

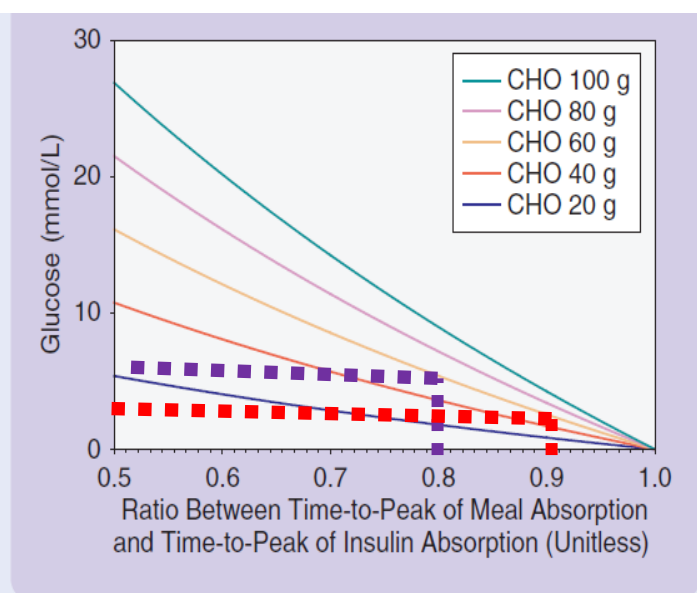
Full closed looping had been around for a while among some OpenAPS low carb loopers, but picked up momentum from ~ late 2020 when **Lyumjev** was launched.

If the user does not bolus for meals, clearly a very fast insulin is needed so, upon realization of a starting meal-related glucose rise, the loop has any chance to eventually keep glucose in range (by common definition, under 180 mg/dl (10 mmol/l))

In the following we look: 1) Into a mathematical modelling study that explains the implications of “faster” insulins on peak height after various meals and 2) into a comparison a FCL looper did in a thorough study using four different insulins.

### General insights from a mathematical modelling study

A modelling study „The Artificial Pancreas and Meal Control“ by A. El Fathi et al (ref.1) can help us understand the effects on glucose peak heights from the course of carb absorption and of insulin activity. The graph shows on the y axis peak over baseline (the overall deltaBG in mmol/l), and on the x-axis the relative speed of insulin absorption to carb absorption. Carb absorption is always faster, therefore all values are under 1.0. But with Lyumjev we move closer to 1. The model calculation shows that **faster insulins** (red dotted) will result in **lower**



**FIGURE S2** A plot of the maximum glucose peak after ingestion of different carbohydrate (CHO) quantities as a function of the ratio between time-to-peak of meal absorption  $\tau_m$  and time-to-peak of insulin absorption  $\tau_i$ . This graph shows that, for instance, following a 60-g meal, the maximum peak of glucose is 5.4 mmol/L for a ratio  $\alpha = \tau_m/\tau_i = 0.8$ . Increasing the ratio to 0.9 (by slowing the meal digestion or providing a faster-acting insulin) may result in decreasing the peak by 46% to 2.5 mmol/L.

glucose **peaks** than slower insulins (violet dotted: reduction by 46% or minus 2.5 mmol/l =

minus 46 mg/dl after a 60 g carb load).

So, this model supports that using a faster insulin will

- lead to less high glucose peaks, notably for bigger meals
- or might **tolerate** a couple of minutes **delayed** first meal bolus while not incurring unacceptable height of peaks.

The latter is a pre-requisite for full closed loop, in which we leave it up to the loop to notice that a meal „must have started“, and to come forward with SMBs that are typically delayed compared to the bolus as given in hybrid closed loop.

This is an encouraging result.

Moreover, the same chart shows us that the spread between the colored curves (they stand for different meal sizes) becomes significantly smaller when we move to the faster insulin with a 0.9 ratio. This means the danger of increasingly high post-meal glucose peaks for high-carb meals is sharply reduced, too. For example, the green curve suggests with the „0.8 insuline“ a peak of 10mmol/l (180 mg/dl) above your glucose level at meal start, but only +4 mmol/l (+70 mg/dl) when using a faster insulin with factor 0.9, which, when starting at or under 110 mg/dl, could keep glucose in range.

The message we can take from this is: **The higher carb loaded our diet, the more important to use the fastest-available insulin.**

Using Lyumjev with a 45 minute time-to-peak and 7 h DIA seems a good setting inoref(1) (AAPS).

Some modelling calculations on effect of dialled-in DIA on insulin kinetics were published by szantos @ de.loopercommunity.org May 2022

<https://de.loopercommunity.org/t/naechtlicher-unterzucker/10626>

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*(ref 1) The Artificial Pancreas and Meal Control. A. El Fathi et al, IEEE Control Systems Magazine Feb.2018 p.67-85. This is a very thorough mathematical modelling study, with 147 references to other literature. However, any modelling must make simplifying assumptions. While our everyday reality is more complex, the authors do carve out, even in quantitative terms, some core mechanisms at play.*

Some loopers reported success in full loop also using slower insulins; they tend to avoid meal extremes, and/or accept going above range for a brief period more often.

In the following, we look at a study using high carb meals that shows the inferiority of slow insulins, notably of Humalog, when you attempt to go FCL:

**n=1 study comparing 4 insulins (Lyumjev, Fiasp, Apidra, Humalog) in a FCL mode - Summary from:**

<https://www.facebook.com/download/831505605647892/What%20about%20insulin%20in%20FCL%20mode.pdf>

(Jiri Borek)

## Method

iAPS using Dexcome g6/7, Dash, iPhone (FCL, but not using autoISF)

SMB+UAM FCL mode without any bolus or carb input or TT setting by the user. For one full week with a standardized sequence of meals (150 – 300 g carb/d; and no exercise after

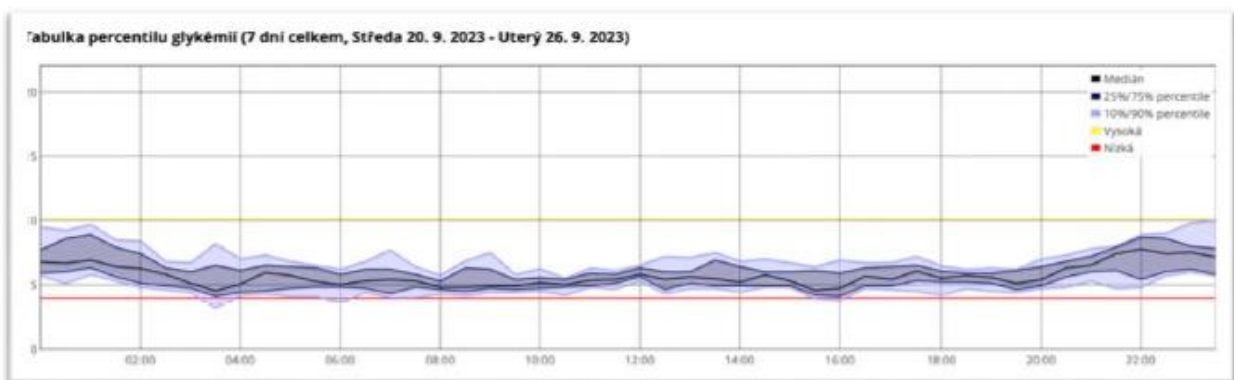
meals), the FCL performance was established for each of the 4 insulins trialled: Fiasp 100 ui, Apidra 100 ui, Humalog 200 ui, and Lyumjev 200 ui.

*And what did I always start with when I changed? Safety is the foundation. So before changing the settings, I first fixed the security limits. Max IOB, Max SMB are the basics. We all want to have nice glucose levels without hyper. But always approach the limits so that the priority is not to protect from hyper, but to not give more insulin than you are able to in case of a problem and cover by finishing the carb. It's silly to put high limits, have it nice and end up in a coma when the sensor jumps! Two hours in hyper has never killed anyone, two hours somewhere alone in a coma can be fatal. Also, never make multiple changes at once while debugging the system. If something doesn't work you won't find out where the error is. Also, before you start pressing anything in the settings be sure of what you are doing. If it's not, please don't do it. Some may be puzzled by the short time to tune the system between insulin. This is due to the fact that I have already studied this system in detail and have been working with the FCL mode since 2020. My first system tune-up (AAPS back then) took maybe half a year, so don't be discouraged by setbacks. And don't bypass security especially, the stress is not worth it. After all, the whole point of FCL is just to take the stress out of dealing with DM.*

## Apidra

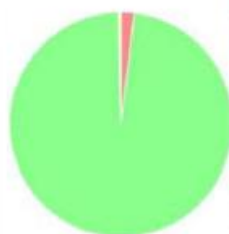
What surprised me about Apidra was the pretty quick onset. It managed the glycemia quite successfully. >But – maybe due to ist longer DIA – I had to feed (against) hypoglycemia a few times. 38 values under 3.9 mmol in 1 week (2% of all values are below range) is not terrible, but created a bit of discomfort taking away from the intended ease in FCL.

### Percentil



## Rozložení glykémie 3,9-10 mmol

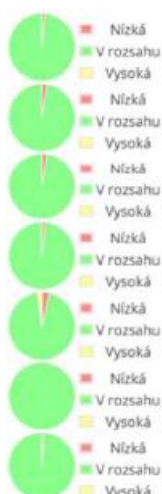
### Rozložení glykémie (7 dní celkem, Středa 20. 9. 2023 - Úterý 26. 9. 2023)



Rozsah	% záznamů	počet záznamů	Průměr	Medián	Standardní odchylka	Předpokládané HBA1c*
Nízká (<3.9):	1.9%	38	3.5	3.7	0.4	5.3% <sub>DCCT</sub>   34 <sub>IFCC</sub>
V rozsahu:	97.8%	1967	5.8	5.7	1.2	
Vysoká (>=10.1):	0.3%	7	10.3	10.4	0.1	
Celkem:		2012	5.8	5.7	1.3	
Průměrná celková denní změna			Doba měnící se glykémie (>0.27 mmol/l/5m)		Doba rychle se měnící glykémie (>0.55 mmol/l/5m)	
51.07 mmol/L			14.0%		4.0%	
Průměrná hodinová změna			GVI		PGS	
2.13 mmol/L			1.28		2.93	
Out of Range RMS						
5.42 mmol/L						

## Denní statistiky 3,9-10mmol

### Denní statistiky

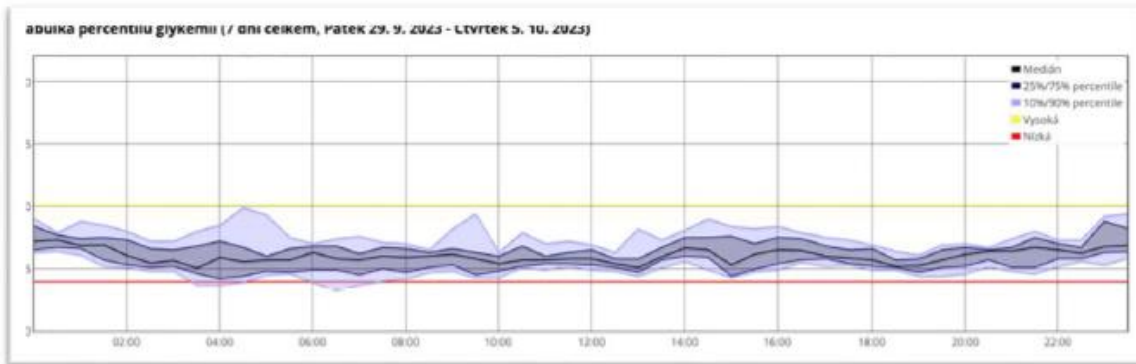


Datum	Nízká	Normální	Vysoká	Záznamů	Min	Max	Průměr	Směrodatná odchylka	25%	Medián	75%
Úterý 26. 9. 2023	1%	99%	0%	278	3.7	8	5.4	1.0	4.7	5.3	6.0
High carb day											
Pondělí 25. 9. 2023	3%	97%	0%	279	3.7	9.7	6.0	1.3	5.1	5.9	6.8
Neděle 24. 9. 2023	3%	97%	0%	277	2.2	8.5	5.5	1.1	4.7	5.4	6.2
Sobota 23. 9. 2023	2%	98%	0%	287	2.9	9.9	6.2	1.5	5.2	5.8	6.9
Pátek 22. 9. 2023	4%	94%	2%	288	2.4	10.7	6.0	1.5	5.0	5.8	6.7
Low carb day											
Čtvrtek 21. 9. 2023	0%	100%	0%	286	4	8.4	5.7	1.0	4.8	5.4	6.4
Středa 20. 9. 2023	1%	99%	0%	285	3.7	8.9	5.8	1.2	4.8	5.8	6.6

## Fiasp

I observed some problems also many others have reported, like or tendency towards partial occlusions and elevated insulin need with cannula age. In FCL operation (with regular pod changes, and the typical smaller boli occurring in FCL) overall Fiasp worked well and fairly much replicated the good results as was reported for Apidra:

## Percentil



## Rozložení glykémie 3,9-10 mmol

### Rozložení glykemií (7 dní celkem, Pátek 29. 9. 2023 - Čtvrtek 5. 10. 2023)



## Denní statistiky 3,9-10mmol

### Denní statistiky





## Humalog

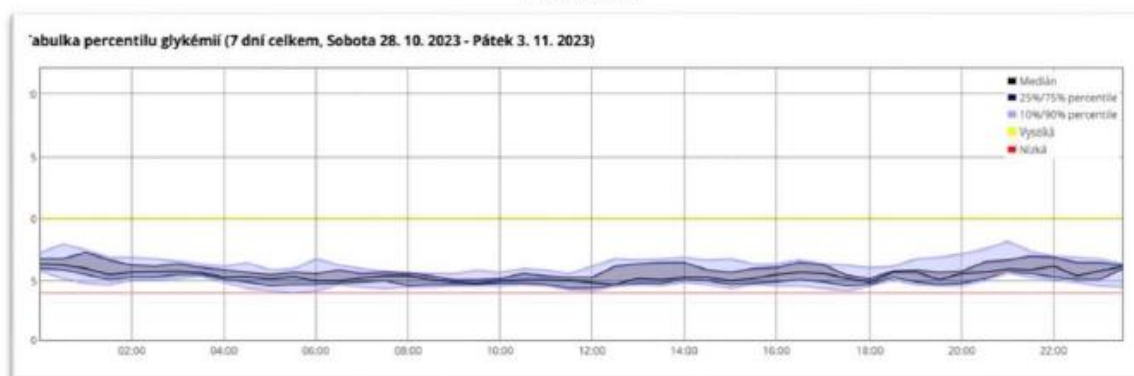
Of the tested insulins, it was the

*slowest and had the longest DIA. Unfortunately, that showed. Even after 14 days, I was not happy with the settings and behavior of the system. Hyper was taking turns with hypo. So I didn't even try FCL with this insulin in the end. The 90% in TIR of 3.9-10 mmol in hybrid mode was enough warning for me not to do it. Hyper wouldn't have mattered anyway. But those hypoglycemic episodes due to his long DIA were pretty uncomfortable and long lasting.*

## Lyumjev

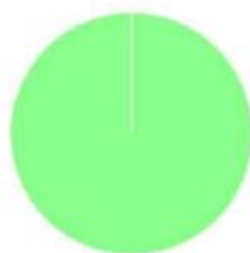
Lyumjev is the insulin with fastest onset and shortest DIA. At the 3.9-10 mmol TIR level, where I have also with Apidra and Fiasp reached ~97%TIR, the difference was less obvious...

### Percentil



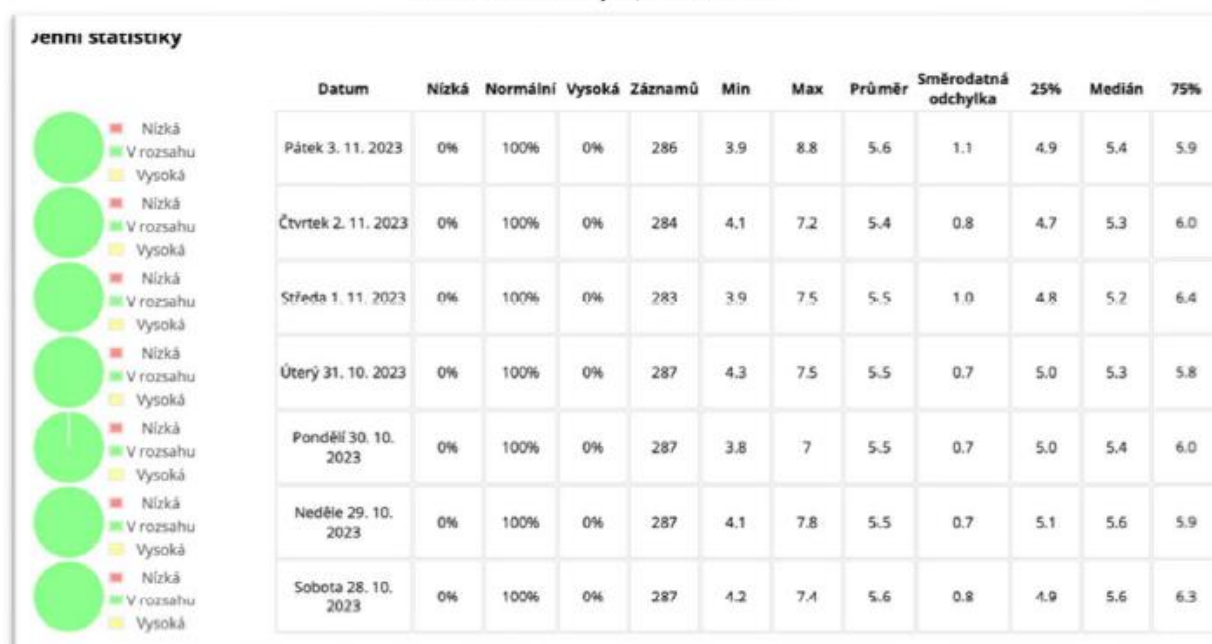
### Rozložení glykémie 3,9-10 mmol

#### Rozložení glykémie (7 dní celkem, Sobota 28. 10. 2023 - Pátek 3. 11. 2023)



Rozsah	% záznamů	počet záznamů	Průměr	Medián	Standardní odchylka	Předpokládané HBA1c*
Nízká (<3.9):	0.0%	1	3.8	3.8	0.0	
V rozsahu:	100.0%	2015	5.5	5.4	0.8	
Vysoká (>=10.1):	0.0%	0	N/A	N/A	N/A	
Celkem:		2016	5.5	5.4	0.8	5.1%DCCT   32IFCC
Průměrná celková denní změna			Doba měnící se glykémie (>0.27 mmol/l/5m)		Doba rychle se měnící glykémie (>0.55 mmol/l/5m)	
34.15 mmol/L			7.0%		1.0%	
Průměrná hodinová změna			GVI		PGS	
1.42 mmol/L			1.14		0	
Out of Range RMS						
5.03 mmol/L						

## Denní statistiky 3,9- 10mmol



It is very interesting that with Lyumjev I reached the lowest predicted HbA1c (5.1%), despite it coming with a vastly lower incidence of low (0,0% <3.9) values when comparing with Apidra (5.3 % HbA1c @ 1,9% <3.9) and Fiasp (5.5 % HbA1c @ 2,1% <3.9).

The superior performance of Lyumjev to control highs is responsible for this – see conclusion.

## Conclusion

**Lyumjev** clearly is the best insulin for my FCL.

- It showed practically no tendency towards hypoglycemia.
- It controlled peaks the best.

This can be best seen when comparing %TIR (3.9 – 7.9 mmol/L)(70-142 mg/dl) between the studied insulins:





**Fiasp and Apidra** had about 10 times as many bg values in the elevated range, above 7.9 mmol/L (142 mg/dl).

It is worth noting here again, that the researched range of meals went up to 300 g carb content (which is a „stress test“, way above my usual range).

Loopers on a lower carb diet (and with strong attention to using proper DIA and ISF profile settings) might see FCL viable even using **Humalog**. See e.g. D. Burren

<https://bionicwookiee.com/2022/04/13/revised-humalog-model-in-a-closed-loop/>

who reports when going Lyumjev to Humalog:

- The TIR for 3.9-7.8 has decreased. 90.3% to 85.1%.
- But the TIR for 3.9-10 has only changed from 97.2% to 97.1% -

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*Disclaimer: Above is a report on testing weeks done by an experienced FCL user (FCL with AAPS or iAPS since nearly 3 years). Prior to each testing week, up to 10 days were spent to fine tune settings for the insulin in use. Effects from sickness, strenuous exercise etc. were excluded. Attention to technical system function (CGM performance, bluetooth stability, timely cannula changes to limit occlusion) was high in these testing weeks, too.*