D 2.1.5
Cross check of the pulsating flow tester at DTI and METAS

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1 Introduction

1.1 Background

In task 2.1, the aim is to develop a performance tester for pulsating flow to study the effects of flux modulation on the outcome of the measurement. Therefore, a cross check of the pulsating flow tester between METAS and DTI is foreseen in Task 2.1.5

1.2 Motivation

This is important because most of the drug delivery systems exhibit some kind of fluctuation and for testing flow sensors the ability of measuring the correct flow rate even in presence of flow fluctuations is very important.

Therefore a syringe pump is characterized at flow rates of 15 ml/h and 1 ml/h. In case that the syringe pump does not reproduce the pulsating flow pattern very well, a Coriolis flow meter is mounted downstream the syringe pump and calibrated in order to compare the deviation of the Coriolis flow meter at the flow rate of 15 ml/h.

1.3 Goal

Cross check of the dynamic flow tester is performed and the uncertainties are validated.

2 Devices under Test

2.1 Flow generator

Syringe pump ALADDIN-300

Manufacturer: World precision instruments (www.wpi-europe.com)
Serial number: 232294
Type: Aladdin-300

Owner: DTI

Figure 1: The Syringe pump consisting of the syringe driver Aladdin-300 with its power supply and 2 syringes of 60 ml. One is marked with “dry” (not used) and the other is marked with “wet” (first use at DTI).

2.2 Syringe used

Manufacturer: TERUMO

Type of syringes used: Plastic, 50 ml, without needle, with Luer Lock connector…..

Brand mark:

2.3 Flow meter

Coriolis mass flow meter M12P

Manufacturer: Bronkhorst Cori-Tech
Serial number: B13200307A
Type: M12P-AGD-11-0-S

3 Set up

3.1 METAS

To perform the measurement with the syringe pump as a flow generator, the «inlet» of the syringe pump is connected (luer lock to 1/8 inch adapter in stainless steel) to the water reservoir and the «outlet» is connected to the piping leading to the beaker on the balance (see Figure 2 and 3). METAS uses a 3-way-valve as the «inlet» and the «outlet» is the same connecting point to the syringe

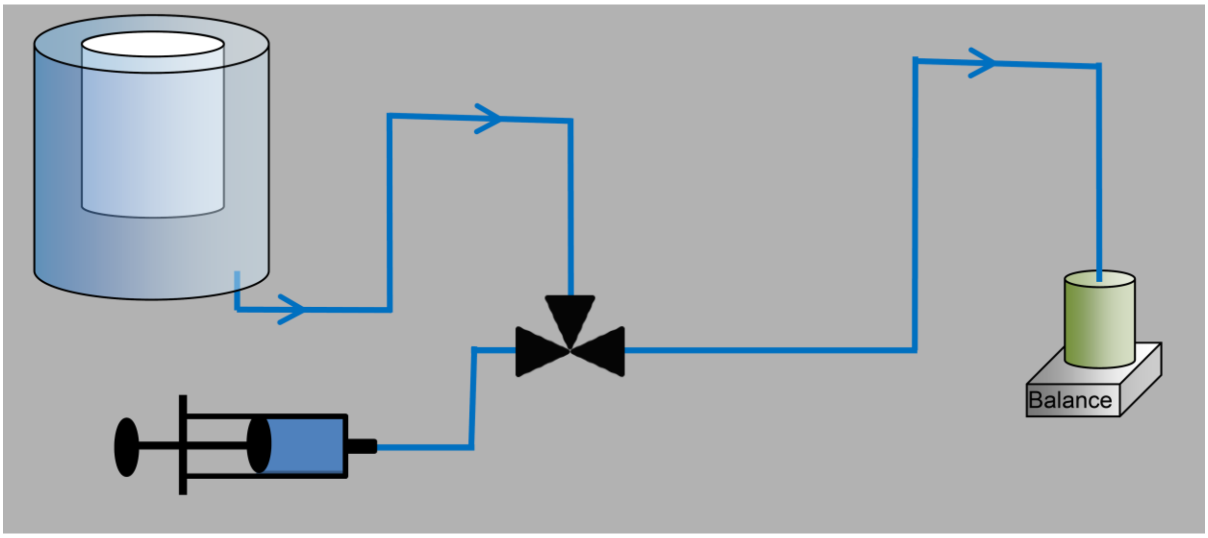

Figure 2, METAS-Setup: The syringe pump is connected to the micro flow facility with its gravimetric method to determine the volume flow rate generated by the syringe pump (micro flow facility METAS).

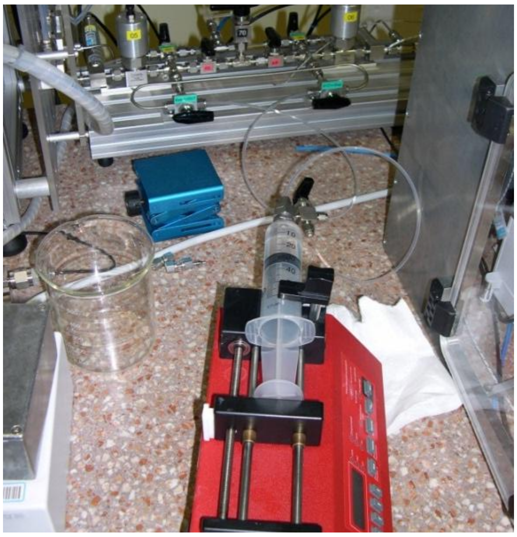

Figure 3, METAS-Setup: The syringe pump is connected to the micro flow facility at METAS.

To perform the measurement with the syringe pump as a flow generator and including the coriolis flow meter inline as a transfer standard, the «inlet» of the syringe pump is connected (luer lock to 1/8 inch adapter in stainless steel) to the water reservoir and the «outlet» is connected to the coriolis flow meter which is then connected to the piping leading to the beaker on the balance (see Figure 4 and 5). METAS uses a 3-way-valve as the «inlet» and the «outlet» is the same connecting point to the syringe.

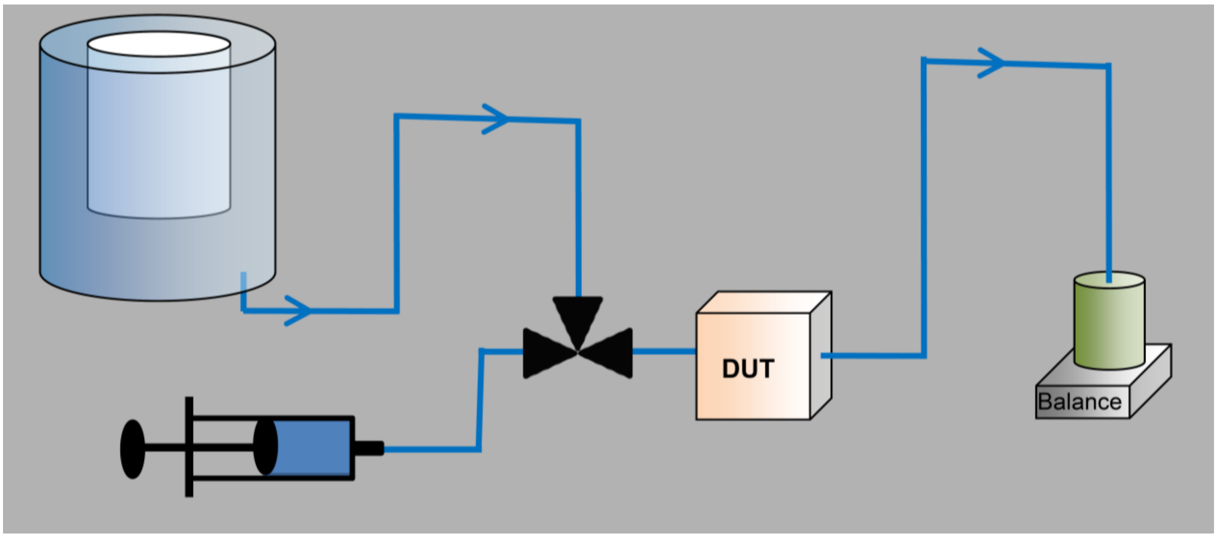

Figure 4, METAS-Setup: The «inlet» of the syringe pump is connected to the water reservoir and the «outlet» is connected to the coriolis flow meter which is then connected to the piping leading to the beaker on the balance (micro flow facility METAS).

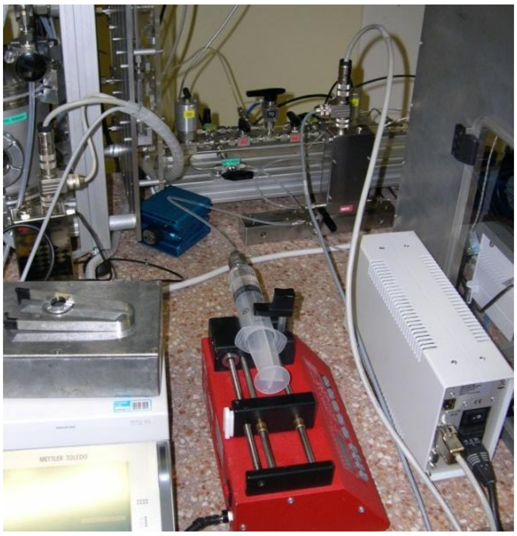

Figure 5, METAS-Setup: The Coriolis flow meter is connected downstream of the syringe pump and to the micro flow facility at METAS.

3.2 DTI

To connect the syringe to the primary standard, a stainless steel “luer-lock to 1/16” tube” adapter is used for the setup at DTI. All connections between device under test and primary standard are of stainless steel. The set-up and connection of the syringe pump to the primary standard at DTI is shown Figure 6.

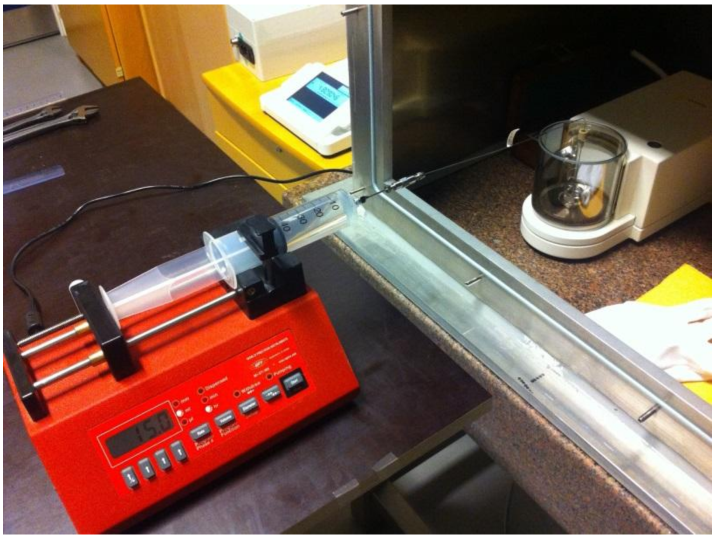

Figure 6, DTI-Setup: The syringe pump is connected to the micro flow facility at DTI.

Further a measurement was performed with a M12P Coriolis flow meter in series. The set-up and connection of the syringe pump with a M12P in series to the primary standard at DTI is shown in Figure 7.

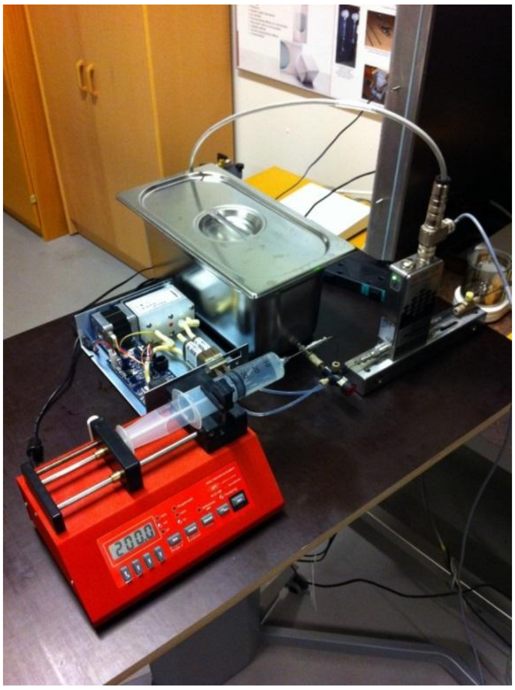

Figure 7, DTI-Setup: The Coriolis flow meter is connected downstream of the syringe pump and to the micro flow facility at DTI.

3.3 Selected parameters at the syringe pump

DTI set the inner diameter of the syringe to 30.0 mm (on purpose). However measurements revealed that the diameter of the syringe is 29.0 mm instead. Therefore the selected flow rates at the syringe pump will deviate from the real flow rates which are described in the Table 1 below.

Selected flow rates		Selected inner diameter	Real flow rates		Real inner Diameter
(ml/h)	(μl/min)	(mm)	(ml/h)	(μl/min)	(mm)
1.0	16.67	30.0	0.934	15.57	29.0
15.0	250.00	30.0	14.017	233.61	29.0

Table 1: The selected flow rates and inner diameter leading to smaller flow rates in reality.

To have the same settings at the syringe pump for the various measurements, METAS has also set the inner diameter to 30.0 mm at the syringe pump.

3.4 Characteristic spindle rotation time

The syringe pump Aladdin-300 has a spindle increment per rotation of 1.27 mm.

Using a syringe of 29.0 mm in diameter we get the following characteristic spindle rotation time τ_{sp} depending on the flow rate selected (see Table 2), which should cause visible oscillations in the flow.

volume syringe	Real flow rates		Real inner Diameter	Spindle rotation time τ_{sp}
(ml)	(ml/h)	(μl/min)	(mm)	(sec)
60	0.934	15.57	29.0	3232.5
60	14.017	233.61	29.0	215.5

Table 2: Characteristic spindle rotation time τ_{sp} depending on the flow rate selected (theoretical approach).

4 Measurement uncertainty

The reported measurement uncertainty is stated as the combined standard uncertainty multiplied by a coverage factor *k* = 2. The measured value (*y*) and the associated expanded uncertainty (*U*) represent the interval (*y* ± *U*) which contains the value of the measured quantity with a probability of approximately 95 %. The uncertainty was estimated following the guidelines of the ISO (GUM:1995).

The measurement uncertainty contains contributions originating from the measurement standard, from the measurement method, from the environmental conditions and from the object being measured. The long-term characteristic of the object being measured is not included.

4.1 METAS

The main contributions those are different from the case of steady flow are the contribution from the linear least square fit ODR and the flow rate stability which both depend on the chosen fit window.
We decided to use for the detection of pulsating flow for 5 fit windows: 3 s, 6 s, 10 s, 20 s, and 40 s.

Q (µl/min)	U (3 s) (fit window) (%)	U (6 s) (fit window) (%)	U (10 s) (fit window) (%)	U (20 s) (fit window) (%)	U (40 s) (fit window) (%)
1000.0	**0.6**	**0.4**	**0.2**	**0.2**	**0.2**
333.0	**0.7**	**0.4**	**0.3**	**0.2**	**0.2**
233.0	**0.7**	**0.4**	**0.3**	**0.2**	**0.2**
100.0	**0.9**	**0.6**	**0.4**	**0.2**	**0.2**
33.0	**2.0**	**1.0**	**0.5**	**0.3**	**0.2**
10.0	5.1	**2.1**	**1.1**	**0.6**	**0.4**
1.0	50.7	21.2	11.6	5.7	**2.7**

Table 3, METAS-Setup: Measurement uncertainty for pulsating flow of the micro flow facility at METAS. The values below 3 % are highlighted in green.

Depending on the fit window used the detection of any sharp change in flow rate is limited by the size of the fit window. Additionally the step response of the balance is also limiting the detection of pulsations to this order of magnitude in time.
The step response of the balance is 0.3 s for the case where water droplet fall onto the beaker and 1.3 s for the case where a force with a tip is acting on the beaker leading to an increase in weight of 650 mg.

4.2 DTI

Q (µl/min)	U (3 s) (fit window) (%)	U (6 s) (fit window) (%)	U (10 s) (fit window) (%)	U (20 s) (fit window) (%)	U (40 s) (fit window) (%)
1000.0	**1,2**	**0,4**	**0,2**	**0,07**	**0,03**
333.0	3,5	**1,2**	**0,6**	**0,2**	**0,07**
233.0	5	1,8	**0,8**	**0,3**	**0,1**
100.0	11,7	4,1	**1,9**	**0,7**	**0,2**
16,7	71	25	12	4	**1,5**

Table 4, DTI-Setup: Measurement uncertainty for pulsating flow of the micro flow facility at DTI. The values below 3% are highlighted in green.

5 Characterization Results and Discussion

In Table 4, we summarized all the measurements that were performed by DTI and METAS.

Set-up	**Flow rates**		**DTI Repetitions**	**METAS Repetitions**
	(ml/h)	(µl/min)		
AL-300	15 ml/h	250.0	3	3
AL-300	1 ml/h	16.7	3	3
AL-300 + M12P	15 ml/h	250.0	1	3
M12P + flow generator of laboratory (steady flow rate)	15 ml/h	250.0	-	3

Table 4: Measurements performed by DTI and METAS

5.1 Mean value and the uncertainty

Later on, we will determine the mean value of 3 values:

Value (a.u.)	Uncertainty (coverage factor 95 %, k=2)
X1	U1
X2	U2
X2	U3

The mean value is determined according to the formula

$$\bar{X} = \frac{1}{n}\sum_{i=0}^{n} Xi$$

The uncertainty is determined according to the formula

$$U(\bar{X}) = \sqrt{[max(U1, U2, U3)]^2 + \left[2 * Stdev(X1, X2, X3)/\sqrt{3}\right]^2}$$

5.2 Results METAS

5.2.1 METAS-Setup - Syringe pump at Q ~ 14 ml/h (233 μl/min)

5.2.1.1 METAS-Setup - Pulsating flow pattern

The instantaneous flow rates determined by the dynamic gravimetric method are shown in Figure 8 resp. 9 where a fit window of 3 s resp. 20 s was used. As the start position of the syringe plunger can't be set really accurate at the beginning of the measurements, the positions on the x-axis were slightly corrected with an offset in order to get an overlap of the pulsating flow pattern (see Table 5). We used 2 syringes of the same type, but one was already used before and was therefore wet (wet marked) and another new syringe (dry marked). The details about the different data can be read in Table 5.

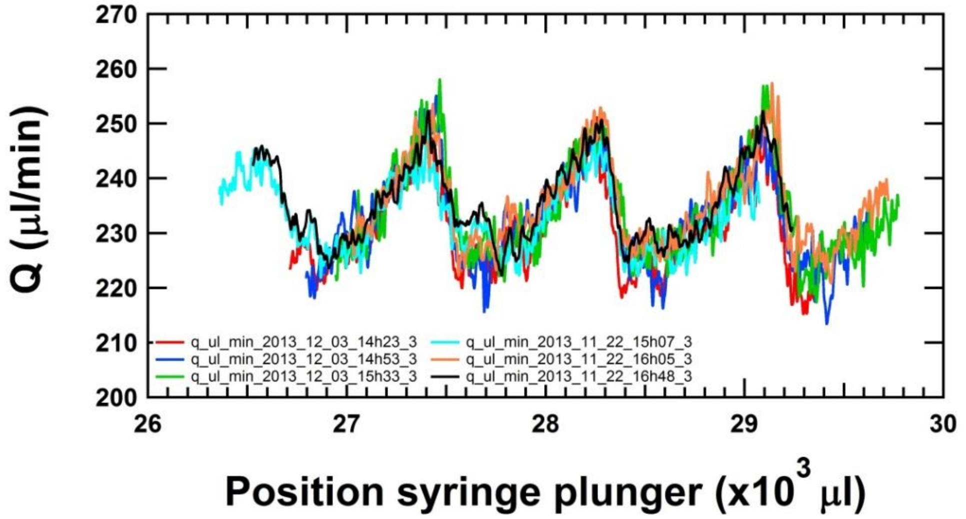

Figure 8, METAS-Setup: Instantaneous flow rates as a function of the position of the syringe plunger where a fit window of 3 s was used for the flow rate determination. Using 2 syringes 6 measurements were performed. Details of the different curves can be found in Table 5.

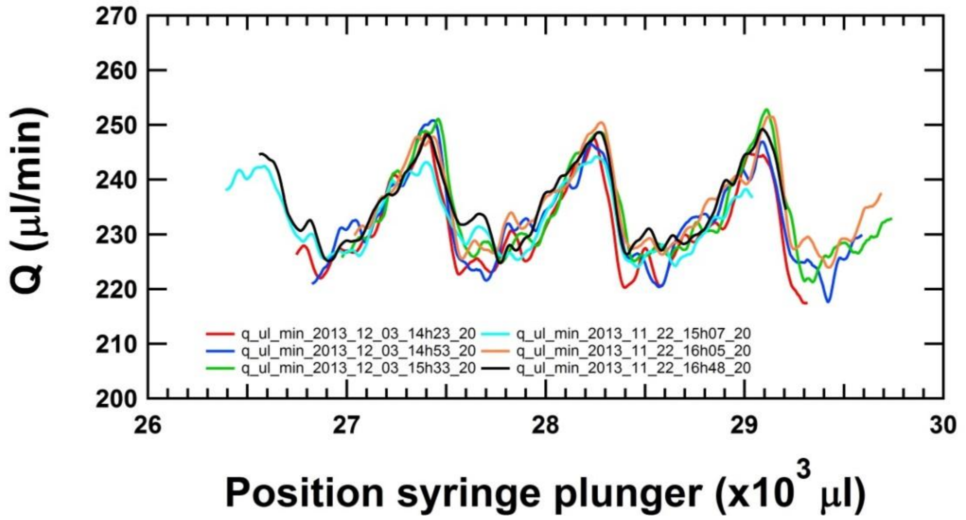

Figure 9, METAS-Setup: Instantaneous flow rates as a function of the position of the syringe plunger where a fit window of 20 s was used for the flow rate determination. Using 2 syringes 6 measurements were performed. Details of the different curves can be found in Table 5.

Name of data	Offset (μl)	Syringe used
2013_12_03 14h23	350	dry marked
2013_12_03 14h53	0	dry marked
2013_12_03 15h33	150	dry marked
2013_11_22 15h07	-550	wet marked
2013_11_22 16h05	100	wet marked
2013_11_22 16h48	-500	wet marked

Table 5, METAS-Setup: Details on the syringe used for each experiment and offset on the x-axis in order to get an overlap of the pulsating flow pattern.

We do not distinguish any evident differences in the pulsating flow pattern by using a wet syringe (used one) or a dry syringe (new one).

5.2.1.2 METAS-Setup - Deviation of averaged flow rate

We determined the mean flow rates over 3 cycles of the spindle rotation time using the fit window of 20 s and show them in Figure 10 and Table 6.

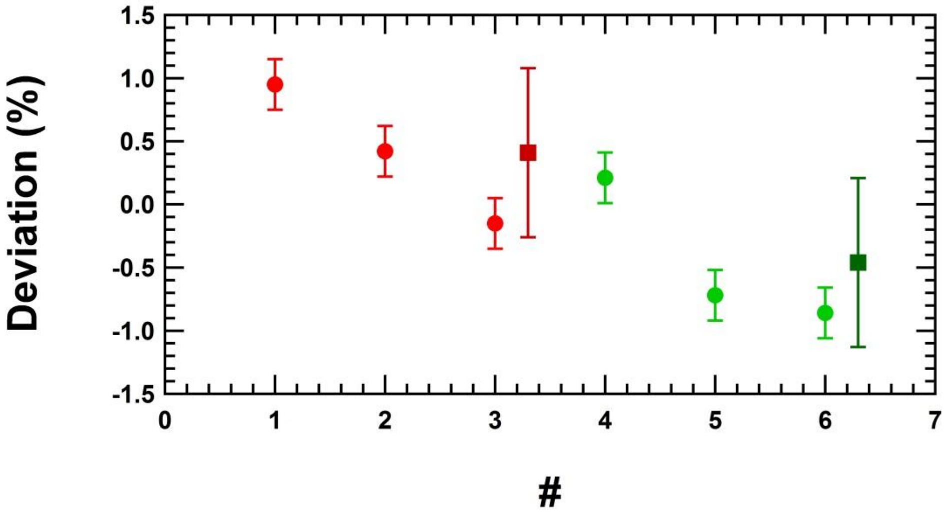

Figure 10, METAS-Setup: Deviations of the syringe pump using a dry syringe (dry marked, red circles) and a wet syringe (wet marked, green) at Q ~ 14 ml/h (233 μl/min). The squares are the mean values of the 3 single points.

Name of data	Deviation (%)	U (k=2) (%)	Mean (%)	U mean (k=2) (%)
2013_12_03 14h23	0.95	0.20	0.41	0.67
2013_12_03 14h53	0.42	0.20		
2013_12_03 15h33	-0.15	0.20		
2013_11_22 15h07	0.21	0.20	-0.46	0.71
2013_11_22 16h05	-0.72	0.20		
2013_11_22 16h48	-0.86	0.20		

Table 6, METAS-Setup: deviations of the mean flow rates over 3 cycles of the spindle rotation time

5.2.1.3 METAS-Setup - Amplitude and periodicity of pulsating flow pattern

To determine the periodicity of the pulsating flow pattern we performed an FFT analysis of the data in Figure 9 (fit window 20 s) and determined additionally the time interval between the maximum peaks and the positions before and after the peaks where the flow rate was equal to the mean flow rate. The results are summarized in Table 7, where the uncertainty is calculated from the standard deviation of the data points.

	Periodicity (s)	U (k=2) (s)
By means of FFT	215.7	23.7
By means of interval determination	214.1	11.4

Table 7, METAS-Setup: Periodicity of the pulsating flow pattern at flow rate Q ~233 μl/min.

The amplitudes were determined by means of averaging the local minima and local maxima. Therefore we get for each measurement the amplitudes with respect to the mean flow rate and then we average the amplitudes of all the measurements to state the amplitudes in positive and negative directions. The uncertainty is calculated from the standard deviation of the data points.

Name of data	Mean flow rate (μl/min)	Average of local maximas (μl/min)	Average of local maximas (%)	U(max) (%)	Average of local minimas (μl/min)	Average of local minimas (%)	U(min) (%)
2013_12_03 14h23	231.41	247.0	6.7	1.6	221.0	-4.5	2.0
2013_12_03 14h53	232.63	248.1	6.7	2	220.1	-5.4	1.6
2013_12_03 15h33	233.95	250.8	7.2	1.8	223.8	-4.3	1.9
2013_11_22 15h07	233.12	243.3	4.4	0.8	224.8	-3.60	0.8
2013_11_22 16h05	235.30	249.9	6.2	1.6	225.2	-4.3	1.2
2013_11_22 16h48	235.63	248.7	5.5	0.5	226.1	-4.0	1.5
Average			**6.1**	**2.1**		**-4.4**	**2.0**

Table 8, METAS-Setup: Amplitudes of the pulsating flow pattern at flow rate Q ~233 μl/min.

5.2.2 METAS-Setup - Syringe pump at Q ~ 0.9 ml/h (15.6 μl/min)

5.2.2.1 METAS-Setup - Pulsating flow pattern

The instantaneous flow rates determined by the dynamic gravimetric method are shown in Figure 11 resp. 12 where a fit window of 3 s resp. 20 s was used. As the start position of the syringe plunger can't be set really accurate at the beginning of the measurements, the position on the x-axis is slightly corrected with an offset of 300 μl for the data of «2013_11_26_12h48» in order to get an overlap of the pulsating flow pattern. We used only the wet syringe (wet marked) at this flow rate.

The sharp spikes of the blue curve in Figure 11 are due to a poor water flow into the beaker as the glass filter was not clean enough and might influence the capillary forces in order to induce a slight step function in the increase of mass. This problem occurred during the measurements of «2013_11_26_12h48» (red) and «2013_11_26_08h49» (blue). To average out this noise effect of the flow detection unit we smoothed the curves over 10 data points for the data with the fit window of 3 s and over 20 data points (~ 5 μl) resp. 30 data points (~ 7.5 μl) for the data with the fit window 20 s of the measurements «2013_11_26_12h48» (red) resp. «2013_11_26_08h49» (blue).This smoothing of the curves was only done for illustration purpose in the Figure 11 and 12.

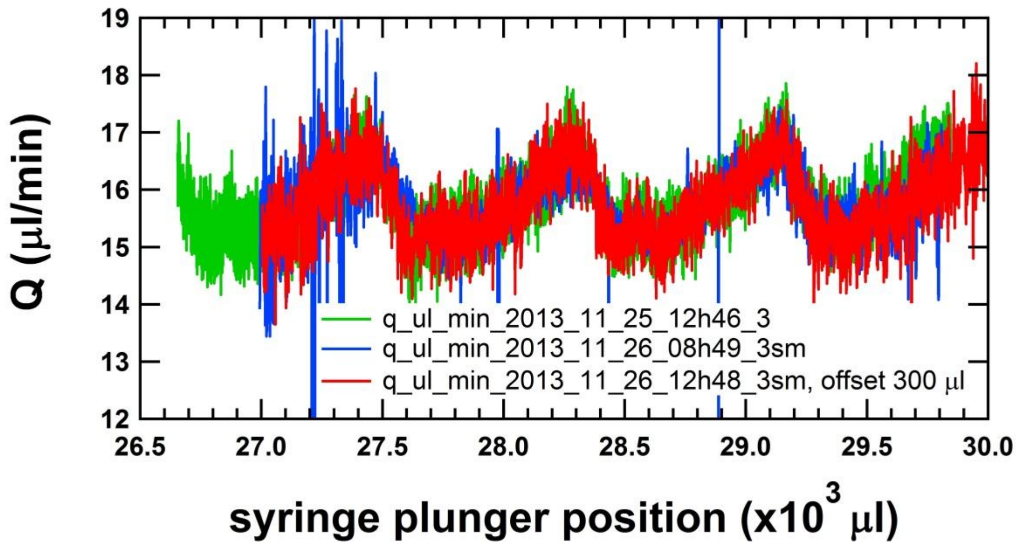

Figure 11, METAS-Setup: Instantaneous flow rates as a function of the position of the syringe plunger where a fit window of 3 s was used for the flow rate determination. 3 measurements were performed with the wet syringe (wet marked). The data of «2013_11_26_12h48» are shifted with an offset of 300 μl in order to get an overlap of the pulsating flow pattern.

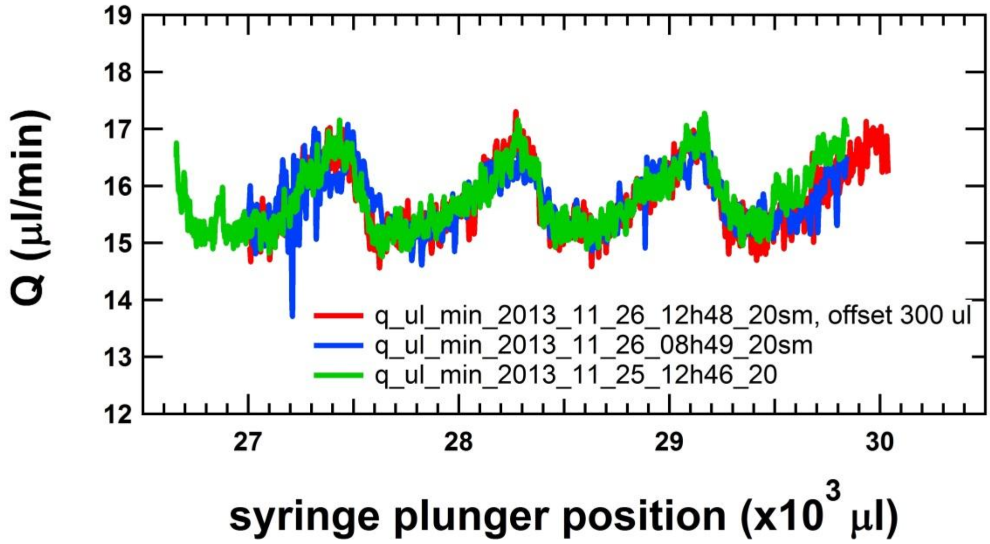

Figure 12, METAS-Setup: Instantaneous flow rates as a function of the position of the syringe plunger where a fit window of 20 s was used for the flow rate determination. 3 measurements were performed with the wet syringe (wet marked). The data of «2013_11_26_12h48» are shifted with an offset of 300 µl in order to get an overlap of the pulsating flow pattern.

5.2.2.2 METAS-Setup - Deviation of averaged flow rate

We determined the mean flow rates over 3 cycles of the spindle rotation time and show them in Figure 13. The original data including the noise effect of the flow detection unit were used and no smoothing was applied prior to the determination of the deviation.

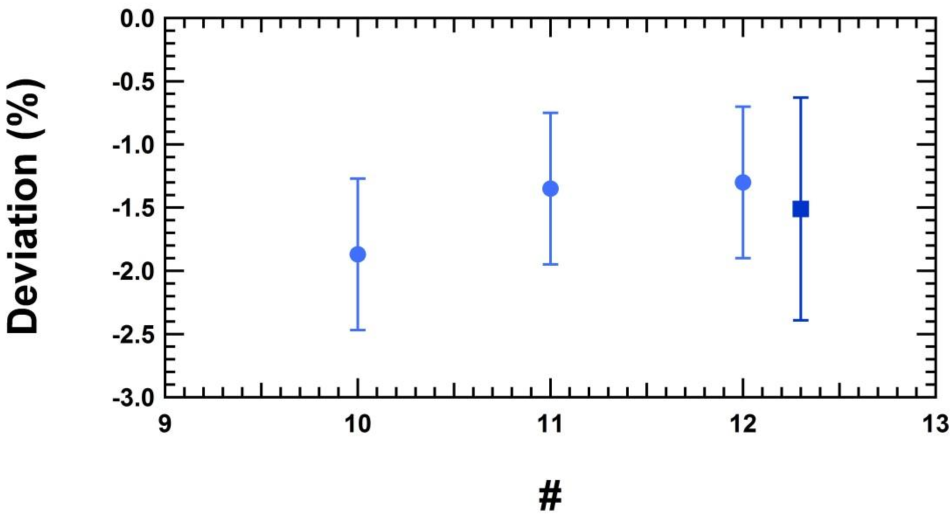

Figure 13, METAS-Setup: Deviations of the syringe pump using a wet syringe Q ~ 0.9 ml/h (15.6 µl/min). The square is the mean value of the 3 single points (circles).

Name of data	Deviation (%)	U (k=2) (%)	Mean (%)	U mean (k=2) (%)
2013_11_25 12h46	-1.87	0.60	-1.51	0.88
2013_11_26 08h49	-1.35	0.60		
2013_11_26 12h48	-1.30	0.60		

Table 9, METAS-Setup: deviations of the mean flow rates over 3 cycles of the spindle rotation time

5.2.2.3 METAS-Setup - Amplitude and periodicity of pulsating flow pattern

To determine the periodicity of the pulsating flow pattern we performed an FFT analysis of the data in Figure 12 (fit window 20 s) and determined additionally the time interval between the maximum peaks and the positions before and after the peaks where the flow rate was equal to the mean flow rate.

As the data show rather large fluctuations and local maxima and minima are difficult to determine we smoothed the curves over 200 points which corresponds to 52 μl as can be seen in Figure 14 for the data of «2013_11_25_12h46».

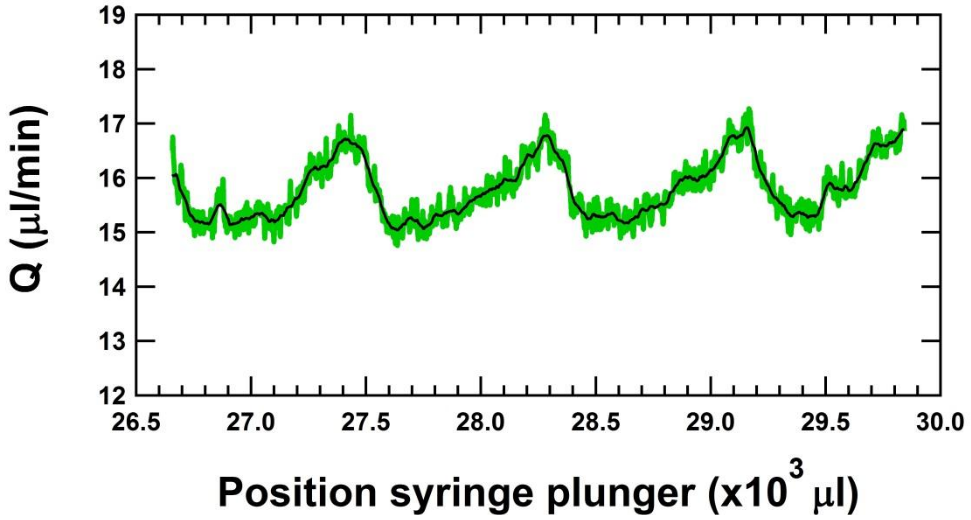

Figure 14, METAS-Setup: the original data of «2013_11_25_12h46» (green line) and the smoothed curve which was averaged over 200 points corresponding to 52 μl (black line).

The results are summarized in Table 10, where the uncertainty is calculated from the standard deviation of the data points.

	Periodicity (s)	U (k=2) (s)
By means of FFT	3241.8	162.4
By means of interval determination	3205.3	284.8

Table 10, METAS-Setup: Periodicity of the pulsating flow pattern at flow rate Q ~15.6 μl/min.

The amplitudes were determined by means of averaging the local minima and local maxima using the data smoothed over 200 points as seen in Figure 14 for example. Therefore we get for each measurement the amplitudes with respect to the mean flow rate and then we average the amplitudes of all the measurements to state the amplitudes in positive and negative directions. The uncertainty is calculated from the standard deviation of the data points.

Name of data	Mean flow rate (μl/min)	Average of local maximas (μl/min)	Average of local maximas (%)	U(max) (%)	Average of local minimas (μl/min)	Average of local minimas (%)	U(min) (%)
2013_11_25 12h46	15.87	16.8	5.9	1.8	15.2	-4.2	2.0
2013_11_26 08h49	15.78	16.6	5.2	3.1	15.1	-4.3	2.0
2013_11_26 12h48	15.77	16.7	5.9	1.2	15.0	-4.9	0.7
Average			**5.7**	**3.1**		**-4.5**	**2.0**

Table 11, METAS-Setup: Amplitudes of the smoothed pulsating flow pattern at flow rate Q ~15.6 μl/min.

5.2.3 METAS-Setup - Coriolis flow meter calibrated with steady flow at Q ~14 ml/h (233 μl/min)

The Coriolis flow meter M12P was first calibrated with the flow generator of the laboratory which generates a stable steady flow rate. One of the measurements is shown in Figure 15 where the raw data of the M12P, the averaged data of the M12P and the averaged data of the reference flow rate determined with a fit window of 300 s are shown.

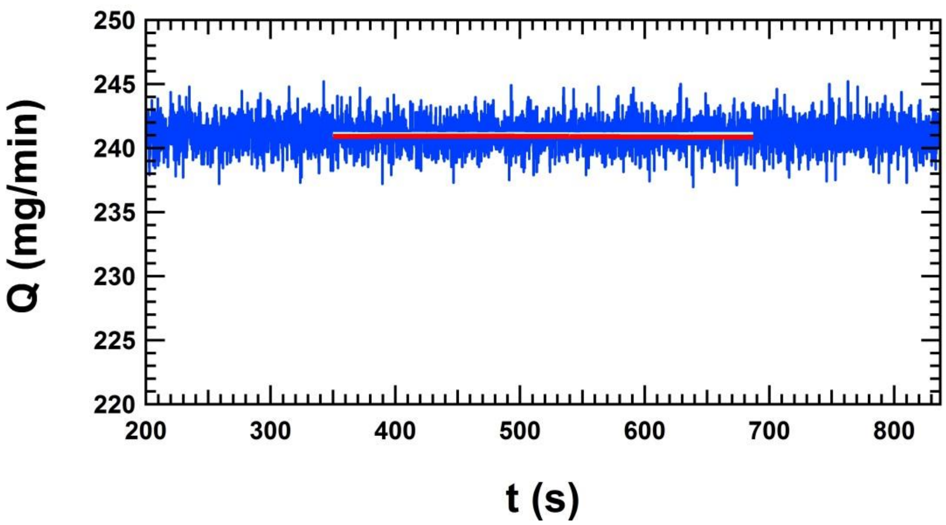

Figure 15, METAS-Setup: raw data of the M12P (blue line), the averaged data of the M12P (cyan line) and the averaged data of the reference flow rate of the experiment «2013_12_02_14h48» (red line). The fit window and the averaging time is 300 s.

We get the following deviations of the M12P using the flow generator of the laboratory as seen in Figure 16 and Table 12.

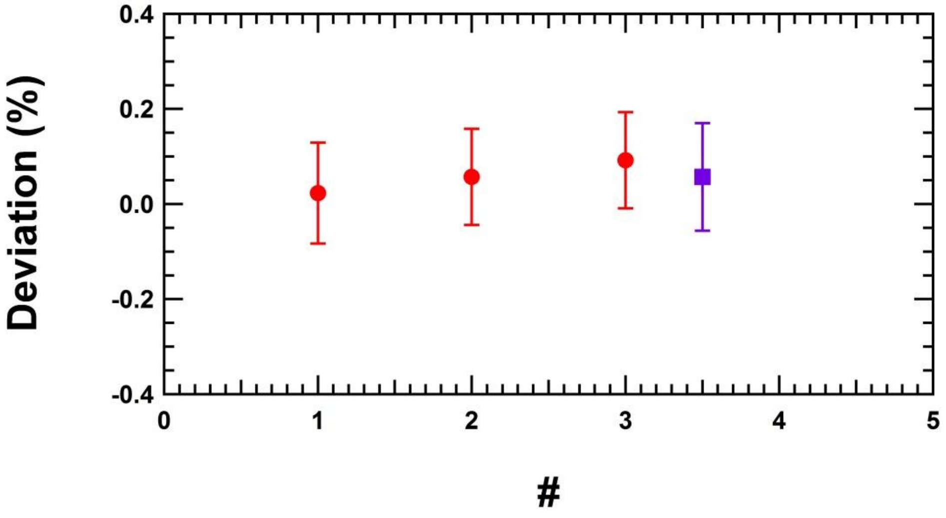

Figure 16, METAS-Setup: deviations of the M12P using the flow generator of the laboratory for stable steady flow. The square is the mean value of the 3 single points (circles).

Name of data	Deviation (%)	U (k=2) (%)	Mean (%)	U mean (k=2) (%)
2013_12_03 10h41	0.023	0.106	-0.057	0.113
2013_12_03 11h09	0.057	0.101		
2013_12_03 13h16	0.092	0.101		

Table 12, METAS-Setup: deviations of the flow rates of the M12P using stable steady flow

5.2.4 METAS-Setup - Coriolis flow meter calibrated with pulsating flow generated by the syringe pump at Q ~14 ml/h (233 μl/min)

The Coriolis M12P is connected between the syringe pump and the piping leading to the beaker on the balance. The generated flow is now pulsating according to the characteristics of the syringe pump.
The instantaneous flow rates determined by the dynamic gravimetric method and the signal from the flow meter as well as the instantaneous deviation are shown in Figure 17 resp. 18 where a fit window of 3 s resp. 20 s was used. In order to compare the data from the same time window the signal of the flow meter was also averaged over 3 s resp. 20 s.

Prior to switching on the syringe pump, residual flow due to system preparation was present. Switching on the pump leads immediately to an increase of the flow. As usual the flow rate at the flow meter and at the Balance is not the same as long as the stabilisation is not reached. Therefore, at the beginning the deviation is larger than after stabilisation as can be seen in Figures 17 and 18.

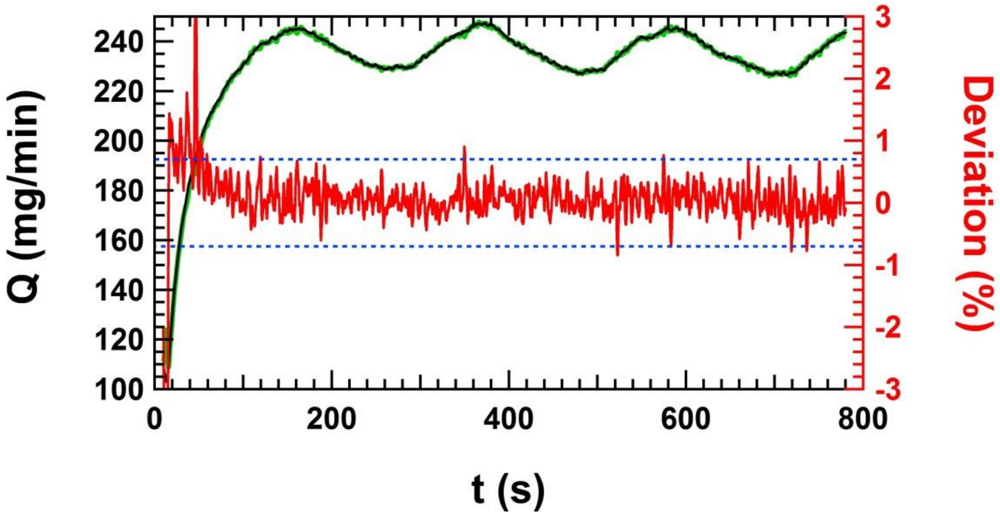

Figure 17, METAS-Setup: The instantaneous flow rate determined by the dynamic gravimetric method for a fit window of 3 s (left axis, green line) and the signal from the flow meter averaged over 3 s (left axis, black line) as well as the instantaneous deviation (right axis, red line). The dashed blue line is the stated uncertainty for the instantaneous flow rate (right axis).

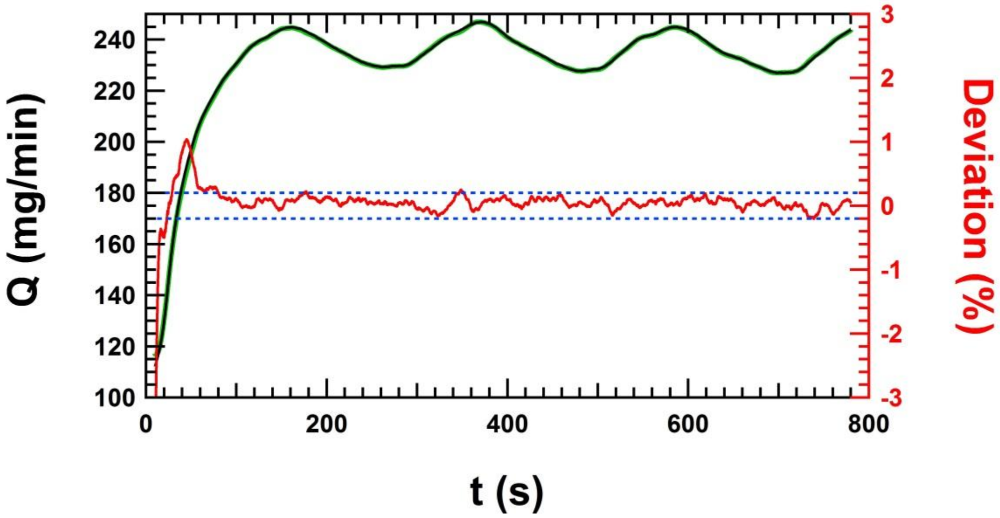

Figure 18, METAS-Setup: The instantaneous flow rate determined by the dynamic gravimetric method for a fit window of 20 s (left axis, green line) and the signal from the flow meter averaged over 20 s (left axis, black line) as well as the instantaneous deviation (right axis, red line). The dashed blue line is the stated uncertainty for the instantaneous flow rate (right axis).

In Figure 19 and 20 we show the same data as in Figure 17 and 18 starting after the stabilisation time. We can clearly see that the instantaneous deviations are within the stated uncertainty and that we expect the distribution of the deviations to be Gaussian around the mean as the deviations are randomly fluctuating (histogram not shown).

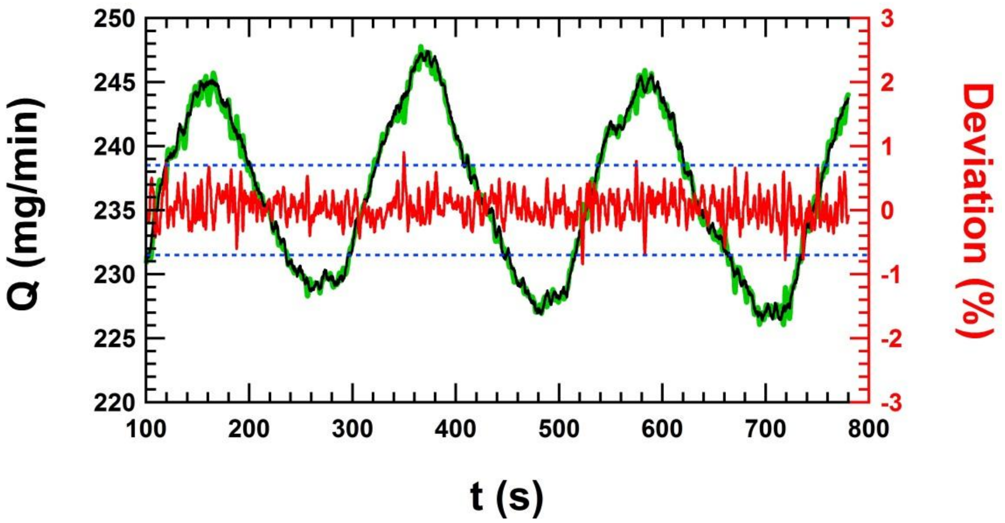

Figure 19, METAS-Setup: The instantaneous flow rate determined by the dynamic gravimetric method for a fit window of 3 s (left axis, green line) and the signal from the flow meter averaged over 3 s (left axis, black line) as well as the instantaneous deviation (right axis, red line). The dashed blue line is the stated uncertainty for the instantaneous flow rate (right axis). Only the data after the stabilization time are shown.

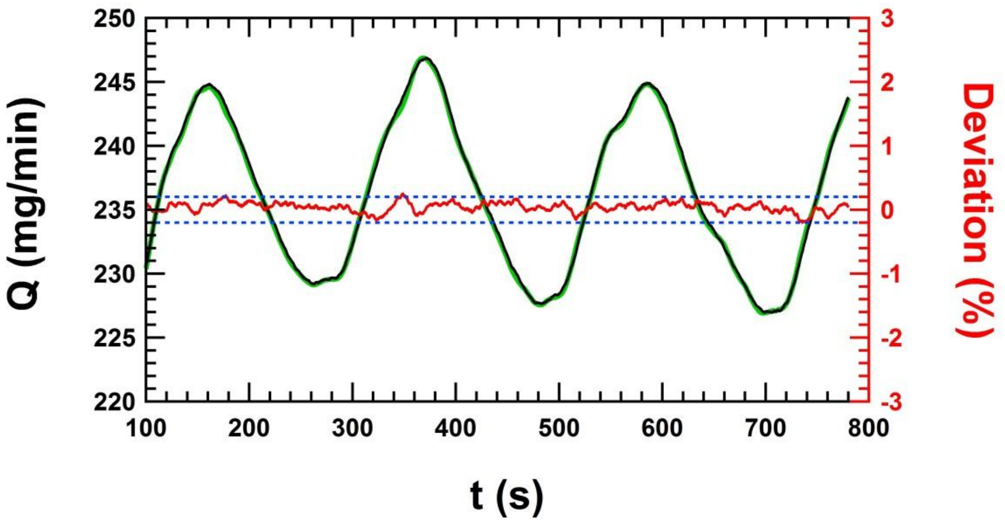

Figure 20, METAS-Setup: The instantaneous flow rate determined by the dynamic gravimetric method for a fit window of 20 s (left axis, green line) and the signal from the flow meter averaged over 20 s (left axis, black line) as well as the instantaneous deviation (right axis, red line). The dashed blue line is the stated uncertainty for the instantaneous flow rate (right axis). Only the data after the stabilization time are shown.

We determined the mean flow rates over 3 cycles of the spindle rotation time (fit window 20 s) and show them in Figure 21 and Table 13. The deviations of the M12P are consistent for both flow generators.

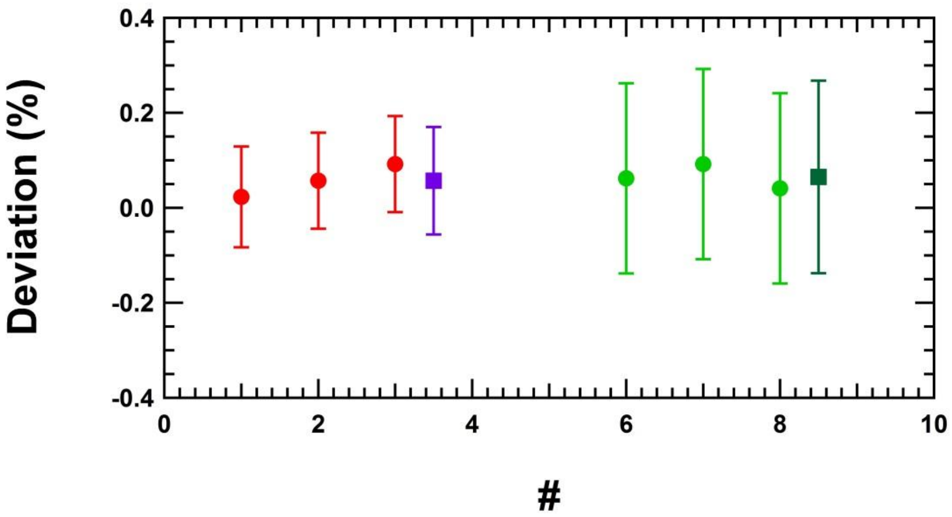

Figure 21, METAS-Setup: deviations of the M12P using the flow generator of the laboratory for stable steady flow (red circles) and the syringe pump for pulsating flow (green circles). The squares are the mean value of the 3 single points (circles).

Name of data	Flow type	Point type	Deviation (%)	U(%)	x-Axis value (#)
2013_12_02 14h21	steady	single	0.023	0.106	1
2013_12_02 14h48	steady	single	0.057	0.101	2
2013_12_03 06h53	steady	single	0.092	0.101	3
	steady	mean	0.057	0.113	3.5
2013_12_03 10h41	pulsating	single	0.062	0.200	6
2013_12_03 11h09	pulsating	single	0.092	0.200	7
2013_12_03 13h16	pulsating	single	0.041	0.200	8
	pulsating	mean	0.065	0.203	8.5

Table 13, METAS-Setup: deviations of the flow rates of the M12P using stable steady flow and pulsating flow

We did also analyze the amplitudes of the pulsating flow rate determined with a fit window of 20 s and get the following results (see Table 14).

Name of data	Mean flow rate (µl/min)	Average of local maximas (µl/min)	Average of local maximas (%)	U(max) (%)	Average of local minimas (µl/min)	Average of local minimas (%)	U(min) (%)
2013_12_03 10h41	235.54	245.3	4.1	0.7	227.6	-3.4	0.9
2013_12_03 11h09	233.92	243.6	4.1	1.1	227.1	-2.9	0.5
2013_12_03 13h16	236.69	246.0	3.9	1.1	228.4	-3.5	1.1
Average			**4.0**	**1.1**		**-3.3**	**1.1**

Table 14, METAS-Setup: Amplitudes of pulsating flow pattern at flow rate Q ~233 µl/min of the syringe pump in line with the Coriolis flow meter M12P.

We observe slightly smaller amplitudes compared to the measurements where only the syringe pump is connected to the piping leading to the beaker on the balance.

5.3 Results DTI

5.3.1 DTI-Setup - Syringe pump at Q ~ 14 ml/h (233 µl/min)

5.3.1.1 DTI-Setup - Pulsating flow pattern

The instantaneous flow rates determined by the dynamic gravimetric method are shown in Figure 22 resp. 23 where a fit window of 3 s resp. 20 s was used. As the start position of the syringe plunger can't be set really accurate at the beginning of the measurements, the positions on the x-axis were slightly corrected with an offset in order to get an overlap of the pulsating flow pattern (see Table 15). We used the syringes (wet marked). The details about the different data can be read in Table 15.

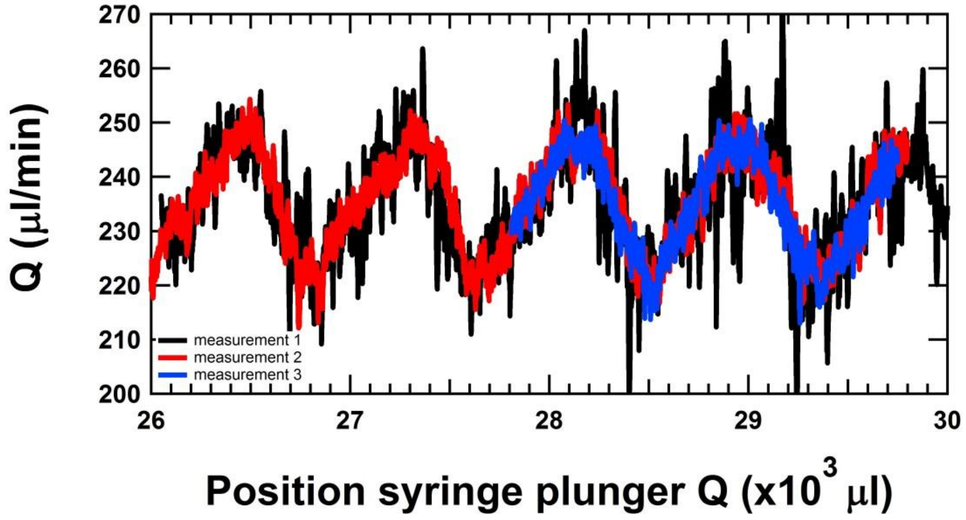

Figure 22, DTI-Setup: Instantaneous flow rates as a function of the position of the syringe plunger where a fit window of 3 s was used for the flow rate determination. Details of the different curves can be found in Table 15.

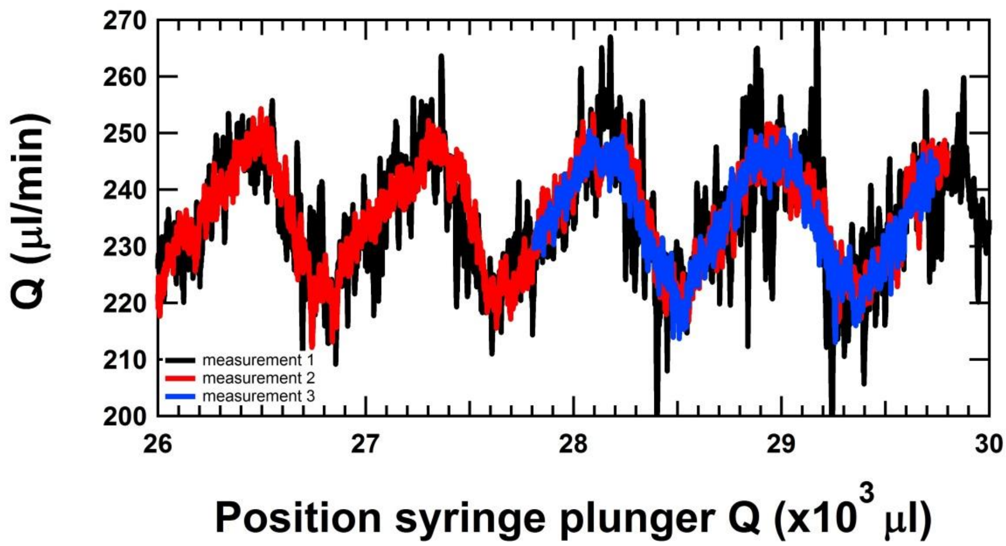

Figure 23, DTI-Setup: Instantaneous flow rates as a function of the position of the syringe plunger where a fit window of 20 s was used for the flow rate determination. Details of the different curves can be found in Table 15.

Name of data	Offset (μl)	Syringe used
Measurement 1	350	wet marked
Measurement 2	0	wet marked
Measurement 3	-100	wet marked

Table 15, DTI-Setup: Details on the syringe used for each experiment and offset on the x-axis in order to get an overlap of the pulsating flow pattern.

5.3.1.2 DTI-Setup - Deviation of averaged flow rate

We determined the mean flow rates over 3 cycles of the spindle rotation time using the fit window of 20 s and show them in Figure 24 and Table 16.

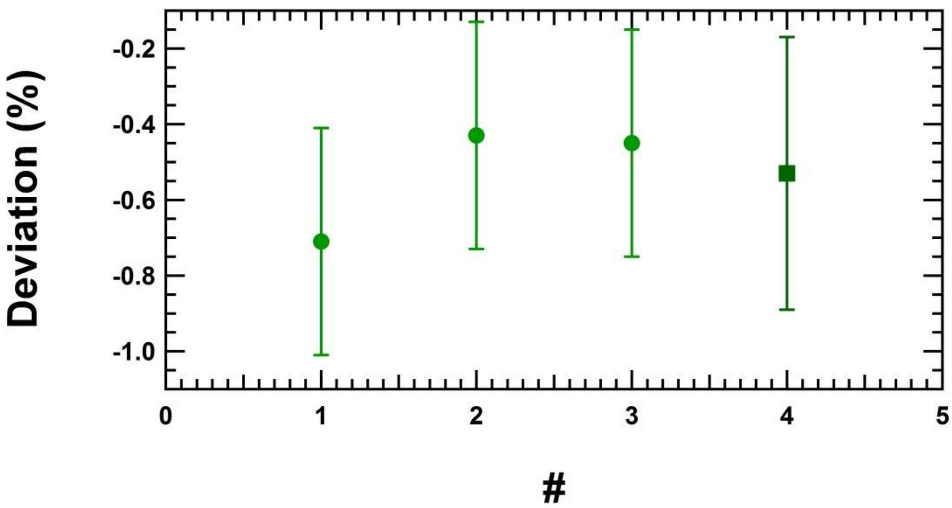

Figure 24, DTI-Setup: Deviations of the syringe pump using a syringe (wet marked, green circles) at Q ~ 14 ml/h (233 μl/min). The squares are the mean values of the 3 single points.

Name of data	Deviation (%)	U (k=2) (%)	Mean (%)	U mean (k=2) (%)
Measurement 1	-0.71	0.3	-0.53	0.36
Measurement 2	-0.42	0.3		
Measurement 3	-0.45	0.3		

Table 16, DTI-Setup: deviations of the mean flow rates over 3 cycles of the spindle rotation time

5.3.1.3 DTI-Setup - Amplitude and periodicity of pulsating flow pattern

To determine the periodicity of the pulsating flow pattern we performed an FFT analysis of the data in Figure 23 (fit window 20 s) and determined additionally the time interval between the maximum peaks and the positions before and after the peaks where the flow rate was equal to the mean flow rate. The results are summarized in Table 17, where the uncertainty is calculated from the standard deviation of the data points.

	Periodicity	U (k=2)

	(s)	(s)
By means of FFT	226.0	51.6
By means of interval determination	213.8	8.0

Table 17, DTI-Setup: Periodicity of the pulsating flow pattern at flow rate Q ~233 µl/min.

The amplitudes were determined by means of averaging the local minima and local maxima. Therefore we get for each measurement the amplitudes with respect to the mean flow rate and then we average the amplitudes of all the measurements to state the amplitudes in positive and negative directions. The uncertainty is calculated from the standard deviation of the data points.

Name of data	Mean flow rate (µl/min)	Average of local maximas (µl/min)	Average of local maximas (%)	U(max) (%)	Average of local minimas (µl/min)	Average of local minimas (%)	U(min) (%)
Measurement 1	235.27	250.0	6.5	1.8	220.0	-6.5	1.3
Measurement 2	234.60	248.3	5.4	0.7	221.7	-5.7	0.4
Measurement 3	234.67	246.7	5.0	1.0	220.0	-6.6	4.3
Average			**5.6**	**1.2**		**-6.3**	**2.0**

Table 18, DTI-Setup: Amplitudes of the pulsating flow pattern at flow rate Q ~233 µl/min.

5.3.2 DTI-Setup - Syringe pump at Q ~ 0.9 ml/h (15.6 µl/min)

5.3.2.1 DTI-Setup - Pulsating flow pattern

The instantaneous flow rates determined by the dynamic gravimetric method are shown in Figure 25 resp. 26 where a fit window of 3 s resp. 20 s was used. As the start position of the syringe plunger can't be set really accurate at the beginning of the measurements, the position on the x-axis is slightly corrected with an offset in order to get an overlap of the pulsating flow pattern. We used only the wet syringe (wet marked) at this flow rate.

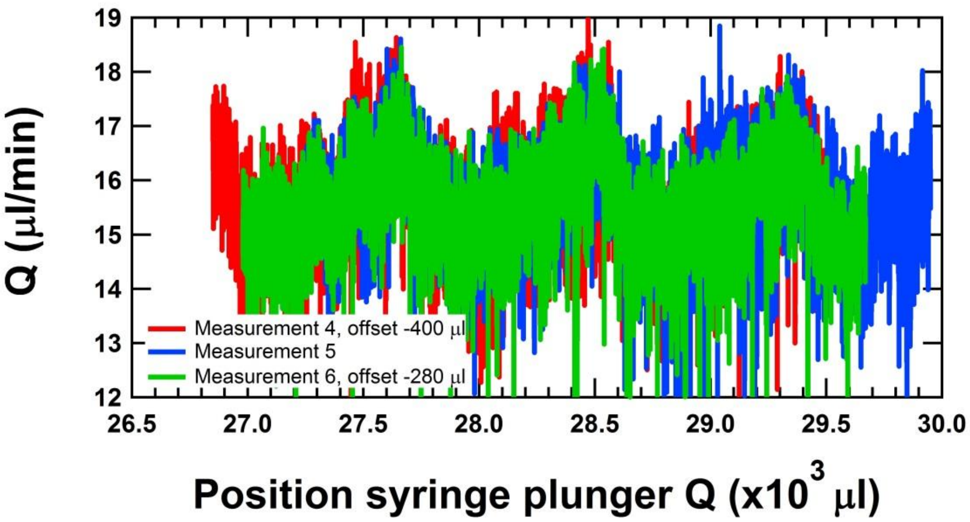

Figure 25, DTI-Setup: Instantaneous flow rates as a function of the position of the syringe plunger where a fit window of 3 s was used for the flow rate determination. 3 measurements were performed with the syringe (wet marked). The data are shifted with an offset in order to get an overlap of the pulsating flow pattern.

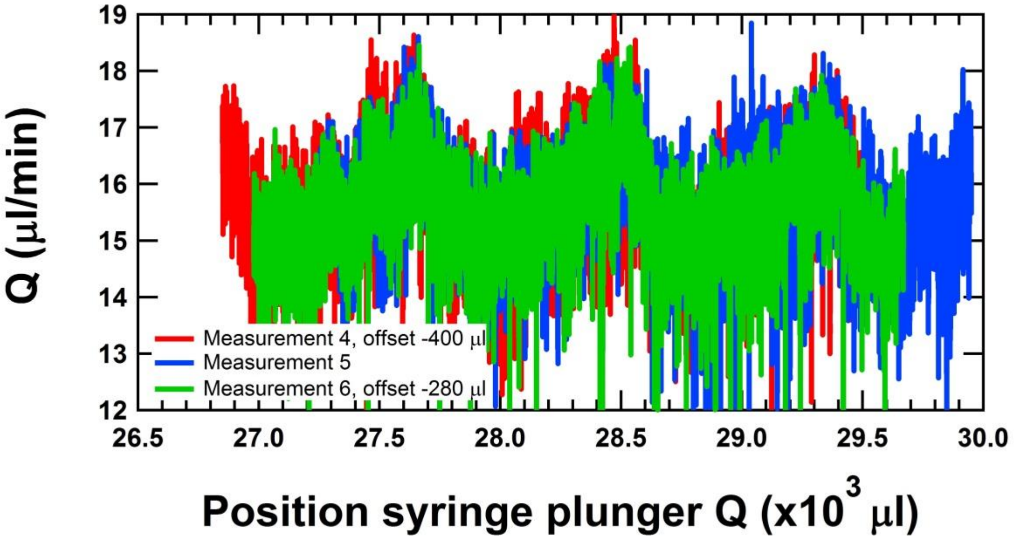

Figure 26, DTI-Setup: Instantaneous flow rates as a function of the position of the syringe plunger where a fit window of 20 s was used for the flow rate determination. 3 measurements were performed with the syringe (wet marked). The data are shifted with an offset in order to get an overlap of the pulsating flow pattern.

5.3.2.2 DTI-Setup - Deviation of averaged flow rate

We determined the mean flow rates over 3 cycles of the spindle rotation time and show them in Figure 27. The original data including the noise effect of the flow detection unit were used and no smoothing was applied prior to the determination of the deviation.

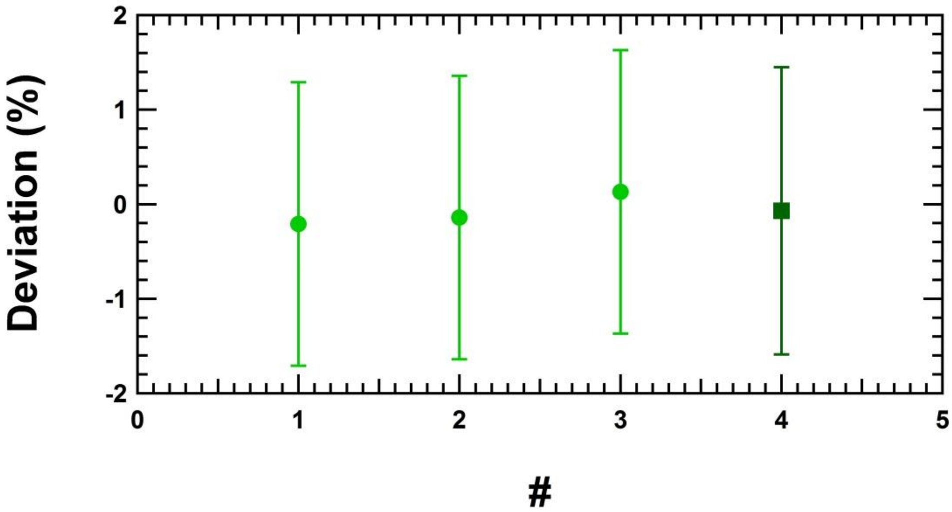

Figure 27, DTI-Setup: Deviations of the syringe pump using a wet syringe Q ~ 0.9 ml/h (15.6 µl/min). The square is the mean value of the 3 single points (circles).

Name of data	Deviation (%)	U (k=2) (%)	Mean (%)	U mean (k=2) (%)
Measurement 4	-0.18	1.5	-0.05	1.52
Measurement 5	-0.12	1.5		
Measurement 6	0.15	1.5		

Table 19, DTI-Setup: deviations of the mean flow rates over 3 cycles of the spindle rotation time

5.3.2.3 DTI-Setup - Amplitude and periodicity of pulsating flow pattern

To determine the periodicity of the pulsating flow pattern we performed an FFT analysis of the data in Figure 26 (fit window 20 s) and determined additionally the time interval between the maximum peaks and the positions before and after the peaks where the flow rate was equal to the mean flow rate.

The results are summarized in Table 20, where the uncertainty is calculated from the standard deviation of the data points.

	Periodicity (s)	U (k=2) (s)
By means of FFT	3587.8	26.0
By means of interval determination	3238.4	152

Table 20, DTI-Setup: Periodicity of the pulsating flow pattern at flow rate Q ~15.6 µl/min.

The amplitudes were determined by means of averaging the local minima and local maxima using the data smoothed over 200 points for example. Therefore we get for each measurement the amplitudes with respect to the mean flow rate and then we average the amplitudes of all the measurements to state the amplitudes in positive and negative directions. The uncertainty is calculated from the standard deviation of the data points.

Name of data	Mean flow rate (µl/min)	Average of local maximas (µl/min)	Average of local maximas (%)	U(max) (%)	Average of local minimas (µl/min)	Average of local minimas (%)	U(min) (%)
Measurement 4	15.60	16.79	7.6	2.4	14.35	-8.0	1.9
Measurement 5	15.59	16.95	8.7	4.2	14.5	-7.0	3.7
Measurement 6	15.55	17	9.3	0.7	14.45	-7.1	2.6
Average			**8.5**	**2.4**		**-7.4**	**2.7**

Table 21, DTI-Setup: Amplitudes of the smoothed pulsating flow pattern at flow rate Q ~15.6 µl/min.

5.3.3 DTI-Setup - Coriolis flow meter calibrated with pulsating flow generated by the syringe pump at Q ~14 ml/h (233 µl/min)

The Coriolis M12P is connected between the syringe pump and the piping leading to the beaker on the balance. The generated flow is now pulsating according to the characteristics of the syringe pump.
The instantaneous flow rates determined by the dynamic gravimetric method and the signal from the flow meter as well as the instantaneous deviation are shown in Figures 28 and 29 where a fit window of 3 s resp. 20 s was used. In order to compare the data from the same time window the signal of the flow meter was also averaged over 3 s resp. 20 s.

Prior to switching on the syringe pump, residual flow due to system preparation was present. Switching on the pump leads immediately to an increase of the flow. As usual the flow rate at the flow meter and at the Balance is not the same as long as the stabilisation is not reached. Therefore, at the beginning the deviation is larger than after stabilisation as can be seen in Figures 28 and 29.

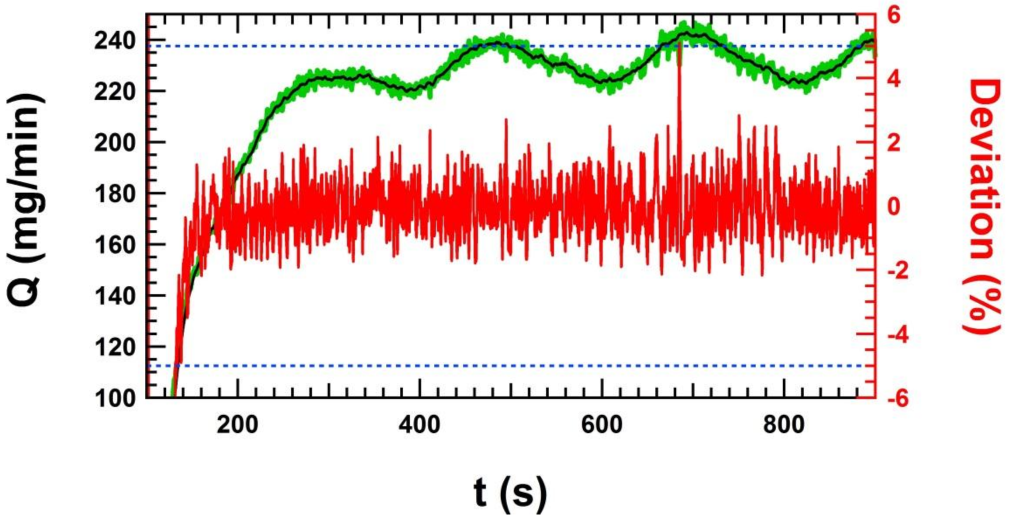

Figure 28, DTI-Setup: The instantaneous flow rate determined by the dynamic gravimetric method for a fit window of 3 s (left axis, green line) and the signal from the flow meter averaged over 3 s (left axis, black line) as well as the instantaneous deviation (right axis, red line). The dashed blue line is the stated uncertainty for the instantaneous flow rate (right axis).

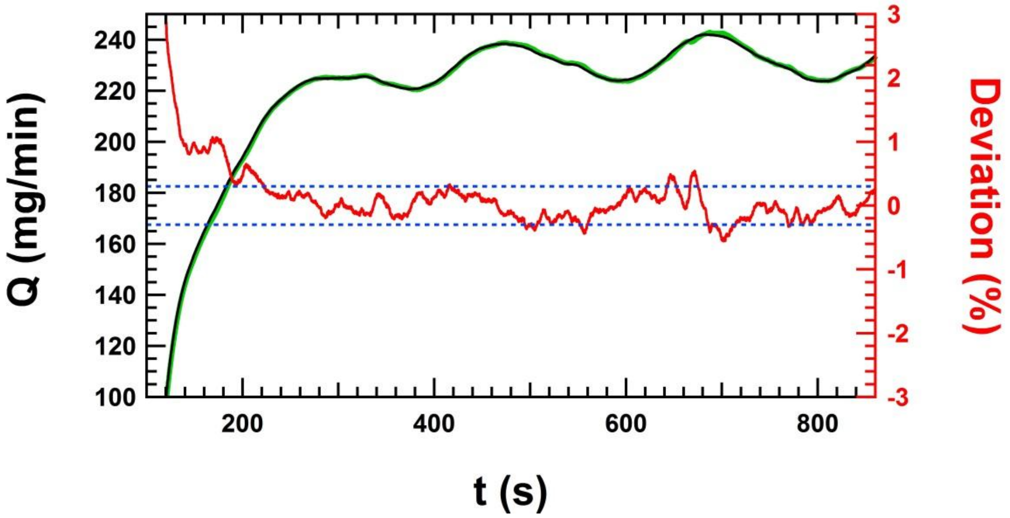

Figure 29, DTI-Setup: The instantaneous flow rate determined by the dynamic gravimetric method for a fit window of 20 s (left axis, green line) and the signal from the flow meter averaged over 20 s (left axis, black line) as well as the instantaneous deviation (right axis, red line). The dashed blue line is the stated uncertainty for the instantaneous flow rate (right axis).

In Figures 30 and 31 we show the same data as in Figures 28 and 29 starting after the stabilisation time. We can clearly see that the instantaneous deviations are within the stated uncertainty and that we expect the distribution of the deviations to be Gaussian around the mean as the deviations are randomly fluctuating (histogram not shown).

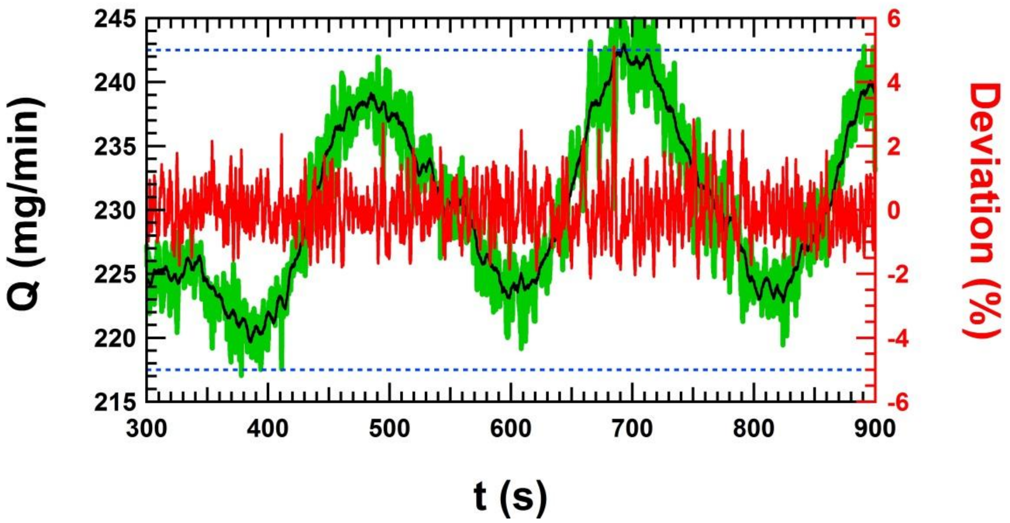

Figure 30, DTI-Setup: The instantaneous flow rate determined by the dynamic gravimetric method for a fit window of 3 s (left axis, green line) and the signal from the flow meter averaged over 3 s (left axis, black line) as well as the instantaneous deviation (right axis, red line). The dashed blue line is the stated uncertainty for the instantaneous flow rate (right axis). Only the data after the stabilization time are shown.

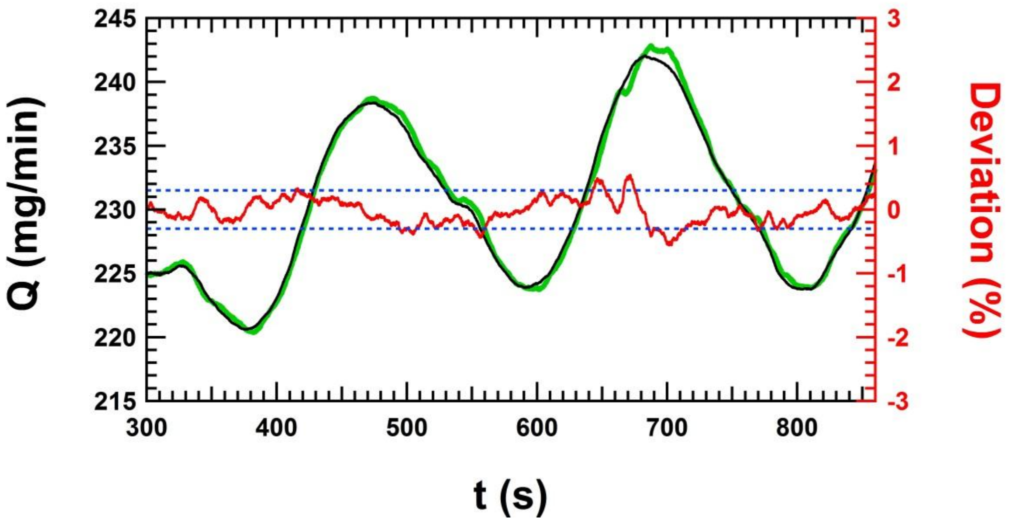

Figure 31, DTI-Setup: The instantaneous flow rate determined by the dynamic gravimetric method for a fit window of 20 s (left axis, green line) and the signal from the flow meter averaged over 20 s (left axis, black line) as well as the instantaneous deviation (right axis, red line). The dashed blue line is the stated uncertainty for the instantaneous flow rate (right axis). Only the data after the stabilization time are shown.

We determined the mean deviation of the M12P being (-0.05 ± 5.00) % for the fit window of 3 s and (-0.04 ± 0.30) % for the fit window of 20 s.

5.4 Validation of the pulsating flow tester

5.4.1 Syringe pump at Q ~ 14 ml/h (233 µl/min)

We summarize the measurements performed with the same syringe (wet marked). The check of consistency is performed according to the formula of the En-value

$$En = |value1 - value2| / \sqrt{(Uncertainty1)^2 + (Uncertainty2)^2}$$

5.4.1.1 Deviation of averaged flow rate at Q ~ 14 ml/h (233 µl/min)

The mean deviations determined by METAS and DTI are consistent within their uncertainties with an En-value of 0.05.

	Mean (%)	U mean (k=2) (%)	**En-value (< 1 !)**
METAS-Setup	-0.46	0.71	**0.09**
DTI-Setup	-0.53	0.36	

Table 22: Validation of averaged flow rate Q ~233 µl/min.

5.4.1.2 Periodicity of pulsating flow pattern at Q ~ 14 ml/h (233 µl/min)

The periodicity of pulsating flow pattern determined by METAS and DTI are consistent within their uncertainties with an En-value of 0.19 and 0.03.

By means of FFT	Periodicity (s)	U (k=2) (s)	**En-value (< 1 !)**
METAS-Setup	215.7	23.7	**0.19**
DTI-Setup	226.0	51.6	

By means of interval determination	Periodicity (s)	U (k=2) (s)	**En-value (< 1 !)**
METAS-Setup	214.1	11.4	**0.03**
DTI-Setup	213.8	8.0	

Table 23: Periodicity of the pulsating flow pattern at flow rate Q ~233 µl/min.

5.4.1.3 Amplitude of pulsating flow pattern at Q ~ 14 ml/h (233 µl/min)

The amplitude of pulsating flow pattern determined by METAS and DTI are consistent within their uncertainties with an En-value of 0.68.

	Average of local maximas (%)	U(max) (%)	**En-value** **(< 1 !)**	Average of local minimas (%)	U(min) (%)	**En-value** **(< 1 !)**
METAS-Setup	6.1	2.1		-4.4	2.0	
DTI-Setup	5.6 *5.2	1.2	**0.21** ***0.37**	-6.3 *-5.8	2.0	**0.68** ***0.50**

Table 24: Amplitudes of the pulsating flow pattern at flow rate Q ~233 µl/min. *According to the report D2.1.3, simulations have shown that the measured amplitudes of the pulsations are larger than the real ones by approximately 8 %. The amplitudes measured by DTI were corrected for this effect.

5.4.2 Syringe pump at Q ~ 0.9 ml/h (15.6 µl/min)

We summarize the measurements performed with the same syringe (wet marked).

5.4.2.1 Deviation of averaged flow rate at Q ~ 0.9 ml/h (15.6 µl/min)

The mean deviations determined by METAS and DTI are consistent within their uncertainties with an En-value of 0.88.

	Mean (%)	U mean (k=2) (%)	**En-value (< 1 !)**
METAS-Setup	-1.51	0.88	**0.84**
DTI-Setup	-0.05	1.52	

Table 25: Validation of averaged flow rate Q ~15.6 µl/min.

5.4.2.2 Periodicity of pulsating flow pattern at Q ~ 0.9 ml/h (15.6 µl/min)

The periodicity of pulsating flow pattern determined by METAS and DTI are consistent within their uncertainties with an En-value of 0.11 for the case of interval determination.
In the case of FFT Analysis, we get an En-value of 2.1. Looking closer at the 4 values of periodicity, we observe that the periodicity determined by means of FFT Analysis by DTI is much larger than the 3 other values.
However, a valid result of the FFT is not possible to obtain for this small flow rate due a limited measurement time (~ 3 hours), which only provides three peaks. This makes the uncertainty of the estimated periodicity by means of FFT large. In order to improve the performance FFT the measurement time have to be increased twofold of even more.

By means of FFT	Periodicity (s)	U (k=2) (s)	**En-value (< 1 !)**
METAS-Setup	3241.8	162.4	**2.10**
DTI-Setup	3587.8	26.0	

By means of interval determination	Periodicity (s)	U (k=2) (s)	**En-value (< 1 !)**
METAS-Setup	3205.3	284.8	**0.11**
DTI-Setup	3238.4	152.0	

Table 26: Periodicity of the pulsating flow pattern at flow rate Q ~15.6 µl/min.

5.4.2.3 Amplitude of pulsating flow pattern at Q ~ 0.9 ml/h (15.6 μl/min)

The amplitude of pulsating flow pattern determined by METAS and DTI are not consistent within their uncertainties with an En-value of 1.31. DTI determined a larger amplitude compared to the one of METAS and additionally the amplitude has increased compared to the amplitude determined by DTI at the flow rate of 233 μl/min. The reason for this might be the very noisy reference flow rate.

	Average of local maximas (%)	U(max) (%)	**En-value (< 1 !)**	Average of local minimas (%)	U(min) (%)	**En-value (< 1 !)**
METAS-Setup	5.7	3.1		-4.5	2.0	
DTI-Setup	8.5 *7.8	2.4	**0.71** **0.54**	-7.4 *-6.8	2.7	**0.86** **0.68**

Table 27: Amplitudes of the pulsating flow pattern at flow rate Q ~15.6 μl/min. *According to the report D2.1.3, simulations have shown that the measured amplitudes of the pulsations are larger than the real ones by approximately 8 %. The amplitudes measured by DTI were corrected for this effect.

5.4.3 Coriolis flow meter calibrated with pulsating flow generated by the syringe pump at Q ~ 14 ml/h (233 μl/min)

The mean deviations determined by METAS and DTI are consistent within their uncertainties with an En-value of 0.04 for the case of steady and pulsating flow at the METAS-Setup and with an En-value of 0.30 for the case of pulsating flow at the METAS-Setup and the DTI-Setup.

<table>
<tr><th></th><th>Flow type</th><th>Deviation (%)</th><th>U(%)</th><th colspan="2">En-value (< 1 !)</th></tr>
<tr><td>METAS-Setup</td><td>steady</td><td>0.06</td><td>0.12</td><td rowspan="2">0.04</td><td></td></tr>
<tr><td>METAS-Setup</td><td>pulsating</td><td>0.07</td><td>0.21</td><td rowspan="2">0.30</td></tr>
<tr><td>DTI-Setup</td><td>pulsating</td><td>-0.04</td><td>0.30</td><td></td></tr>
</table>

Table 28: deviations of the flow rates of the M12P using stable steady flow and pulsating flow

6 Conclusion

DTI and METAS have developed pulsating flow tester.
The METAS setup covers a flow rate range from 1 ml/min to 1 µl/min with uncertainties ranging from 0.2 % to 2.7 % depending on the flow rate and the fit window used.

The DTI setup covers a flow rate range from 1 ml/min to 17 µl/min with uncertainties ranging from 0.03 % to 1.5 % depending on the flow rate and the fit window used.

The validation of the pulsating flow tester showed consistency in the mean flow rates, the periodicity and the amplitudes of the pulsating flow.

It is worthwhile to mention at this point that the stated measurement uncertainties only correspond to the instantaneous flow rate determination and not to the periodicity and the amplitude of the pulsating flow. Nevertheless, the periodicity and the amplitude of the pulsating flow can be indicated as additional information where the uncertainty is taken only from the variation of the different values obtained from several series of measurements.

The instantaneous flow rate and the mean flow rate averaged over an integer value of full pulsation cycles are the only traceable results.