Supplementary Material:

Physical activity informed bolus algorithm details

The physical activity related mealtime insulin bolus modulation relies on a wearable activity tracker-based calculation of accumulated physical activity through a weighted sum of the historical steps taken within the previous 12 hours. The resulting metric, denoted as AOB, corresponds to the accumulated physical activity performed previously and is still actively impacting glucose uptake. The AOB at a sampling time index *k* is calculated as follows:

$$AOB(k) = \langle \rho, \sigma \rangle, = \sum_{t=k-143}^{k} \rho(k-t)s(t)\,, k \geq 143,$$

where "*s(t)*" is the step-count accumulated over 5 minutes (aligning with common CGM sampling intervals), and *t* spans from *k* (current time) to *k-143* (144×5min=12 hours ago), $\rho = (\rho(0), \rho(1), \ldots, \rho(143))$ is a 144-dimensioanl weighting vector, consisting of the percentage of the residual glycemic impact from the previously performed physical activity obtained based on an activity accumulation curve (Supplemental Figure 1). In other words, *AOB(k)* is a weighted summation of the recent 12-hour physical activity.

$$PA\ informedbolus = ST\ Bolus - \frac{AOB_{d,m} - AOB_{profile,m}}{AF}$$

ST Bolus is the amount of insulin bolus calculated according to the standard insulin therapy. The $AOB_{d,m}$ is the AOB calculated for the meal *m* consumed on day *d*. $AOB_{profile,m}$ is the profile that captures the routine daily accumulated physical activity of a participant around a selected standard meal *m* such as breakfast, lunch or dinner. AF translates the anticipated glycemic change generated by the physical activity deviations into insulin units with a similar impact. In order to obtain the $AOB_{profile,m}$, optimum mealtime CR, and optimum AF we followed the steps below:

Step 1—Extraction of the participant-specific AOB lunch profile ($AOB_{profile,lunch}$)*:* Lunchtime $AOB_{profile,lunch}$ was computed as the median AOB between 11 am and 2 pm during the data collection phase.

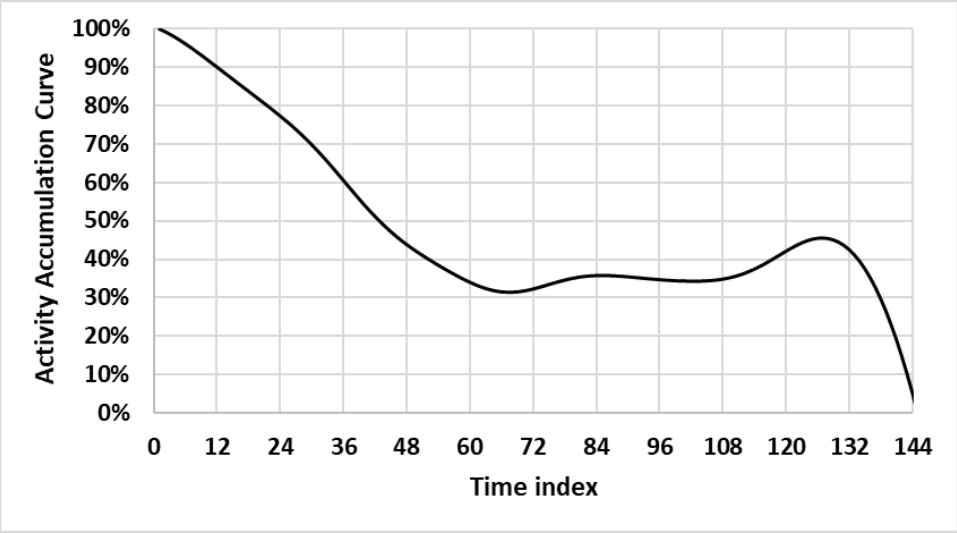
Step 2– Physical activity informed CR optimization: The main parameter of a meal bolus is the CR. This parameter is designed to provide optimum CHO/insulin value to compensate for the expected BG increase from the CHOs in meals. If the glycemic impact of previous physical activity was similar at the time of every meal, an optimized CR could compensate for the combined impact of meal and accumulated physical activity without a need for an additional physical activity correction. However, because deviations in the physical activity behavior are a part of daily life, the performance of a meal bolus without such correction is limited. This limitation is addressed with the AF in the physical activity informed bolus formula. Therefore, we first optimize CRs for the meals we are interested in –in our case, lunch, and a late evening meal – separately by running *in silico* CGM replays on the data obtained during the data collection phase. The objective of this data-driven optimization is to minimize the post-meal glycemic risk computed as explained in [1] by factoring out the physical activity-induced changes in the insulin needs. In order to separate the cofounding effect of physical activity,

we use the physical activity information while determining whether the emphasis should be on the low BG risk (LBGI) or high BG risk (HBGI) in the cost function as explained in [2]. The resulting optimum lunch CRs are used in both outpatient study visits, whereas the optimum CRs for the selected late evening meal are only used to obtain AFs for each participant as elaborated in Step 3.

Step3—AF optimization: Using the optimum dinner CR, we find the AF for each participant as the parameter that minimizes the total glycemic risk –with equal emphasis on LBGI and HBGI— evaluated on the CGM traces obtained when physical activity-informed bolus formula is applied *in silico* at and following sizable meals that occur later in the evening (between 4:30-10:00pm). The reason we selected to evaluate post-*meal* BG behavior after a sizable meal that occurs later in the evening for AF optimization is in order to (i) capture glycemic impact from a wide range of physical activity accumulated throughout the day, and (ii) relatively better isolation of the analysis window from significant disturbances, such as another large meal. We used a time and meal-size based dinner detection algorithm to label the dinners.

The CGM replays for both CR and AF optimizations are performed using the net effect technology developed previously by Patek et al. [3]. This technique allows us to replay the participant's post-meal BG traces with physical activity informed boluses while keeping in the real-life observed BG variations due to disturbances including and beyond meal and insulin. Before performing the replays, we pre-processed the collected data to check for validity based on the following criteria:

- A day was rejected from analyses if more than 2 hours of CGM data was missing between 4:30 pm and 10 pm or if no insulin was administered for a meal during this interval.
- Physical activity data had to be available in the morning (6 am to noon), afternoon (noon to 5 pm) and evening (5 pm to 10 pm), as defined by no more than 2-hours of missing data in any of these three intervals.



Supplemental Figure 1 Activity accumulation curve

Participant-level breakdown of lunchtime insulin bolus variables

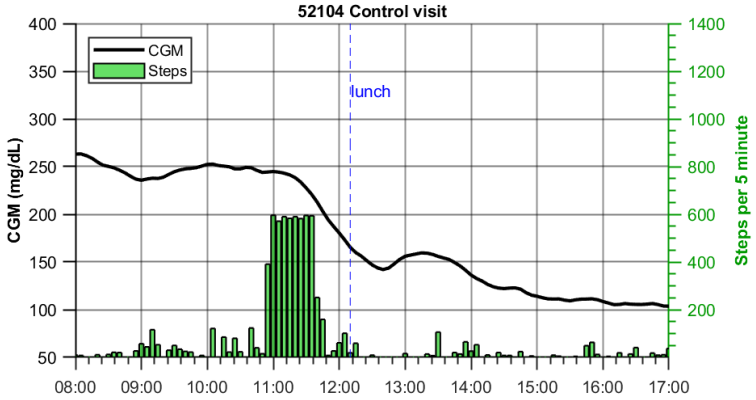
Supplemental Table 2 Lunchtime values per participant used during the control visit and resulting post-lunch CGM slopes

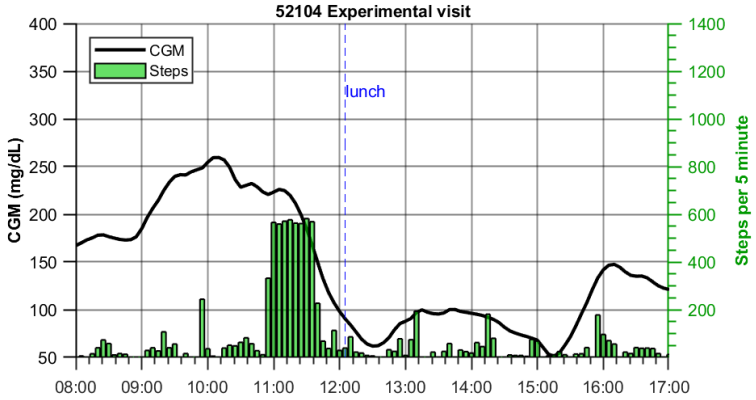
Subject	IOB (U)	BG (mg/dL)	CR (g/U)	AF (acc. Steps/U)	Bolus (U)	AOB Profile (acc. Steps)	AOB Lunch (acc. Steps)	Post-lunch [0h,2h] Slope (mg/dL/5min)	Post-lunch [2h,4h] Slope (mg/dL/5min)
52104	0.15	163	14.0	2200	2.7	3917	6224	-0.5	-0.9
52106	0	137	7.5	2200	7.7	3973	5700	3.5	-2.9
52107	0.13	145	10.7	2594	7.2	990	6192	-0.9	6.4
52108	0	91	11.4	2200	5.3	1402	4470	8.4	-2.3
52109	0	130	15	2198	4.6	3157	6467	0.4	0.1
52110	0	149	17	2200	2.9	1065	3966	2.7	0.0
52111	0.03	111	7.9	4405	8	1857	4617	-0.3	0.9
52113	0	73	11.8	2200	4.9	1197	4078	0.1	1.1
52114	0	91	7.4	3235	7.3	3300	6132	1.0	0.3
52116	0	163	16.7	2836	4	2108	5573	0.3	-0.4
52117	0.09	157	13.6	4921	3.9	1827	4819	-0.3	-0.8
52118	0.14	218	7.0	1666	7.9	1735	4665	-3.6	-0.9
52119	0	73	18.8	1621	2.6	930	1621	5.0	-1.0
52121	0.07	92	10.6	1573	4.8	2063	7529	-1.7	4.1
52122	0	83	7.4	2200	8	673	4682	4.7	0.3

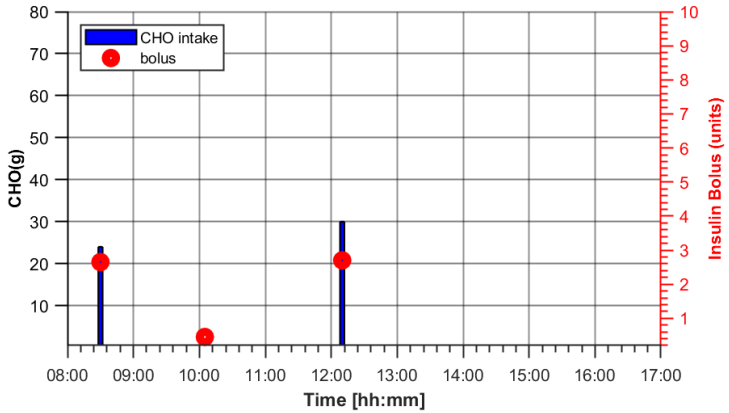
Supplemental Table 2 Lunchtime values per participant used during the experimental visit and resulting post-lunch CGM slopes

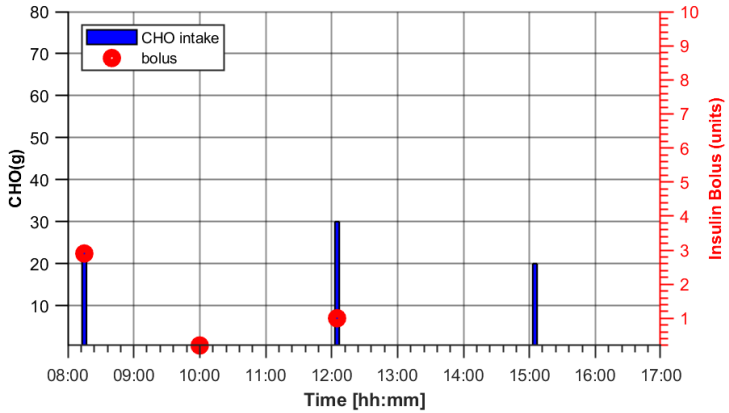
Subject	IOB (U)	BG (mg/dL)	CR (g/U)	AF (acc. Steps/U)	Bolus (U)	AOB Profile (acc. Steps)	AOB Lunch (acc. Steps)	Post-lunch [0h,2h] Slope (mg/dL/5min)	Post-lunch [2h,4h] Slope (mg/dL/5min)
52104	0.08	89	14.0	2200	1	3917	6172	1.4	1.1
52106	0.11	181	7.5	2200	8.2	3973	5945	2.1	-2.5
52107	0	138	10.7	2594	6.1	990	3916	1.7	4.4
52108	0	128	11.4	2200	4.6	1402	3953	5.3	1.5
52109	0	101	15	2198	2.5	3157	6059	7.0	0.0
52110	0.03	153	17	2200	1.8	1065	4242	1.3	2.8
52111	0	154	7.9	4405	8.7	1857	4985	-0.2	-0.6
52113	0.02	89	11.8	2200	3.6	1197	4066	0.8	2.5
52114	0.01	120	7.4	3235	6.9	3300	5796	0.4	-0.3
52116	0	132	16.7	2836	2.2	2108	5772	2.6	0.0
52117	0.07	198	13.6	4921	3.9	1827	4334	1.9	-0.7
52118	0	111	7.0	1666	3.3	1735	5014	0.9	-0.6
52119	0.03	76	18.8	1621	1.3	930	4535	6.2	-1.0
52121	0	134	10.6	1573	2.9	2063	7208	0.9	-2.6
52122	0.05	93	7.4	2200	5.9	673	5038	2.9	-0.4

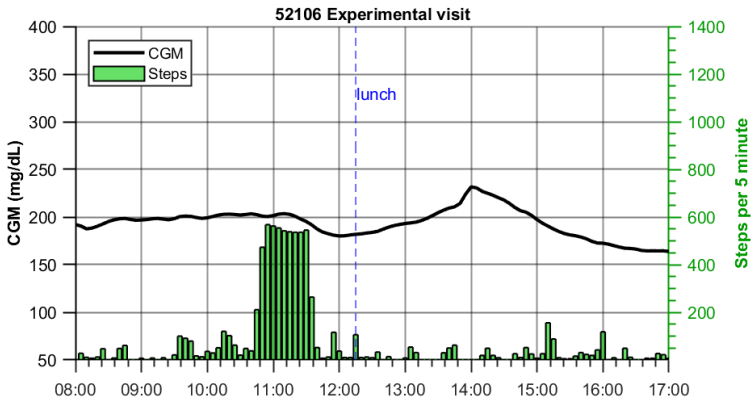
Individual Clinical Results







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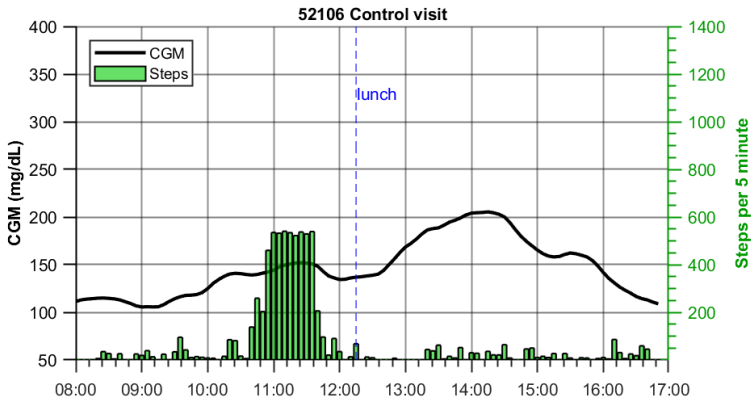
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute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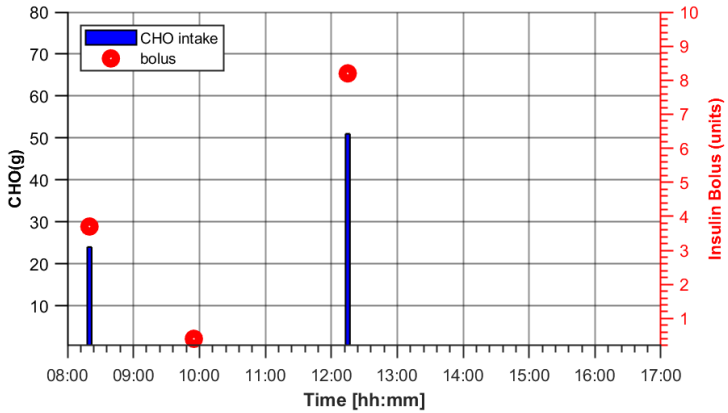
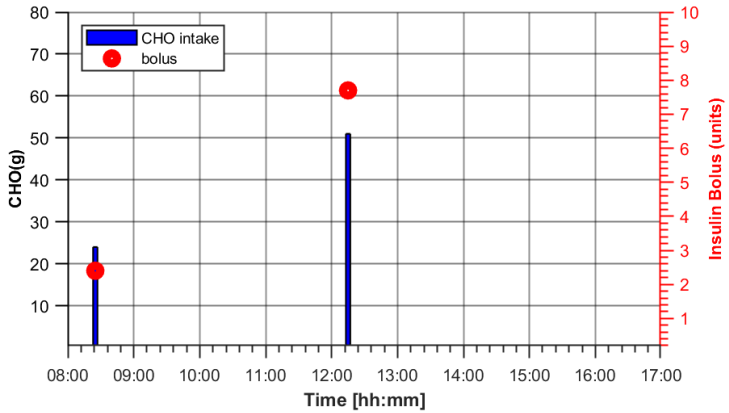
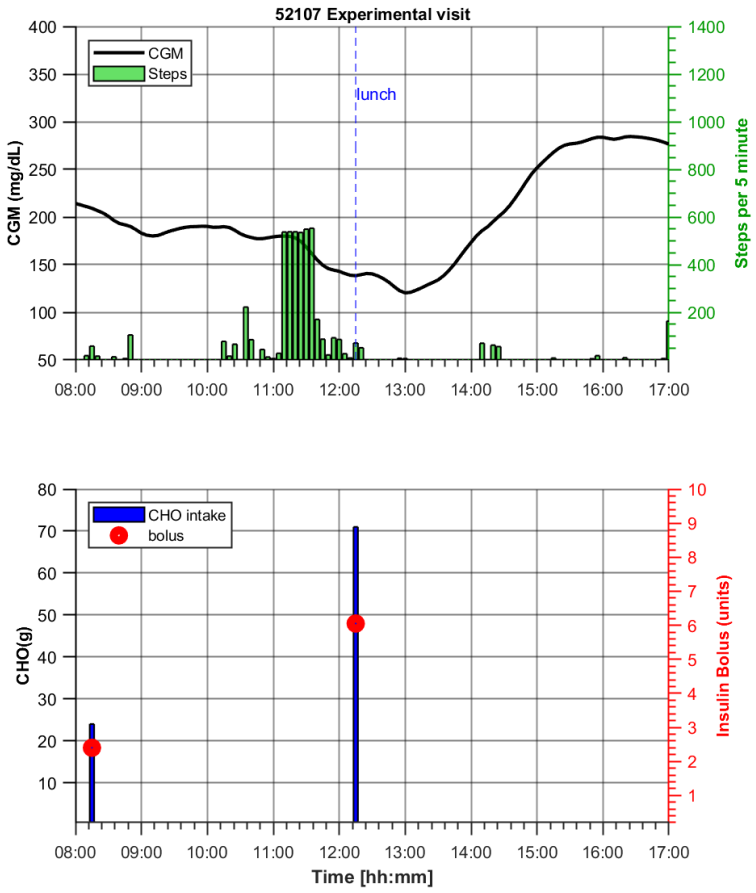
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute


CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]


CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]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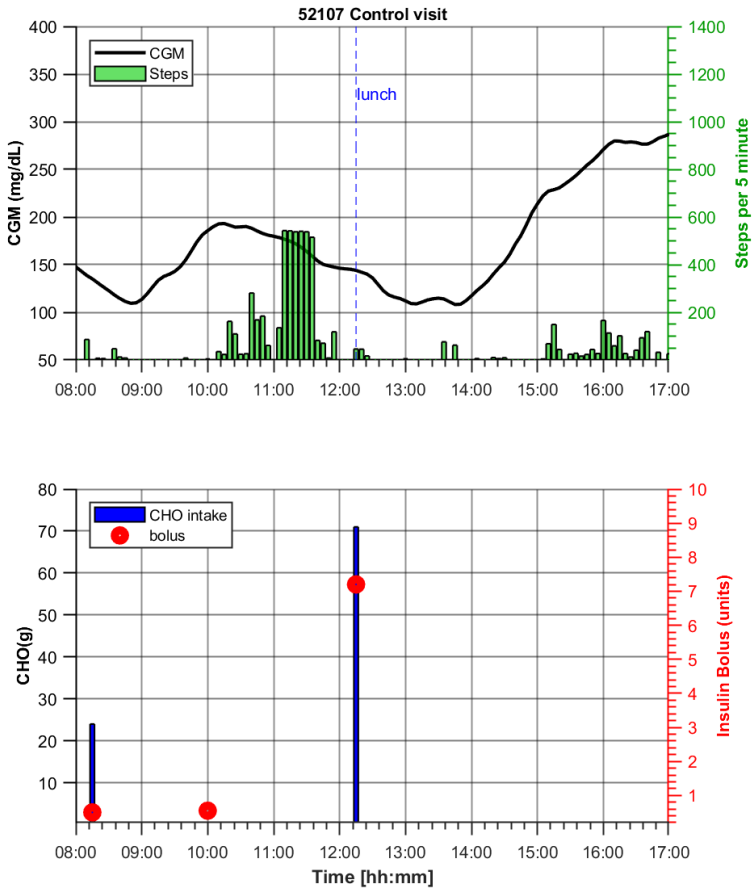
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute
CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]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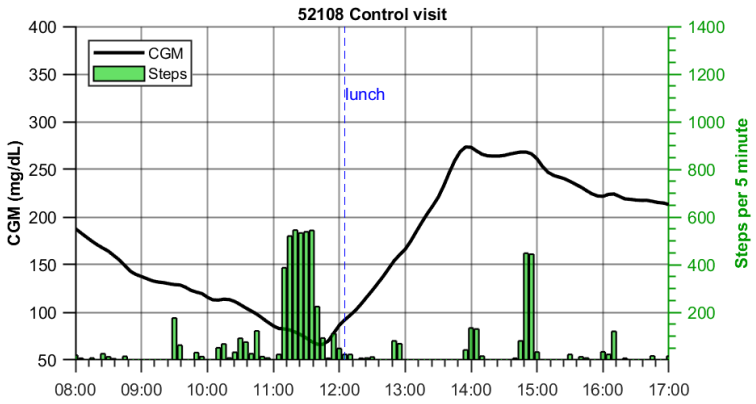
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute
CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]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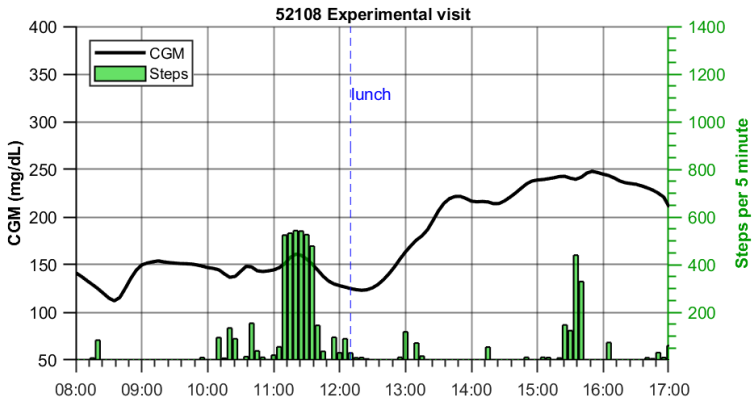
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute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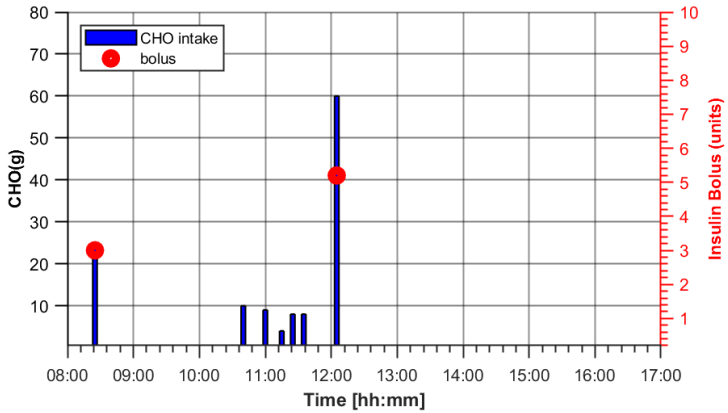
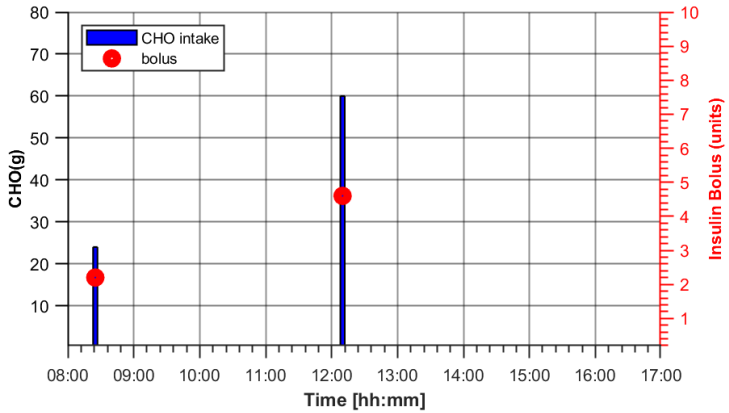
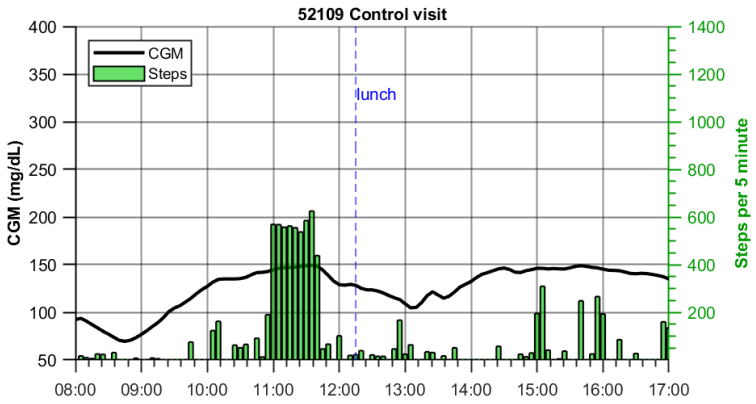
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute


CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]


CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]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CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute
400
350
300
250
200
150
100
50
1400
1200
1000
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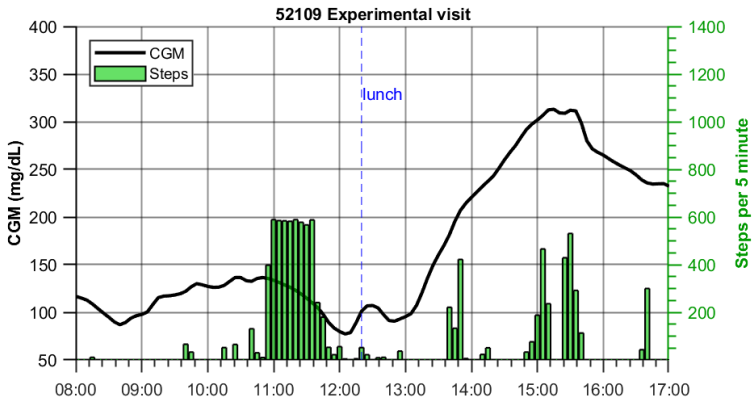
16:00
17:00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CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute
400
350
300
250
200
150
100
50
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1200
1000
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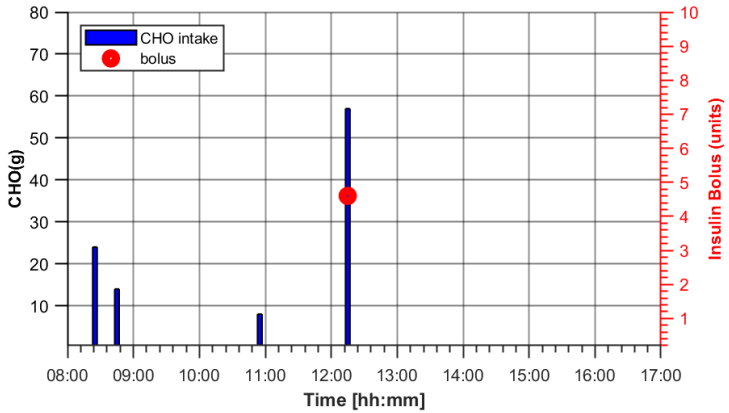
CHO intake
bolus
CHO(g)
Insulin Bolus (units)
80
70
60
50
40
30
20
10
10
9
8
7
6
5
4
3
2
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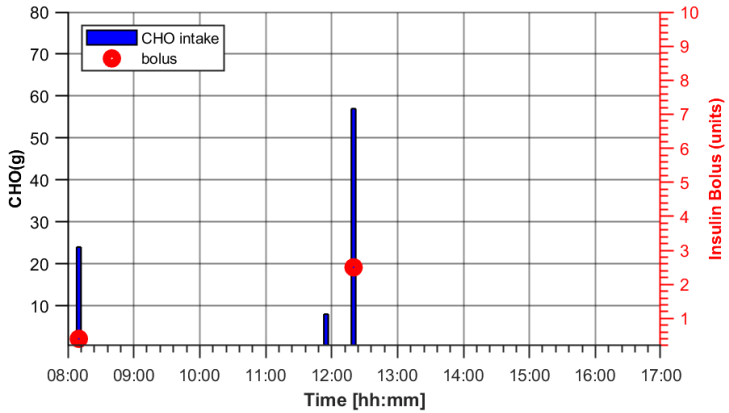
14:00
15:00
16:00
17:00
Time [hh:mm]


CHO intake
bolus
CHO(g)
Insulin Bolus (units)
80
70
60
50
40
30
20
10
10
9
8
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6
5
4
3
2
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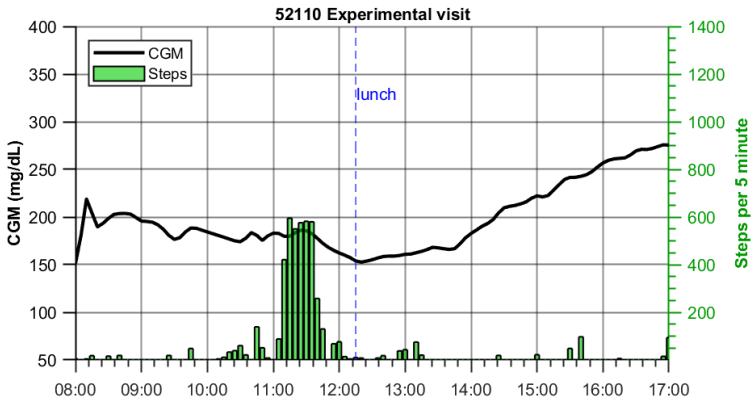
14:00
15:00
16:00
17:00
Time [hh:mm]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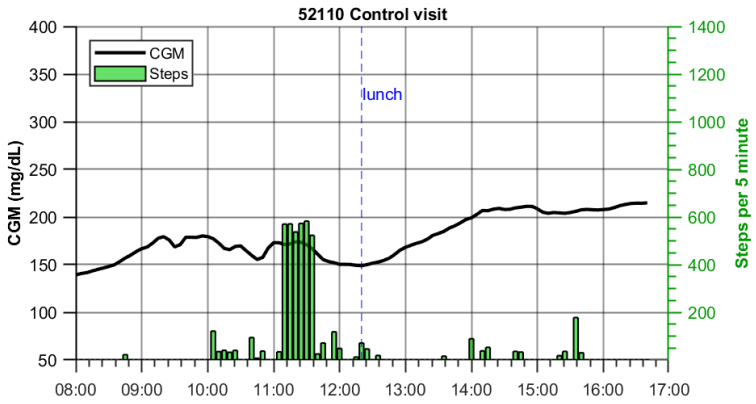
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute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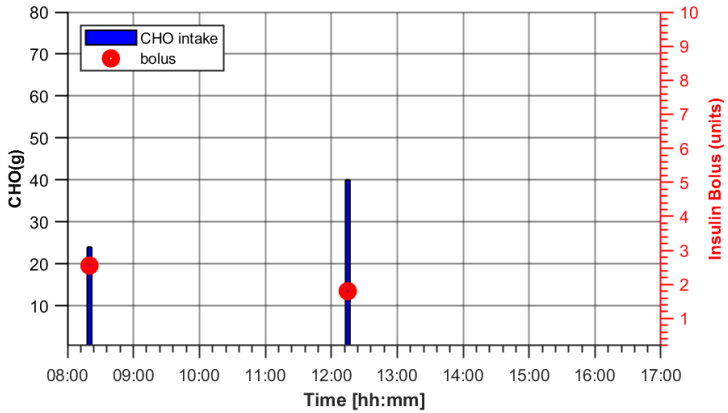
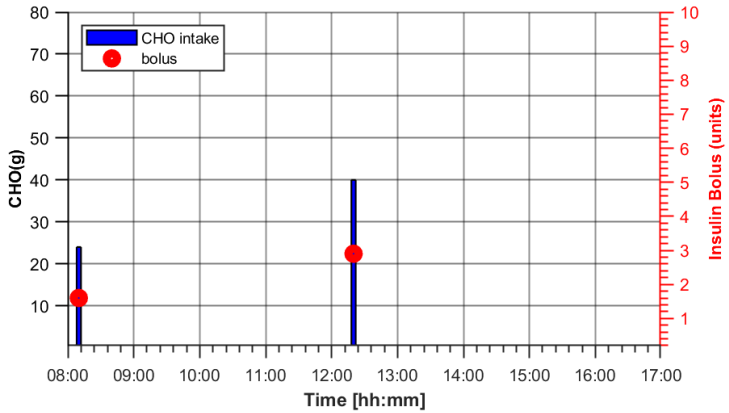
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute


CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]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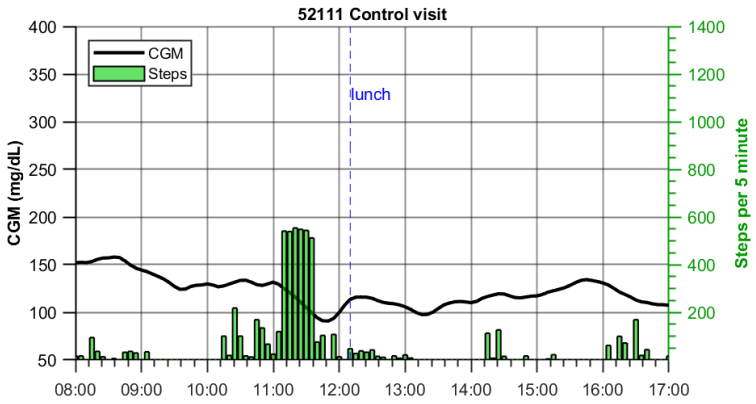
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]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CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute
400
350
300
250
200
150
100
50
1400
1200
1000
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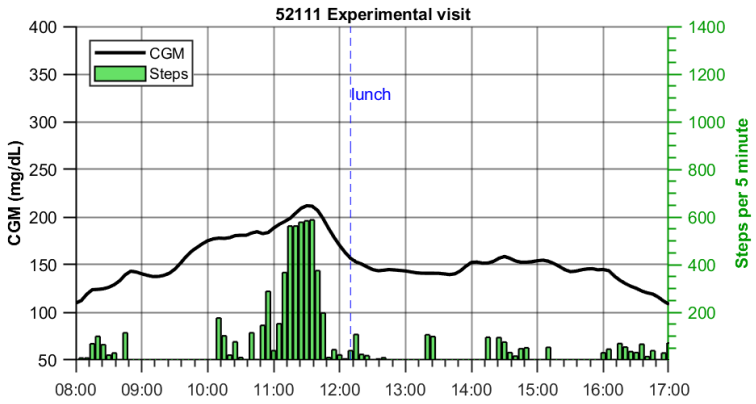
17:00


52111 Experimental visit
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute
400
350
300
250
200
150
100
50
1400
1200
1000
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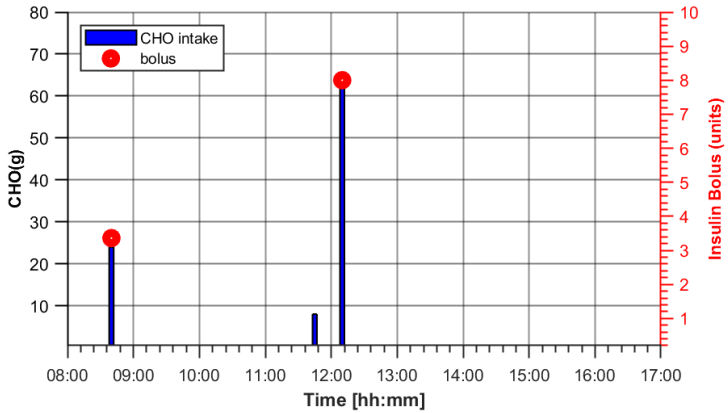
CHO intake
bolus
CHO(g)
Insulin Bolus (units)
80
70
60
50
40
30
20
10
10
9
8
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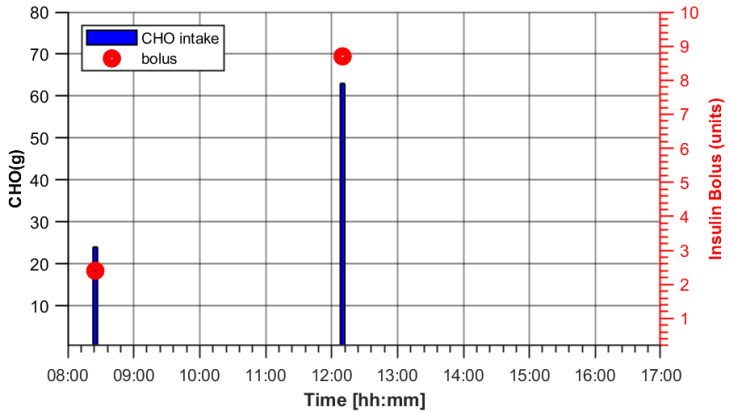
6
5
4
3
2
1
08:00
09:00
10:00
11:00
12:00
13:00
14:00
15:00
16:00
17:00
Time [hh:mm]


CHO intake
bolus
CHO(g)
Insulin Bolus (units)
80
70
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40
30
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9
8
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6
5
4
3
2
1
08:00
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12:00
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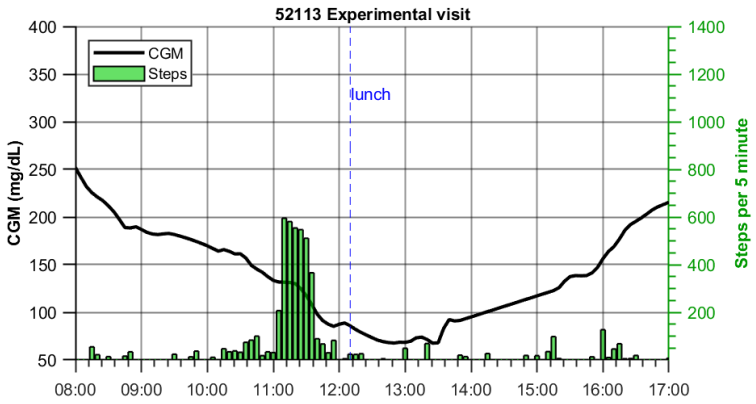
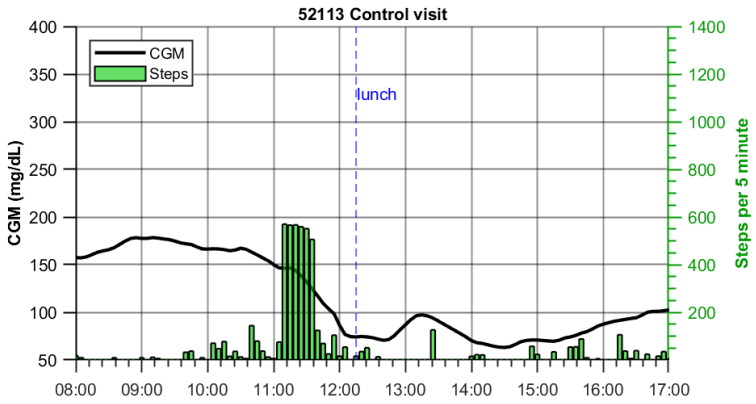
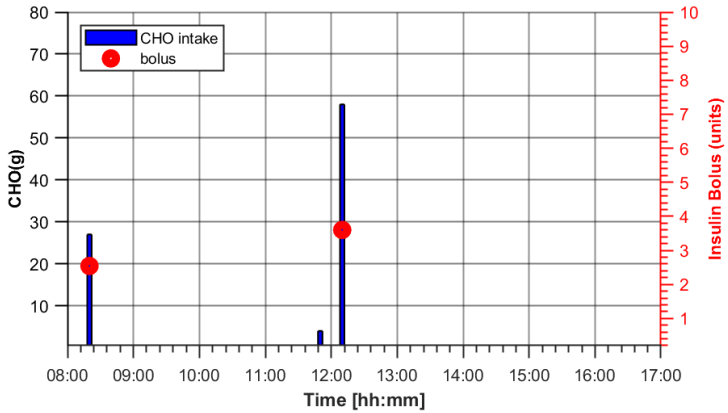
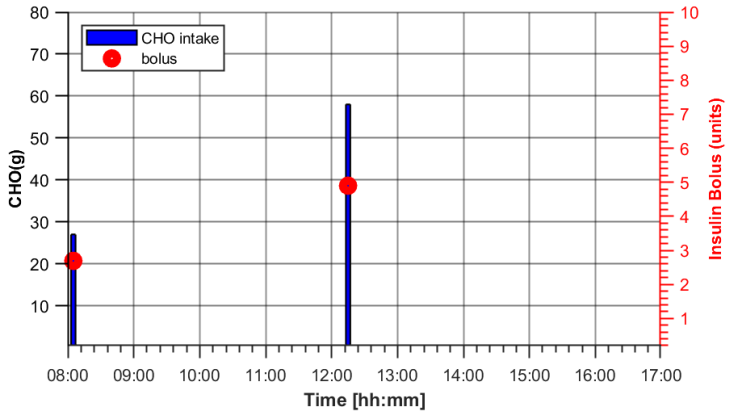
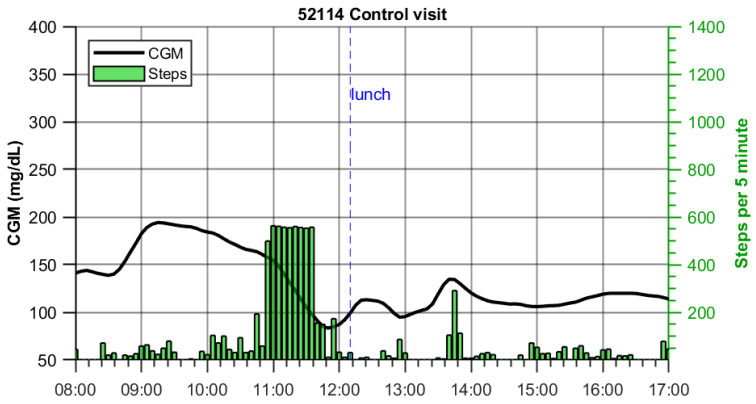
15:00
16:00
17:00
Time [hh:mm]

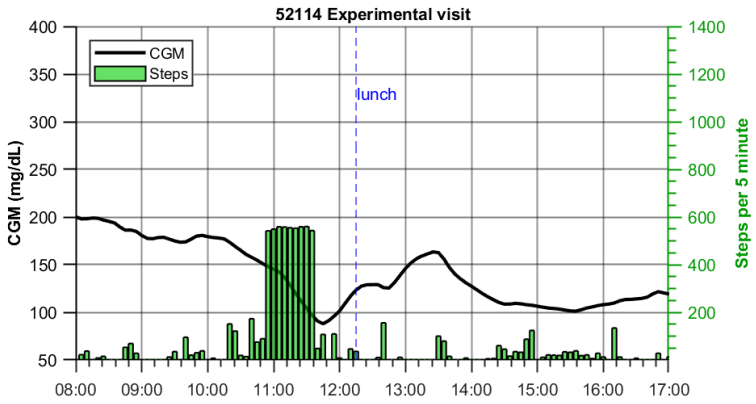

52113 Experimental visit
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute

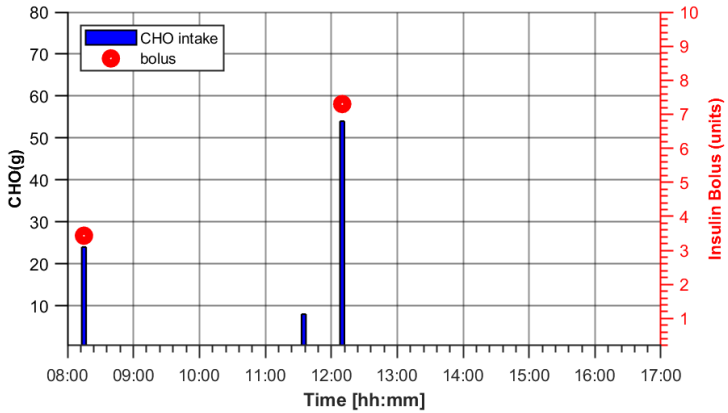

52113 Control visit
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute

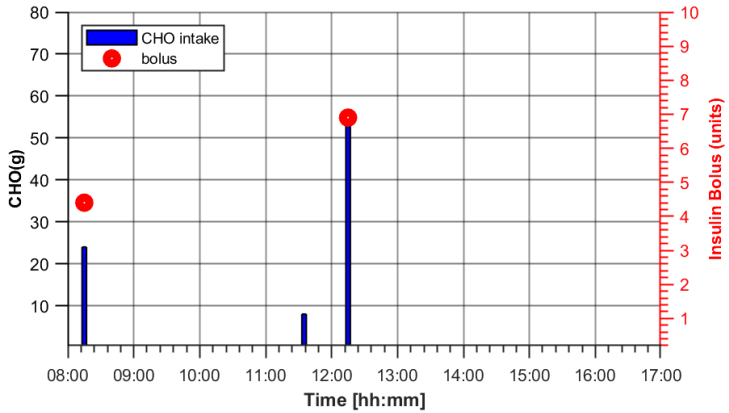

CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]

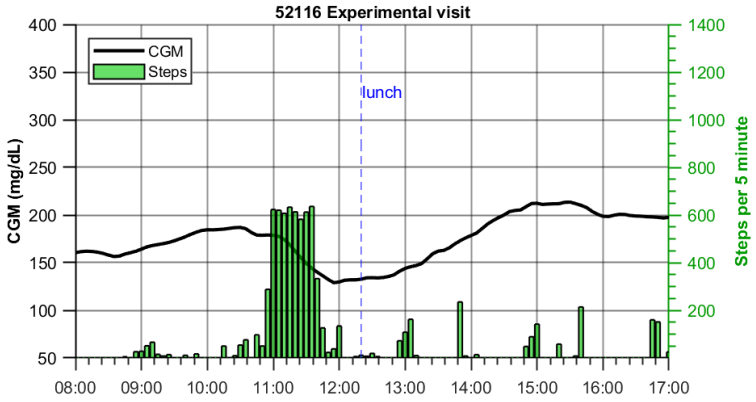

CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]

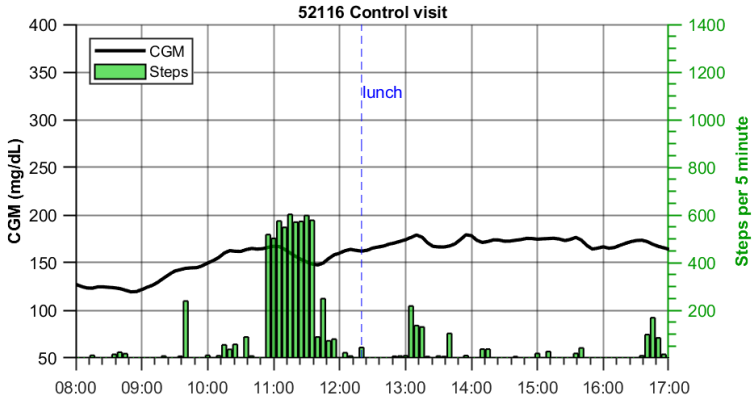

52114 Control visit
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute

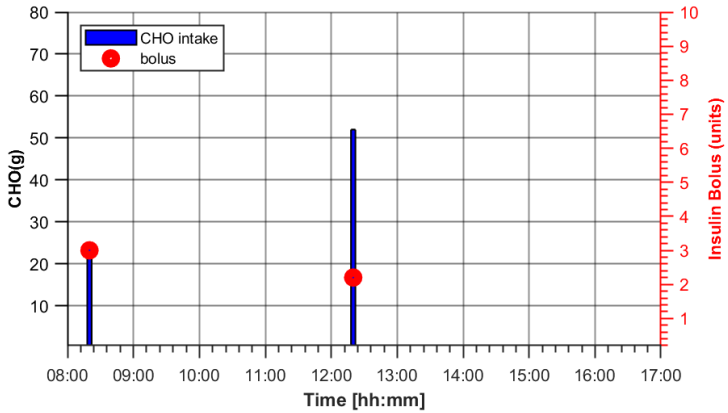

52114 Experimental visit
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute

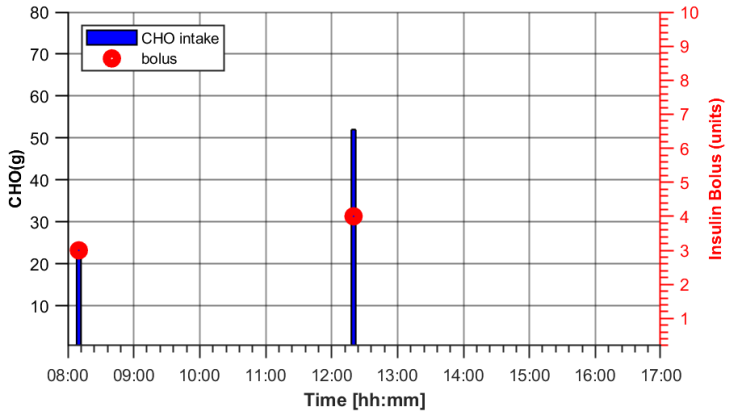

CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]

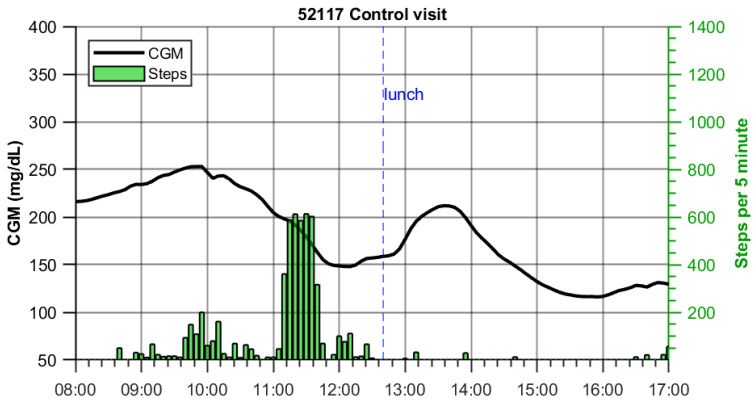

CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]

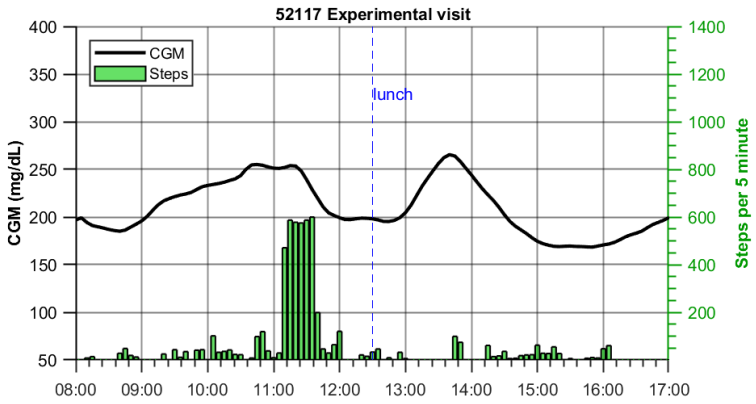

52116 Experimental visit
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute

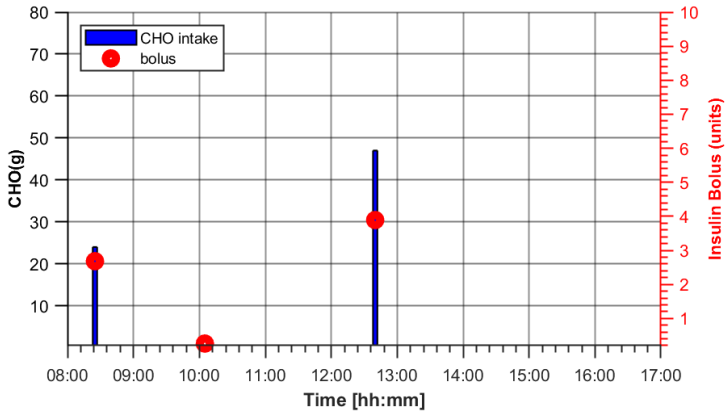

52116 Control visit
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute

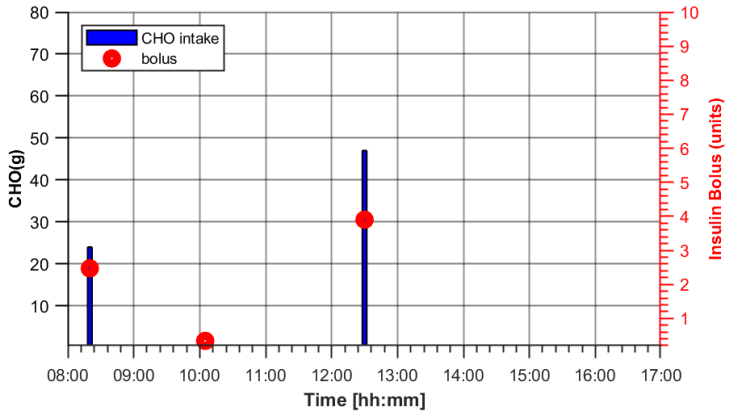

CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]

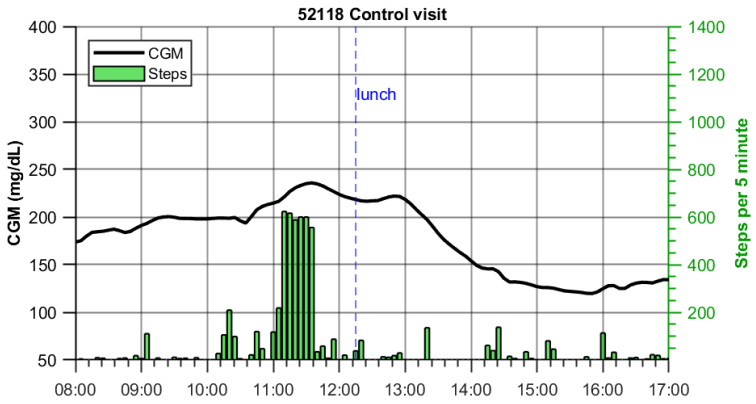

CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]

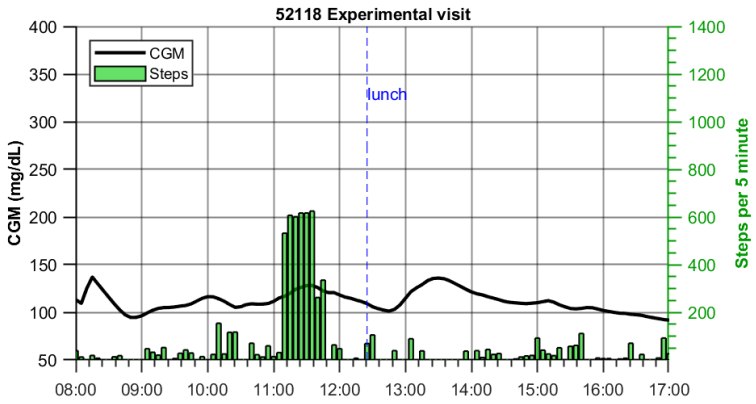

52117 Control visit
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute
400
350
300
250
200
150
100
50
1400
1200
1000
800
600
400
200
08:00
09:00
10:00
11:00
12:00
13:00
14:00
15:00
16:00
17:00

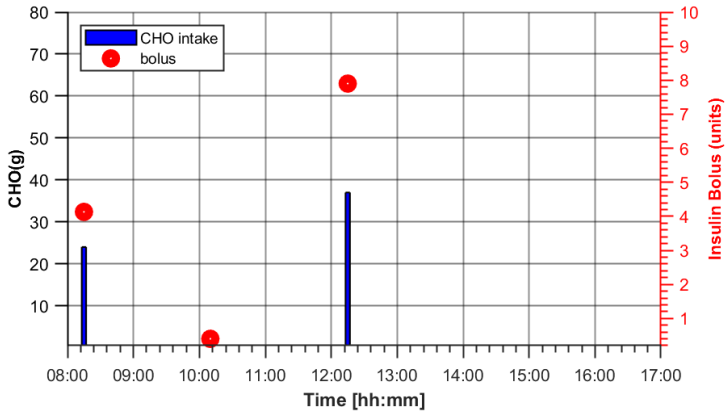

52117 Experimental visit
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute
400
350
300
250
200
150
100
50
1400
1200
1000
800
600
400
200
08:00
09:00
10:00
11:00
12:00
13:00
14:00
15:00
16:00
17:00

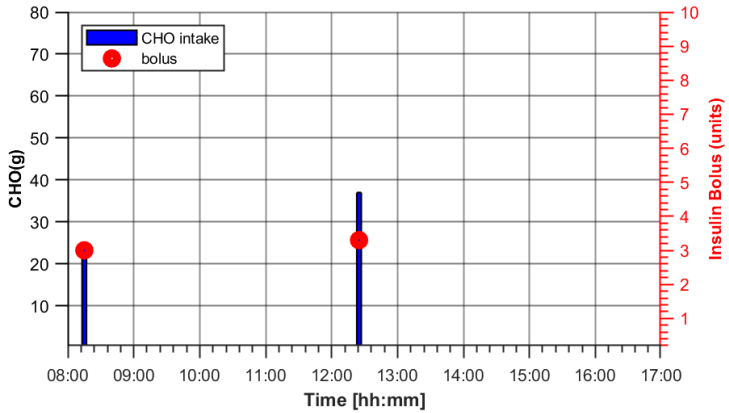

CHO intake
bolus
CHO(g)
Insulin Bolus (units)
80
70
60
50
40
30
20
10
10
9
8
7
6
5
4
3
2
1
08:00
09:00
10:00
11:00
12:00
13:00
14:00
15:00
16:00
17:00
Time [hh:mm]

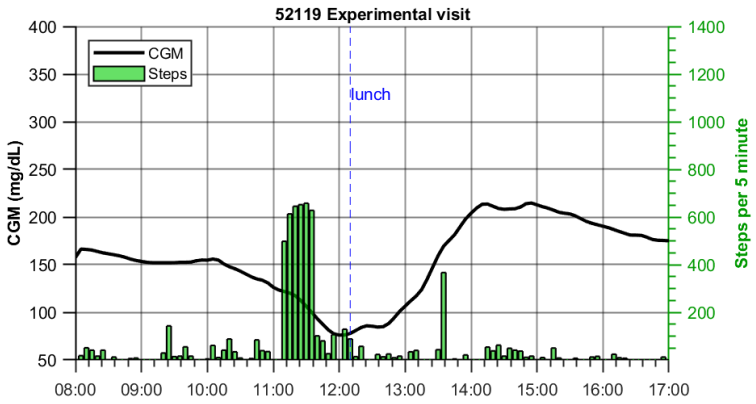

CHO intake
bolus
CHO(g)
Insulin Bolus (units)
80
70
60
50
40
30
20
10
10
9
8
7
6
5
4
3
2
1
08:00
09:00
10:00
11:00
12:00
13:00
14:00
15:00
16:00
17:00
Time [hh:mm]

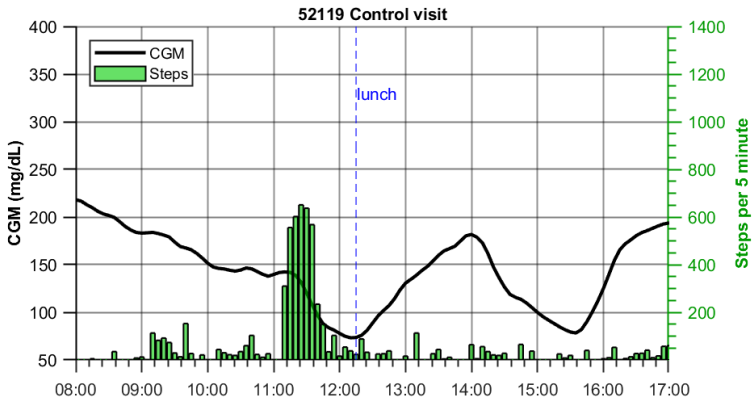

52118 Control visit
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute

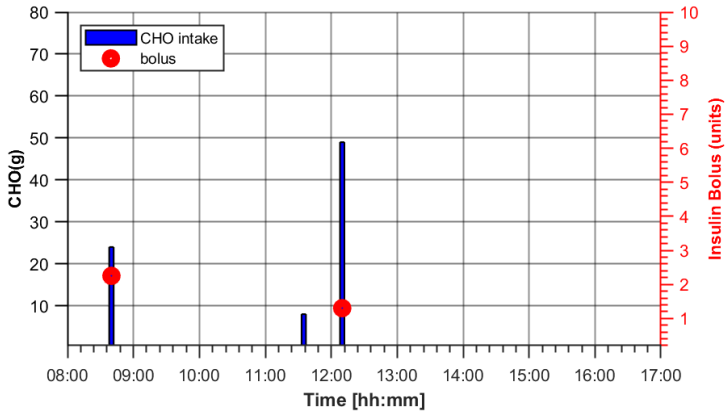

52118 Experimental visit
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute

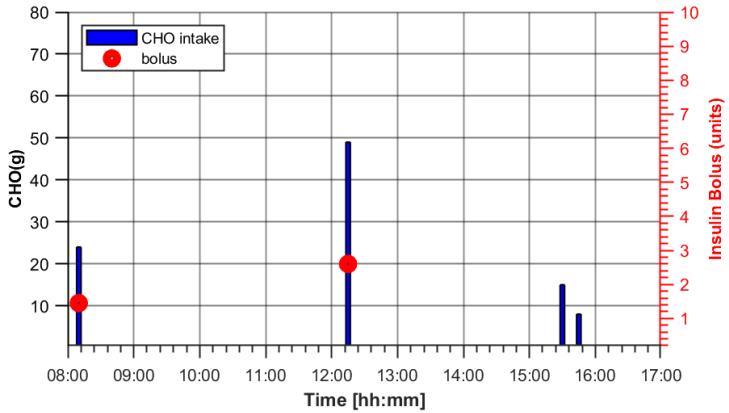

CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]

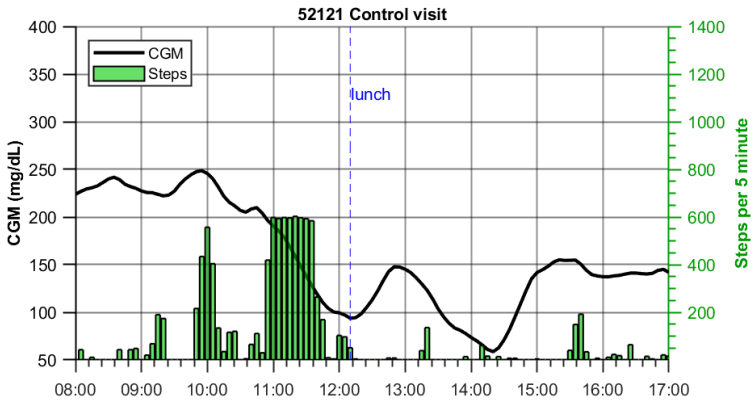

CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]

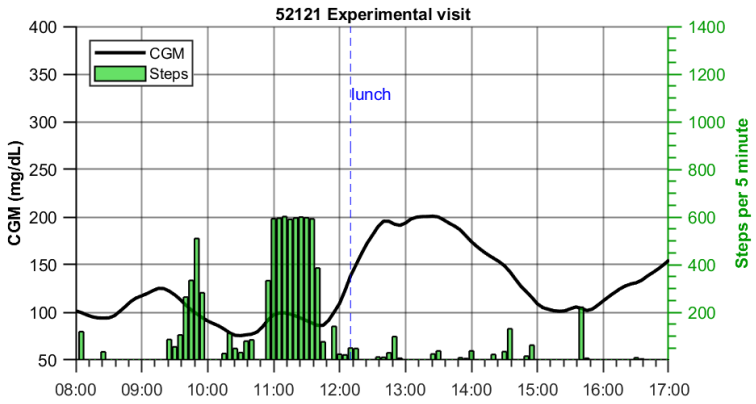

52119 Experimental visit
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute

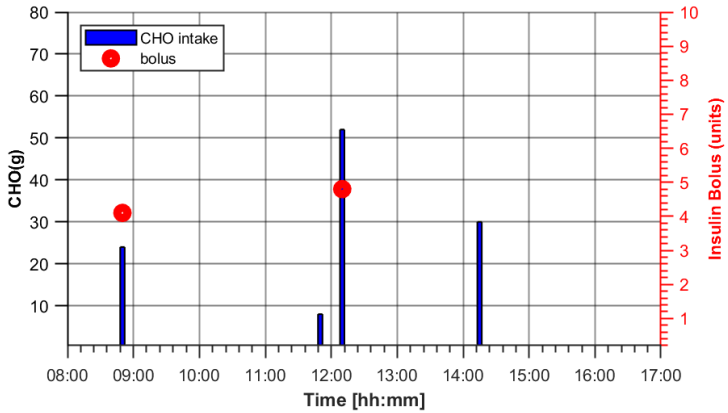

52119 Control visit
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute

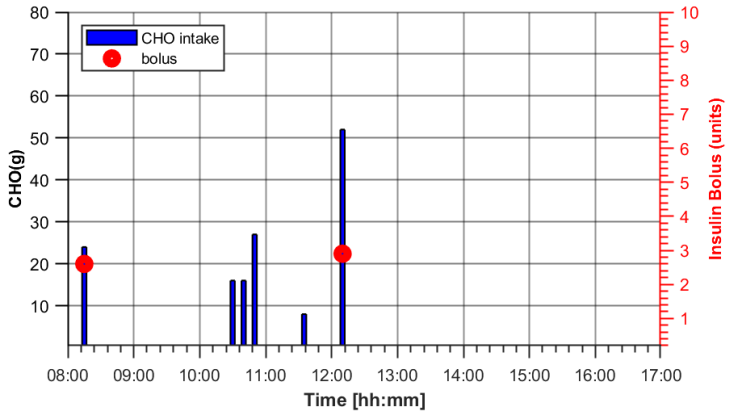

CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]

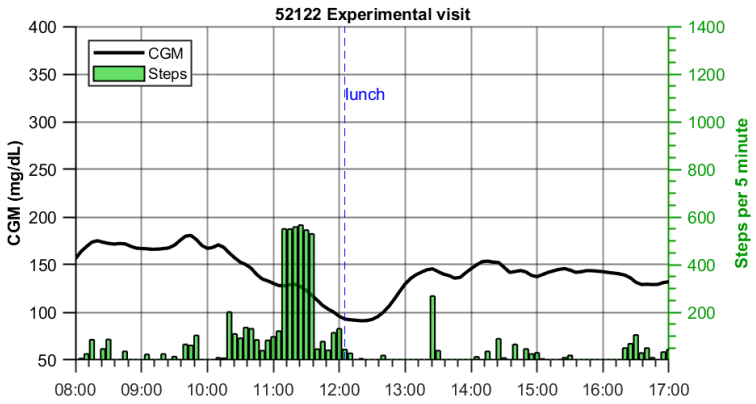

CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]

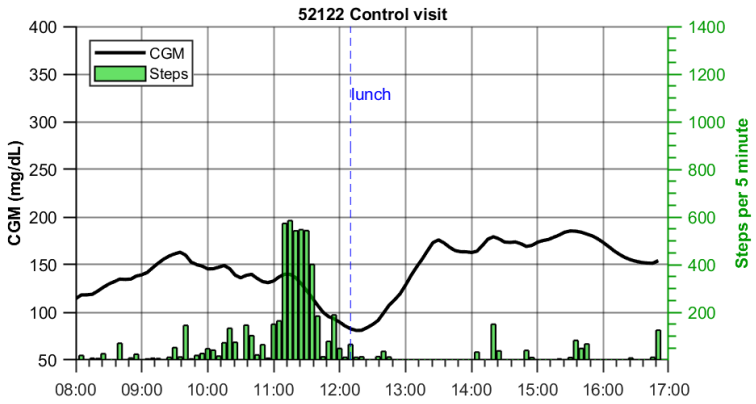

52121 Control visit
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute

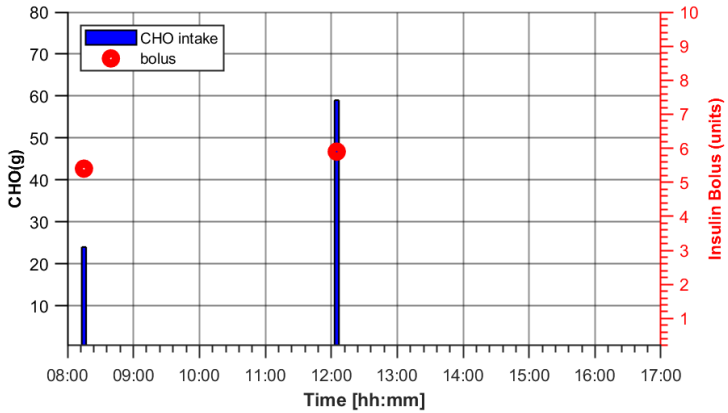

52121 Experimental visit
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute

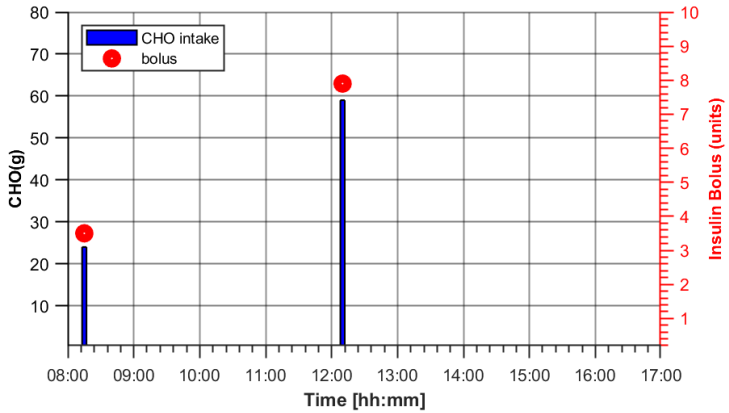

CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]


CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]


52122 Experimental visit
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute


52122 Control visit
CGM
Steps
lunch
CGM (mg/dL)
Steps per 5 minute


CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]


CHO intake
bolus
CHO(g)
Insulin Bolus (units)
Time [hh:mm]

References

[1] B. P. Kovatchev, M. Straume, D. J. Cox, and L. S. Farhy, “Risk Analysis of Blood Glucose Data: A Quantitative Approach to Optimizing the Control of Insulin Dependent Diabetes,” *Comput. Math. Methods Med.*, vol. 3, no. 1, pp. 1–10, 2000, doi: 10.1080/10273660008833060.

[2] B. Ozaslan, C. Fabris, S. D. Patek, and M. Breton, “Automatically Accounting for Physical Activity in Insulin Dosing for Type 1 Diabetes,” *Comput. Methods Programs Biomed.*, vol. In Press.

[3] S. D. Patek *et al.*, “Empirical Representation of Blood Glucose Variability in a Compartmental Model,” in *Prediction Methods for Blood Glucose Concentration*, Springer, Cham, 2016, pp. 133–157.