandial glycemia in pump therapy is proposed. Superior performance of this new strategy is demonstrated through a formal analysis of attainable performances in an *in silico* study.

***Methods:***

The set inversion via interval analysis algorithm has been applied to obtain the feasible set of basal and bolus doses that, for a given meal, mathematically guarantee a postprandial response fulfilling the International Diabetes Federation (IDF) guidelines (i.e., no hypoglycemia and 2 h postprandial glucose below 140 mg/dl). Hypoglycemia has been defined as a glucose value below 70 mg/dl. A 5 h time horizon has been considered for a 70 kg *in silico* T1DM subject consuming meals in the range of 30 to 80 g of carbohydrates.

***Results:***

The computed feasible sets demonstrate that current separated basal/bolus strategy dramatically limits the attainable performance. For a nominal basal of 0.8 IU/h leading to a basal glucose of approximately 100 mg/dl, IDF guidelines cannot be fulfilled for meals greater than 50 g of carbohydrates, independent of the bolus insulin computed. However, coordinating the basal and bolus insulin delivery can achieve this. A decrement of basal insulin during the postprandial period is required together with an increase in bolus insulin, in appropriate percentages, which is meal dependent. After 3 h, basal insulin can be restored to its nominal value.

***Conclusions:***

The new strategy meets IDF guidelines in a typical day, contrary to the standard basal/bolus strategy, yielding a mean 2 h postprandial glucose reduction of 36.4 mg/dl without late hypoglycemia. The application of interval analysis for the computation of feasible sets is demonstrated to be a powerful tool for the analysis of attainable performance in glucose control.

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**Abbreviations:** (I:C) insulin-to-carbohydrate ratio, (IA) interval analysis, (IDF) International Diabetes Federation, (IU) international units [of insulin], (SIVIA) set inversion via interval analysis, (T1DM) type 1 diabetes mellitus

**Keywords:** glucose control, insulin pump therapy, interval analysis, set inversion, type 1 diabetes mellitus

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