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Supplementary Appendix. Model Used For Optimal Model Predicted Bolus (MPB)

Model optimization was based on the 3rd order insulin pharmacokinetic/pharmacodynamic model developed by Sherwin and colleagues (1) combined with the 1st order Bergman minimal model (2; 3), and a piecewise linear approximation of the 2nd order meal absorption model proposed by Hovorka and colleagues (4). The combined model allowed 9 parameters to be identified: 3 insulin PK/PD rate constants, the effect of glucose per se to increase glucose uptake and decrease endogenous glucose production (p_1), insulin sensitivity normalized to insulin clearance (S_I), 3 parameters characterizing the initial rise, maximum rate, and fall in glucose appearance following the meal (T_{rise}, $T_{constant}$, and $T_{decrease}$), and the glucose distribution space (V_G). Model equations:

$$\frac{dI_{SC}}{dt} = \frac{1}{\tau_1}\Delta ID - \frac{1}{\tau_1}I_{SC}$$

$$\frac{dI_p}{dt} = \frac{1}{\tau_2}I_{SC} - \frac{1}{\tau_2}I_p$$

$$\frac{dI_{ISF}}{dt} = \frac{1}{\tau_3}I_P - \frac{1}{\tau_3}I_{ISF}$$

$$\frac{dG}{dt} = -\left[p_1 + S_I\Delta I_{ISF}\right]G + p_1 G_B + \frac{R_{A[MEAL]}}{V_G}$$

$$R_{A[MEAL]} = if\ T_{MEAL} \le t < T_{rise}\ SLOPE_1\left[t - T_{MEAL}\right]$$

$$if\ T_{rise} \le t < T_{constant}\ R_{A[MAX]}$$

$$if\ T_{constant} \le t \le T_{decrease}\ SLOPE_2[t - T_{constant}]$$

were implemented in Microsoft Excel (Office 2013), with the added constraint that the total area under curve for $R_{A[MEAL]}$ equal the grams of carbohydrate in the meal, and that $SLOPE_1 = R_{A[MAX]}/[T_{rise} - T_{meal}]$ and $SLOPE_2 = R_{A[MAX]}/[T_{constant} - T_{decrease}]$. Parameters for each HFHP meal were obtained using a nonlinear generalized reduced gradient algorithm available in Microsoft Excel. We have previously used a similar model to characterize the effect of meal fat content on insulin requirements (5) and characterize intraday changes in metabolism (6; 7).

SUPPLEMENTARY DATA

Supplementary Appendix References

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Supplementary Table 1. Nutritional composition of test foods

Meal	Ingredient	Weight (g)	Energy (kCal)	CHO (g)	Glycemic Index (%)	Fat (g)	Protein (g)
Low Fat, Low Protein (LFLP)	Pizza Base	93	249	46	52	3	8
	Marinara Sauce	42	24	4	-	1	1
	TOTAL	135	273	50		4	9
High Fat, High Protein (HFHP)	Pizza Base	93	249	46	52	3	8
	Marinara Sauce	42	24	4	-	1	1
	Cheese	125	491	0	-	40	27
	TOTAL	260	764	50		44	36
Difference			+ 491	-		+ 40	+ 27

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Supplementary Table 2. Mealtime insulin dosing and 6 hour postprandial glucose profiles in 10 adults with type 1 diabetes.

	LFLP	HFHP	HFHP – Optimized Dose
Mean Insulin Dose (units)	4.7	4.7	7.9
Mean Insulin Combination Wave Split (%/%)	50/50	50/50	30/70
Mean Insulin Combination Wave Duration (minutes)	120	120	144
Glucose iAUC (mg/dL.min)	13320 ± 2960	27092 ± 1709	11712 ± 3172
Mean Incremental plasma glucose (mg/dL)	+23 ± 11	+73 ± 4	+24 ± 11
Mean Incremental Peak plasma glucose (mg/dL)	+82 ± 13	+118 ± 7	+61 ± 13
Time to Mean Incremental Peak plasma glucose (minutes)	105 ± 14	255 ± 21	207 ± 33

LFLP = Low fat, low protein meal; HFHP = High fat, high protein meal; iAUC = incremental Area Under the Curve