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Development of Smart Flow Regulation for Lab-on-a-Chip Applications

Master's thesis

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Nutika voolu reguleerimise seadme arendamine kiiplaborsüsteemide rakenduste jaoks

Magistritöö

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Author’s declaration

Hereby I declare that, the thesis has been done independently and it has not been submitted by anyone else. All used material from written literature, authors and other sources has been referred in this work.

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Abstract

In the field of flow chemistry, it is essential to have precise flow control. Lab-on-a-Chip (LoC) systems require controlling different liquids on a milliliter to microliter scale. Therefore, a pumping system consisting of a peristaltic pump, DC/DC converters, lithium-ion batteries, ESP32 DevkitC microcontroller and a 3D printed enclosure were designed and fabricated and tested. Into the system multiple pumps can be added; up to two slave pumps and each pump can be controlled through Wi-Fi AP separately through a common interface. The system is portable so it is possible to use it at the Point-of-Care or in the field.

The design involved choosing commercially available hardware and creating the schematics and 3D models for 3D printable parts. There were calculations and simulations done for the electrical concept. A user-friendly interface was developed.

The pump is controlled by using the PWM output of the microcontroller to control the pump control board threshold voltages to have a voltage control up to 12V. The pumping system was initially designed with closed-loop control. Because the designed flow sensor system did not give the expected results, the pump was open-loop controlled and was calibrated using water viscosity. The calibration process involved generating a specific characteristic curve (PWM vs. flow rate) for the pump.

In the end, a proof-of-concept experiment was done on LoC applications and new, optimized chip layouts were designed and simulated. Overall, the pumping system reached 12ml/min-72ml/min flow rate and was able to run for half an hour on battery at maximum flow rate. It is currently applicable in millifluidic applications and environments, where liquid does not get into touch with external parts. However, design improvements and recommendations for future development were proposed.

Thesis is written in English language and has 59 pages, 9 chapters, 28 drawings, 7 tables.

Annotatsioon

Mikrofluiidikas on oluline täpne vedeliku voolu juhtimine. Mikrofluiidika süsteemid või kiiplaborsüsteemid nõuvad erinevate vedelike voolu juhtimist mikroliiter skaalal. Sellepärast, töös arendati, valmistati ja testiti pumpamise süsteemi, mis koosneb peristaatilisest pumbast, alalisvoolu muunduritest, liitiumioon akudest, ESP32 DevkitC mikrokontrollerist ja 3D priditust korpusest. Süsteemi saab lisada mitmeid pumpasid kuni 2 lisa pumpa. Igat pumpa saab juhtida eraldi läbi Wi-Fi kasutades ühist kasutajaliidest.

Disain sisaldas endas riistvara valikut, mis on turul saadaval. Automaaika jooniste ja 3D mudelite loomises. Elektri kontseptsiooni simuleeriti ja arvutati läbi. Kasutajasõbralik liides arendati.

Pumpa juhitakse mikrokontrolleri pulsilaiusmodulatsiooniga, mis juhib pumba disainitud juhtelektroonikat, mis lubab juhtida pinget kuni 12 voldini. Pump on avatud tagasisidemega ja kalibreeriti vee tiheduse järgi. Protsess nõudis pumba jaoks spetsiifilise karakteristiku kõvera leidmist. Algul oli pump disainitusd suletud tagasiside süsteemina. Kuna voolu juthimise andurid ei töötanud nii nagu eeldati, siis need eemaldati lõplikus disainis.

Kontseptsiooni testidi kiiplaborsüsteemide rakendustel ja uus kiibi kavand disainiti. Disainis tehti uuendusi ja lisati soovitusi edaspidiseks arenduseks. Pumpamise süsteem arendas voolu kiirust 12ml/min-72ml/min. Lisaks sellele maksimaasel kiirusel suutis pump töötada pool tundi. Süsteemil on suur potentsiaal millifluiidika rakendustes ning keskkondades, kus vedelik ei puutu kokku välispindadega.

Lõputöö on kirjutatud ingliskeeles ning sisaldab teksti 59 leheküljel, 9 peatükki, 28 joonist, 7 tabelit.

List of abbreviations and terms

ADC	Analog to digital converter
AP	Access point
API	Application
BMS	Battery management system
CPU	Central processing unit
CSI	Camera Serial Interface
DAC	Digital to analog converter
DC	Direct current
DDS	Data distribution service
DSI	Digital Serial Interface
GPIO	General purpose output input
HMDI	High Definition Multimedia Interface
IJPEM	International Journal of Precision Engineering and Manufacturing
IJRET	International Journal of Research in Engineering and Technology
I2C	Inter-Integrated Circuit
IoT	Internet of Things
IR	Infrared
ID	Inside diameter
JTAG	Joint Test Action Group (hardware interface)
LAN	Local area network
LoC	Lab-on-a-Chip
MCU	Microcontroller unit
MIPI	Mobile Industry Processor Interface
MOSFET	Metal–oxide–semiconductor field-effect transistor
NI	No information
OD	Outside diameter
OSI	Open system interconnection

PC	Personal computer
PDMS	Polydimethylsiloxane
PoC	Point-of-care
PoE	Power over Ethernet
PWM	Pulse width modulation
RAM	Random Access Memory
SD	Secure Digital
SoC	State of Charge
SPI	Serial Peripheral Interface
UART	Universal asynchronous receiver-transmitter
USB	Universal Serial Bus
Wi-Fi	Wireless Fidelity

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1 Introduction

A Lab-on-a-Chip (LoC) is a miniaturized device that integrates into a single chip one or several analyses, which are usually done in a laboratory; analyses such as DNA sequencing or biochemical detection.[1] LoC research is focusing on several applications including human diagnostics, DNA analyses and synthesis of chemicals. The LoC field is relying on two core technologies: microfluidics and molecular biology.

LoC systems are consisting of microchannels where the liquid is being manipulated and biochemical reactions created. The reagents and fluid quantities can go from microliters down to picoliters. The system is requiring pumps, electrodes, valves, electrical fields.

Even though there is a lot of research being done the devices in the hospitals and which are available in the market are still quite large. Smaller and more compact applications are still expensive. And they are not so portable. The goal of the thesis was to research and develop a low-cost, open-source, portable peristaltic pump for Lab-on-a-Chip applications in the field.

The development involved electronics, mechanical and software design as well as experimental and simulated analyses of prototype design solutions.

1.1 Design requirements

Below are the initial requirements, which were taken into consideration when it came to designing the pumping system/module:

1. The size of the device: max 10cmx15cmx10cm
2. The flow rate: 1-100ml/min
3. Volume accuracy: 1%
4. Remote control: yes

5. Number of channels: 1

6. Voltage: 6V/12V

7. Tubing Silicone tubing, ID 1mm, OD 2mm

1.2 Objectives

The objective of this thesis is to develop a low cost, open-source, portable smart flow regulation system for droplet generation applications and on the field diagnosis.

The development involved:

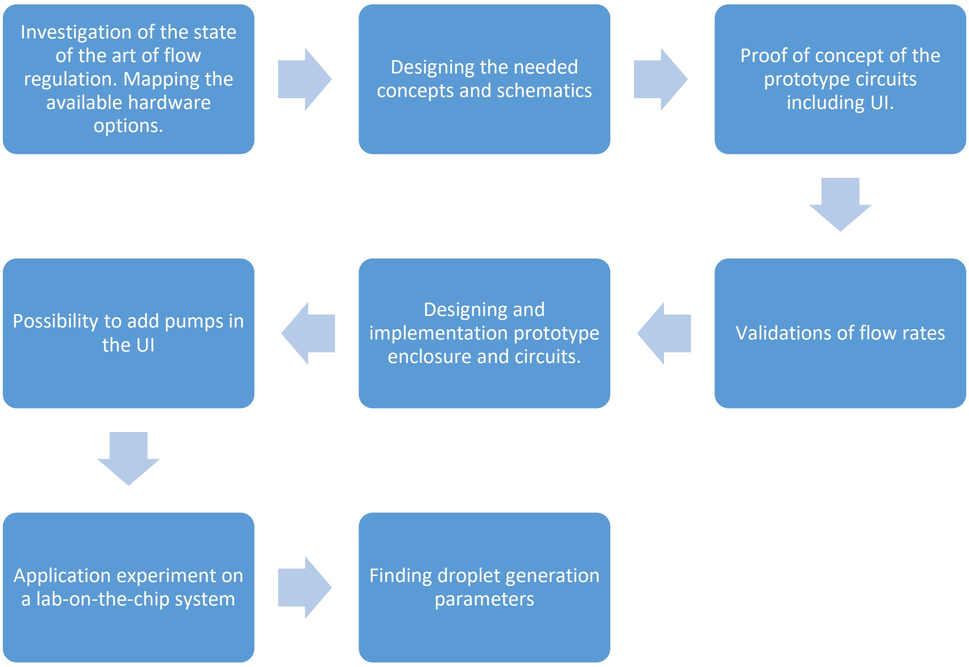

Figure 1.Development flow

2 State of the art

In this chapter was researched the possibilities and hardware for designing the pumping system. Different pump working principles and research papers were analyzed. Different sensors having a closed loop feedback system were taken into account. Then a brief overview of batteries and microcontrollers were done.

2.1 Pumps

This chapter is looking into different pumps which are available in the market. As described in "Fundamentals and applications in microfluidics" book [2] then the pumps are being divided into two big categories. To mechanical pumps and to nonmechanical pumps, this can be seen in Figure 2. There are two sub-categories to mechanical pumps: displacement pumps and dynamic pumps. In displacement pumps the energy is used in one or in more movable boundaries for the pressure increase of chambers which by so achieves the liquid movement. For example, check-valve pumps, peristaltic pumps, valveless rectification pumps, and rotary pumps work so. Normally the flow rate in microscale for these pumps are 1-10 ml/min.

In the dynamic pumps the energy is used for increasing fluid velocity in the machine. Higher velocity increases pressure on the outlet. For example, centrifugal pumps and ultrasonic pumps. The flow rate for these pumps are 10ul/min

In the nonmechanical pumps another nonmechanical energy is converted into kinetic energy. When mechanical pumps are used in macroscale and large size and high flow rates then nonmechanical pumps are more used in microscale. The flow rate is 10ul/min. For example, electrohydrodynamic, electrokinetic, magnetohydrodynamic pumps.

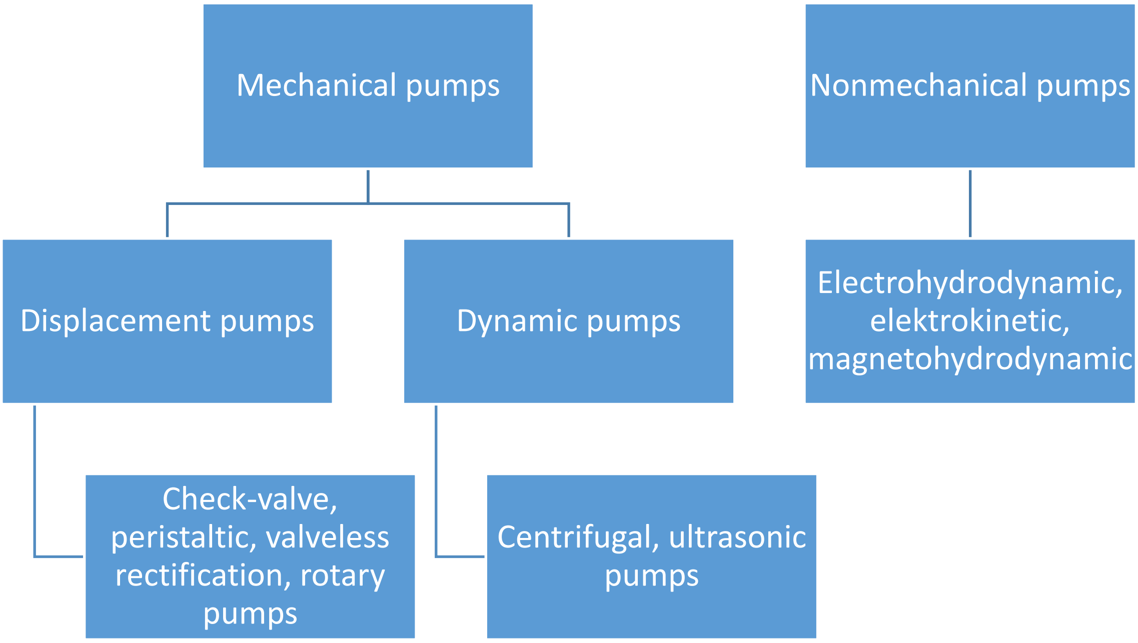

Figure 2. Pump classification

From Louisiana State University a research group investigated a micro-cam actuated linear peristaltic pump for microfluidic applications.[3] They fabricated the pump using 3D printing technology. A maximum flow rate of 274 ul/min was achieved, where the back pressure was 36 kPa.

In 2020 American Control conference in Denver a research group presented the possibilities to model, identify and control flow for a microfluidic device using a peristaltic pump.[4] The system involved a DC peristaltic pump with a feedback loop using a pressure sensor. It demonstrated that a response rate under 1ms can be achieved for adjusting the pressure of the system.

In 2020 Scientific Reports was discussed about an open-source, 3D printed peristaltic pumps for small volume point-of-care liquid handling.[5] In this paper a 3D printed peristaltic pump was built, which cost 65$. The total system was twice of the pump cost – 120$. To drive the pump a stepper motor was used. Design had an Arduino microcontroller, DC converters and stepper motor drives. The flow rate was 0,46 ml/min for tubing ID 0,79 and for tubing ID 1mm 1,62ml/min.

Diaphragm pumps

A diaphragm pump is a positive displacement pump. It is also called as a membrane pump. These pumps are widely used to handle a wide range of fluids in many industries.

They can be used for high, low and medium viscosity fluids and also for acids as depending on materials used in the pump.[6]

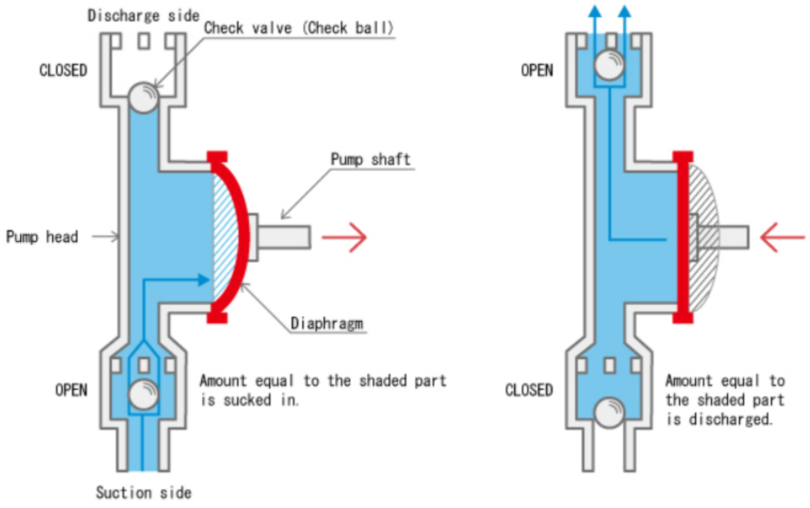

Figure 3. Structural diagram of the pump head of a diaphragm dump [7]

In the Figure 3 the diaphragm pump can be seen. The head has two check valves. One in the suction side and one in the discharge side. When the pump shaft (diaphragm) is being pulled outwards then the check valve on the suction side opens and the liquid is coming inside. When the diaphragm is pushed in then in the suction side the check valve closes and discharge check valves opens and liquid goes outside.

Table 1. In the market available diaphragm pumps.

	Cole-Parmer[1]	Bartels Mikrotechnik[2]	SMC[3]
Price [€]	285,75	NI	NI
Flow rate [ml/min]	0,055-38	4, 6	5uL up to 200ul
Remote control	no	no	no
Tubing OD [mm]	6,35	1,9	NI
Voltage [V]	24 DC	220 AC	12 DC
Power [mW]	NI	50	NI

[1]https://www.coleparmer.com/i/dc-powered-diaphragm-pump-24-vdc-4-20-ma-proportional/7420113

[2] https://www.bartels-mikrotechnik.de/wp-content/uploads/simple-file-list/EN/Manuals-and-Data-Sheets/DE_EN_comparison_charts_micropumps.pdf

[3] https://content2.smcetech.com/pdf/LSP.pdf

The diaphragm of the pump head can be differently actuated. There are air operated diaphragm pumps, motor driven diaphragm pumps and Wanner hydra-cell pumps.[6]

In Table 1 can be seen some diaphragm pumps which are available in the market. The diaphragm pumps can vary in flow rates. For controlling the pump, it depends on the actuator of the pump head.

While doing research then nowadays aren't talked so much about diaphragm pumps rather more about the piezoelectric pumps. It is because it's not so popular anymore to drive these pumps with pneumatic actuators or with motors. For example, articles about diaphragm pumps are actual in late 90s or early beginning of 2000s. An article in 2000 was published about "A check-calved silicone diaphragm pump"[8], where the actuator was pneumatic and was talked about diaphragm pump. After that is talked more about piezoelectric pumps, where the actuator is an electromagnet and the diaphragms are just mention as a contractual element.

Piezoelectric pumps

Piezoelectric pump is a type of diaphragm pump. A piezoelectric actuator is used for the pumps. The functional principle of piezoelectric pump involves control of the pump diaphragm. By applying voltage, the membrane is formed and deformed. The resulting down stroke is pushing out the liquid from the chamber. The check valves on the side of chambers define flow direction. In Figure 4 Bartels Mikrotechnik double diaphragm piezoelectric pump can be seen. [9]

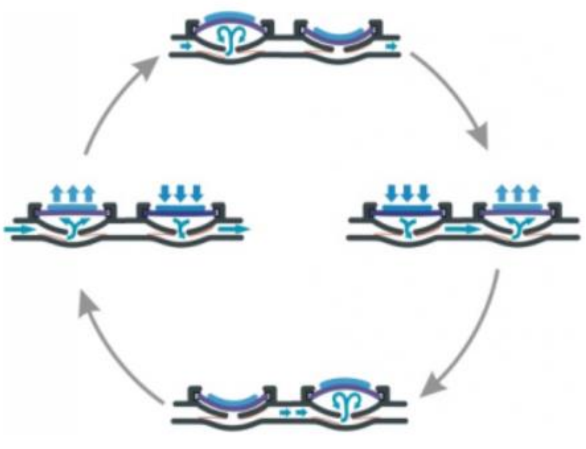

Figure 4.Functional principle of Bartels Mikrotechnik double piezoelectric micropump[9]

In the Table 2 a comparison of piezoelectric pumps can be seen, which are available in the market. Different pump sizes have different flow rate characteristics. A flow rate up to 20ml/min can be achieved. Because the manipulation of the diaphragm involves alternating current then a controller is needed to generate it. The companies offer controllers as well, but then the overall expense is adding up for the pumping system.

Table 2. In the market available piezoelectric pumps

	Dolomite	Takasago	Bartels mikrotechnik
Price [€]	380	78-152	249[1]
Flow rate [ml/min]	3,7,20	3,7,15,20	6,7, 20
Remote control	No	No	No
Tubing ID [mm]	0,6, 1,2, 1,8	0,6, 1,2, 1,3, 2,1, 1,8	1,77, 1,85
Voltage [Vp-p]	60-250	60-340	250
Frequency [Hz]	10-60	10-60	100
Power [mW]	47,76	NI	50

The sizes of the pumps are quite small. The piezoelectric pumps can be used in many ways in medical and analytical technology, mechanical engineering, space research and in many other applications.[9]

In 2017 Scientific reports was published “a controllable and integrated pump-enabled microfluidic chip and its application in droplets generating”[11] research article. In there was investigated and demonstrated the piezoelectric pump as a valid solution for droplet generation. A flow rate of 0-300 ul/min was achieved.

[1] On the table the Bartels Mikrotechnik price is for the mp6-basic set, which consists of 3 mp6 pumps, controller board and tubing.[10]

Peristaltic pumps

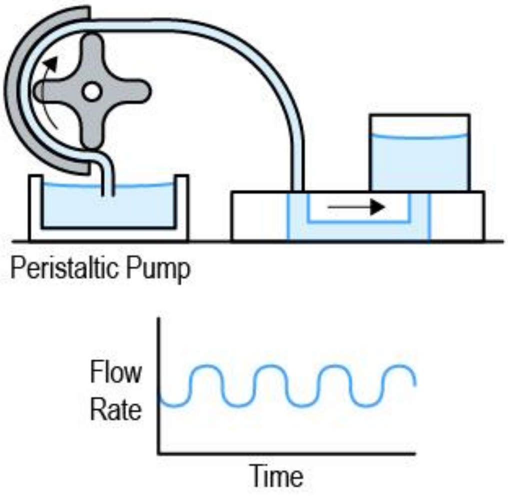

Figure 5. Peristaltic pump working principle[12]

Peristaltic pump is based on the compression and the relaxation of flexible tubing. [13] Vacuum is created in the tubing by the roller inside of the pump. This is inexpensive method and it is used in microfluidic laboratories. The working principle can be seen in Figure 5. The disadvantages are that the compression of tubing is creating pulses in the flow which is not suitable for most microfluidic applications where the flow precision is important. To avoid damage the tubing is regularly needed to be changed.

In the Table 3 can be seen that peristaltic pumps can achieve higher flow rates up to 100ml/min. Overall the flow rate depends on the pump tubing and what kind of motor is used for driving the pump. In many pumps DC motors are used, but there are pumps with stepper motors also. Dolomite peristaltic pump is using a DC motor and it is really small. It can achieve microliter flow rates.

Table 3. In the market available peristaltic pumps.

	Dolomite[1]	Cole-Parmer[2]	INTLLAB[3]	No brand on eBay[4]
Price [€]	190	732-795	5,73	4,91
Flow rate [ml/min]	0,45	0,002-43	2-100	11-80
Remote control	no	yes	no	no
Tubing ID [mm]	OD 2,5, ID 1,5	0.19, 0.25, 0.51, 0.89, 1.14, 1.42, 2.06, and 2.79	1, 2, 3	1,2,3
Voltage [V]	3 DC	230 AC	12 DC	12 DC
Power [W]	0,13	90-260 VAC	4,8	NI

Cole Parmer had more expensive pumps. In the market can be found inexpensive pumps with dc motors also. For example, Broading Shenchen precision pumps are 13€-35€ and different tubing and motors can be ordered. So it is possible to get pumps for flow rates 14ml/min up to 150ml/min.[14] These pumps are a little bit more bigger and might be little bit bulky for handheld devices, but still usable.

In the thesis was an Adafruit peristaltic pump chosen, mainly because it was cheap. In the design process was taken into account that a flow rate of 100ml/min should be achieved. It’s also simple to control DC motors.
A positive point is when the pump is working then liquid is not in touch of the moving parts of the pump. A negative side is that the flow is pulsating and is not fully laminar.

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[1] https://www.dolomite-microfluidics.com/product/peristaltic-pump/

[2] https://www.coleparmer.com/p/masterflex-c-l-analog-variable-speed-pump-systems-with-single-channel-pump-head/49284

[3] https://www.alibaba.com/product-detail/INTLLAB-2-17-mL-min-DC_62251903929.html?spm=a2700.shop_pl.41413.23.4cad59d5BK79Bo

[4] https://www.ebay.com/b/Other-Industrial-Pumps/46547/bn_16563447

In the 2020 American control conference paper hold in Denver was used the same pump from Adafruit.[4]
The design of the peristaltic pump is still actual and research is being done to make it better, smaller and more precise. In 2017 IJPEM was 3D printed a peristaltic minipump. It achieved 40-230 ml/min flow rate and it was able to work even with backpressure as high as 25 kPa.[15] In 2020 Research gate was also 3D printed a peristaltic pump which demonstrated flowrates from microliter scale up to 2ml/min depending on tubing.[5]

Syringe pump

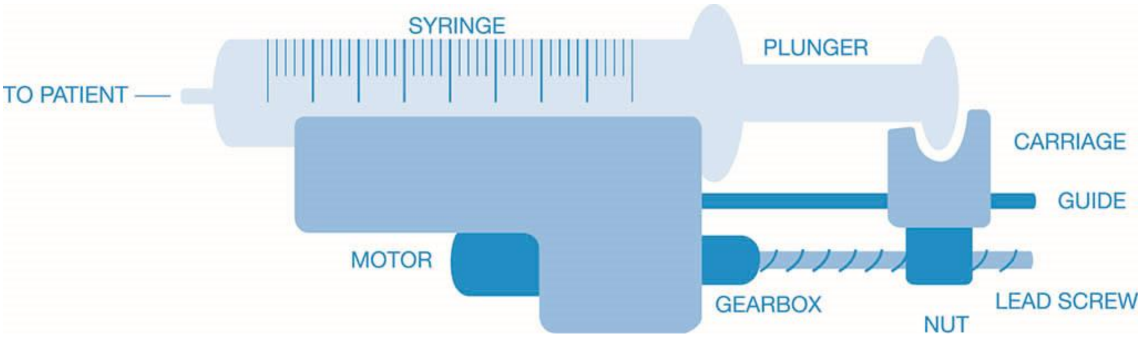

Figure 6. Syringe pump structural concept[16]

Syringe pumps are most commonly used in microfluidics.[13] The syringe piston is controlled by a motor by pushing and pulling the piston. In the Figure 6 the structural concept of the syringe pump can be seen.

There are two categories of syringe pumps. Syringe pumps which are quite inexpensive which generate flow oscillations in microfluidics. And pulseless microfluidic pumps. The main disadvantage is the responsiveness of the pump and that the fluid dispensed in the pump is limited volume.

In 2016 Chemical Education[17] an inexpensive open-source pump was constructed. It costed roughly 100$ with the controllers. There were two syringes and they could be controlled independently.

In 2019 eNeuro journal an open source syringe pump was constructed. [18] In the system was used 3D printed parts, stepper motor, a PCB for control, OLED display. The pump demonstrated microliter fluid control and the cost was below 250$.

Pressure pump

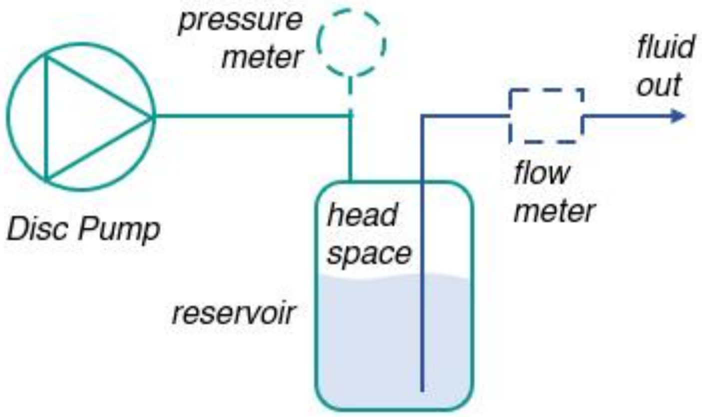

Figure 7. Microfluidic system with pressure pump[19]

In pressure pump the sample is pressurized inside the tank. This is good when it is needed to have responsiveness and stability in the system. In Figure 7 can be seen the structural diagram of microfluidic system, where the sample gets pressurized in a tank. There is no delay in the flow and flows are smooth in despite of the different flow rates. Only disadvantage might be that when the pressure is unbalanced then it is possible to have back flows when using flow switches with multiple inputs. [13]

In 2011 “A portable pressure pump for microfluidic Lab-on-a-Chip systems using a porous PDMS sponge”[20] paper was published. In there was discussed how a porous PDMS sponge can be used as a pressure pump. The idea is that it’s inexpensive and can work as a microfilter as well. In the paper wasn’t discussed about the flow rates rather more about the sponge compression rate.

In 2016 Technical Note was presented a fully-programmable pressure source, which was low-cost and could be used in microfluidic applications.[21] The system tested two pressure sensors. PD23 pressure sensor from Keller and Flow sensor 0182 from Gesim. The sensors were mounted on Wago 750-468 fieldbus and pressure was controlled from 0mbar to 1000mbar with 25mbar step. The results were compared to commercially available pressure pump AF1 from Elveflow. Furthermore, they demonstrated the possibility of the designed system to be used in droplet generation application.

Commercially available pumping systems

Cole-Parmer

Cole-Parmer is offering low flow peristaltic pumps, which can run dry without damage to pump and flow rates from 0,03 to 4ml/min. The prices range from 47-345€.[22]

Cole-Parmer is offering pump systems, where the flow rate can vary from 0,005 to 600 ml/min these are varying from 312-540€.[13]

Cole-Parmer offers Ismatec multi-channel pumping systems also. They can be PC controlled and the flow rate can vary, which range from 1,7k -6,2k€.[23]

ElveFlow

ElveFlow is offering multichannel pressure and vacuum controllers, single channel autonomous pumps, different valves, flow and pressure sensors and even bubble detectors.

In the pressure pumps the input pressure is 1,5-10 bar and the output pressure ranges from 0 to 6000 mbars.[22]

Dolomite

Dolomite is also providing different pumping solutions. Mitos pressure pump solution is 5000€ [24]. Dolomite peristaltic pump is costing 190€. Flow rate is 0,45ml/min and 0,12W power. Mainly I was looking for flow sensors and the Dolomite ones are from nanoliter scale to milliliter scale. They are fast and accurate and cost 1600€.

To sum up, then full pumping solutions for various low flow rate applications are quite expensive. In the market is room for cheaper solutions.

Open-source pumping systems

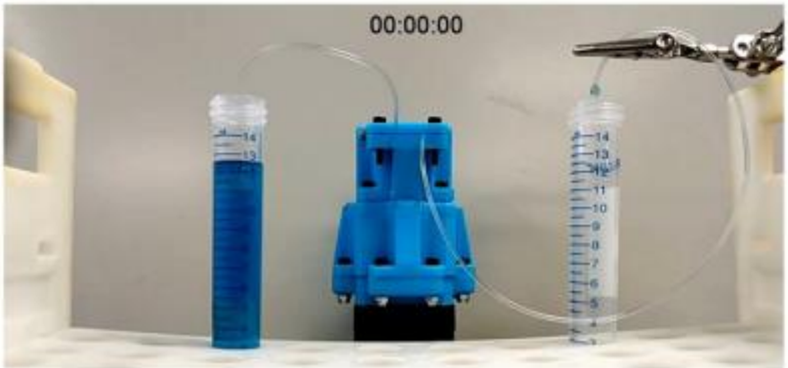

Figure 8. 3D printed peristaltic pump.

In 2020 Scientific report[5] the 3D peristaltic pump solution cost was 120$. In the Figure 8 can be seen the printed peristaltic pump. In the system was used also NEMA-17 stepper motor, Arduino microcontroller, stepper drive and power supply.

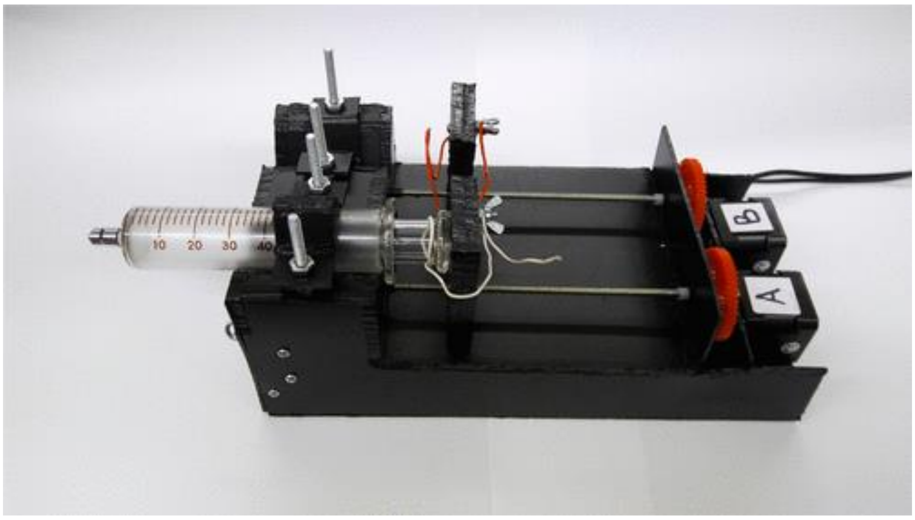

Figure 9. Dual syringe pump

In 2016 Chemical Education[17] the syringe pump solution was costing 100$. This can be seen in Figure 9. Because the article is needed to be purchased then deeper knowledge about the system wasn't researched.

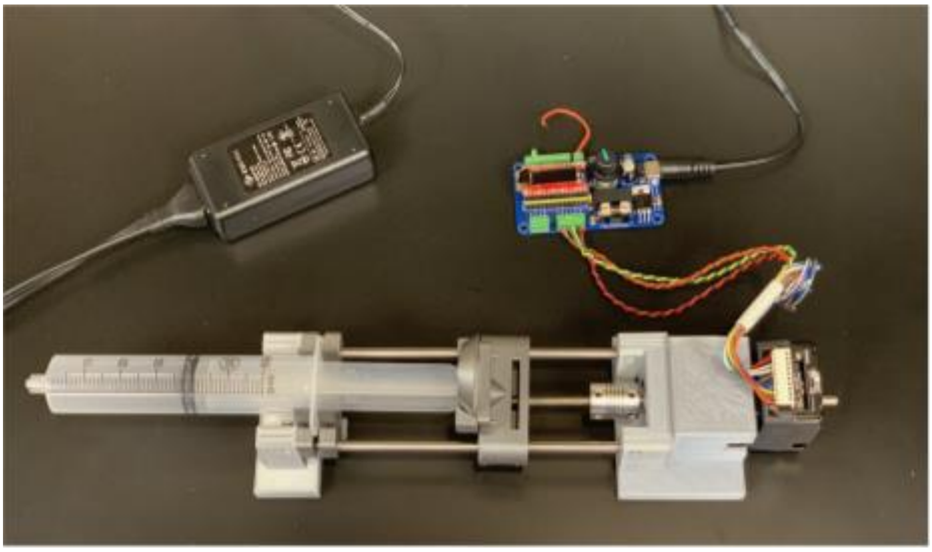

Figure 10. Syringe pump setup

In Figure 10 can be seen eNeuro syringe pump setup.[18] The system is consisting of 60ml syringe, 3D printed holder, NEMA-17 stepper motor and drive, pump controller and 15V power supply. The total cost was below 250$.

When we are talking about the open-source solutions then the cost is mainly the hardware cost. Into the cost isn't taking account the design, coding and developing hours which normally the commercial solutions do. Therefore, the cost is cheaper than the commercial offerings.

2.2 Flow sensors and valves

In designing process was considered that the pumping system should have a closed looped feedback control. Pressure or flow rate should be monitored and the system can automatically adjust the pumping flow rate for different liquids.

Liquid flow meters are compulsory elements of microfluidic systems requiring a control of the sample volume dispensed and obviously the sample flow rate. Many liquid flow meters have been developed for large scale industries like food and beverage, pharmaceuticals or oil and gas companies. Microfluidics require rather high accuracy low flow liquid flow meters for the microliters and nanoliters per minute range.[25]

Differential pressure low flow liquid flow meters

These low flow liquid flow meters are based on Bernoulli's laws from fluid mechanics stating that flow velocity variations are correlated with pressure drops. Thus, by adding restrictions within the fluid channel, the increased velocity along the restriction induces a pressure drop measured with connected pressure sensors and then correlated with flow velocity and consequently flow rate.[25]

Vortex flow meter

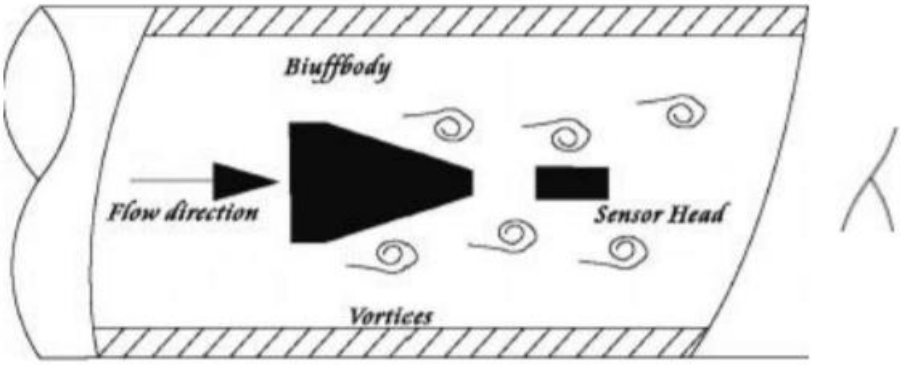

Figure 11. Vortex flow meter working principle[26]

Vortex flow sensors use a bluff body through a sample flow. Can be seen in Figure 11. This obstacle creates vortexes right behind it and alternatively from each of its sides. The frequency of these alternating vortexes is correlated to the flow velocity and measured thanks to a mechanical piezoelectric sensor or an ultrasonic beam placed in the vortexes path. For low flow rate ranges, vortexes may be too weak to be detected. In this case, a channel restriction may be needed to increase flow section and thus velocity. Like with differential pressure low flow liquid flow meters, this kind of set-up can be so complicated for versatile applications of vortex flow sensors and notably microfluidics using already narrow channels. Vortex flow sensors are rather adapted to the industrial handling of very large volume since its minimal flow rate range remains around several liters per minute.[25]. In the 2020 Automation, Telemechanization and Communication and Oil Industry journal was an article about the vortex flow meter.[27] Operational ranges of DYMETIC-1261 flow meter were discussed. K.Muzipov. described the technical characteristics and applicable scope. Because it's for oil industry and for high flow rates and isn't suitable for microfluidics then the research wasn't going into the article deeper.

Ultrasonic flow meter

This technology uses the fact that ultrasonic sound waves propagate faster in the flow direction than in it's opposite direction. Sensors are called often time-of-flight ultrasonic flow sensors or transmit-times ultrasonic flow sensors.[25] In the sensor are ultrasonic transducers and reflectors. They are placed so that the ultrasonic pulses will be propagated in the flow direction and in its opposite way. The ultrasonic pulses propagated in the flow direction accelerate while the ones propagated in the opposite direction are slowed down. The differential times of these ultrasonic signals are proportional to the fluid velocity.[25]

One main advantage of the sensor is that they can be used by avoiding any contact with samples. They can be used for very large flow volume 4m diameter tube. [25] The disadvantage is that they are very sensitive for air bubbles in the liquid and the flow must be laminar to avoid any acoustic dispersion.[25] In the 2013 Ultrasonics Journal[28] was proposed a methodology for different viscous fluids to use ultrasonic transducers.

Electromagnetic flow sensors

The idea of electromagnetic flow sensors comes from the principle that moving liquids generate low electromagnetic field. The faster the liquid moves the stronger is the electromagnetic field. During the thesis there were considered some hall sensors, but because there are papers of it and no real practical application then the design of a flow sensor was out of scope from this thesis. Also infrared sensors where tested to calculate the initial flow rate. Because the flow is pulsating then these sensors can be used for bubble detection. In 2014 IJRET was published a Raspberry pi based liquid flow monitoring and control[29] paper. In there was a Hall Effect sensor for the flow used.

Pressure Sensors

Pressure sensors should be mounted in the tube for directly measuring the pressure. Because the pressure sensors are coming with contact with the liquid then they weren't really considered. In the 2020 American conference paper [4] was used an Honeywell pressure sensor for control.

Solenoid valves

In designing the system there was briefly taken a look about solenoid valves. Solenoid valves could have been good for protection against back pressure or stopping the liquid in the tubing coming out. There are several companies offering solenoid valves for liquids, for example Darwin microfluidics offers 2-way normally closed and normal open valves and 3-way valves. Price was 299€.[30] Burkert fluid control systems also offer solenoid valves for liquids, but a price request should be done.[31] Overall because the solenoid valves added complexity into the system and they were expensive, therefore they were excluded from the design.

2.3 Microcontrollers

The variety of microcontrollers in the market is large. The most known companies are Arduino, Texas Instruments, Espressif systems, Raspberry Pi and there are more. In choosing the microcontroller was considered that the device which should be built, should have remote control via Bluetooth or Wi-Fi. It should have couple of inputs for flow and pressure sensors and outputs to control the pump directly or via driver or transistors. Below is a comparison table of the controllers.

Table 4. Comparison table of microcontrollers

	Arduino[1]	Texas Instruments[2]	Espressif systems[3]	Raspberry Pi[4]
Model	ARDUINO NANO 33 IOT	CC3200-LAUNCHXL	ESP32 DevkitC	Raspberry Pi 4
Cost [€]	16	24,51	14	29-62
CPU	SAMD21 Cortex®-M0+ 32bit low power ARM MCU	SimpleLink™ 32-bit Arm Cortex-M4	32-bit ESP-WROOM-32	BCM2711 ARM,64-bit Quad core Cortex-A72 (ARM v8)
SPI flash	256KB	1MB	4MB	4 MB
RAM	32KB	256KB	520KB	2GB,4GB, 8GB
ROM	-	-	448KB	-
Interfaces	Micro-USB	JTAG, SWD, micro-USB	SD card, micro-USB	USB 3.0, USB 2.0, micro-HDMI, MIPI DSI,

[1] https://store.arduino.cc/arduino-nano-33-iot

[2] https://www.ti.com/tool/CC3200-LAUNCHXL#description

[3] https://www.espressif.com/en/products/devkits/esp32-devkitc

[4] https://www.raspberrypi.org/products/raspberry-pi-4-model-b/specifications/

				MIPI CSI, 4-pole stereo audio and composite video port, Micro-SD, PoE
Interfaces	UART, SPI, I2C, ADC, DAC, External inerrupts, IMU	UART, SPI, I2C, McASP, SD/MMC, watchdog timer, ADC, Hardware crypto engine AES, DES, 3DES, SHA2, MD5 CRC and Ckecksum	UART, SPI, SDIO, I2C, PWM, I2S, IR, pulse counter, GPIO, capacitive touch sensor, ADC, DAC	UART, SPI, I2C, PWM, I2S, GPIO, ADC, DAC
GPIOs	14pins	27 pins	26 pins	28pins
DAC	1pin	4 pins	2 pins	4pins
Wireless communication	802.11b/g/n 2,4GHz	802.11b/g/n 2,4GHz and 5GHz	802.11b/g/n 2,4GHz, Bluetooth V4.2 BR/EDR, Bluetooth LE	802.11a/c wireless 2.4 GHz and 5.0 GHz, Bluetooth 5.0, BLE
External power	Up to 21V	5V or 3,3V-2,3V	5V or 3,6V-3V	5V or 3,3V

Espressif systems is offering ESP32 DevkitC[32] microcontroller which is quite cheap.

ESP32 has Wi-Fi, Bluetooth low energy, Bluetooth classic. Power consumption is low 2.2-3.6V so it can run on a battery. The controller has several configurable digital and analog inputs and outputs. And it can be programmed with Arduino IDE or with Espressif system own IDE. Because Arduino IDE has a lot of open-source projects then that was used for programming. In the 2020 American conference paper was used a Raspberry Pi microcontroller.[4] In 2014 IJRT [29] paper was also a Raspberry Pi controller used. In there it was acting as a web server. Instead of Wi-Fi they used LAN.

2.4 Battery

In the market there are 3.7 Li-ion 18650 and 1,5V alkaline batteries. Because the trend is going toward lithium batteries then the pumping system will use them as well.

In the system was used two Li-ion batteries in parallel to get the capacity up, which makes the device to run longer. The battery capacities are different but the most reliable and biggest one is now 3500mAh lithium-ion batteries.
For powering the microcontroller 3,3V was needed. A step down converter was used to power the microcontroller. The pump requires different voltage to run. The easiest and cheapest was to use an opamp, a MOSFET, 12V step up converter and a microcontroller PWM output to drive the pump.

In the 2017 Renewable and sustainable energy reviews [33] was talked about the lithium-ion batteries. How complicated it is to have the SOC (State of Charge) and have proper models for the deration process of the batteries.

3 System design

The hardware which was used for one pumping system is as follows:

1. ESP32 DevkitC microcontroller
2. Adafruit peristaltic pump 12V with 3mm tubing, 1mm tubing, 3D printed converters
3. 2 Panasonic NCR18650B lithium-ion batteries and battery holder
4. LM2596 step down DC/DC converter
5. LM2577 step up DC/DC converter
6. Prototyping board, 1N4007 rectifier diode, 2 1k resistors, 10k resistor, LMC7101 opamp, IRF520N MOSFET.
7. ON/OFF button
8. Female and male headers
9. Wires

10. Bolts and nuts

11. 3D printed enclosure

The price for the hardware was from 95€ to 105€. The pumping system is quite inexpensive. It is possible to do some cost reduction with wire costs and circuit design. For the prototype the initial price was good.

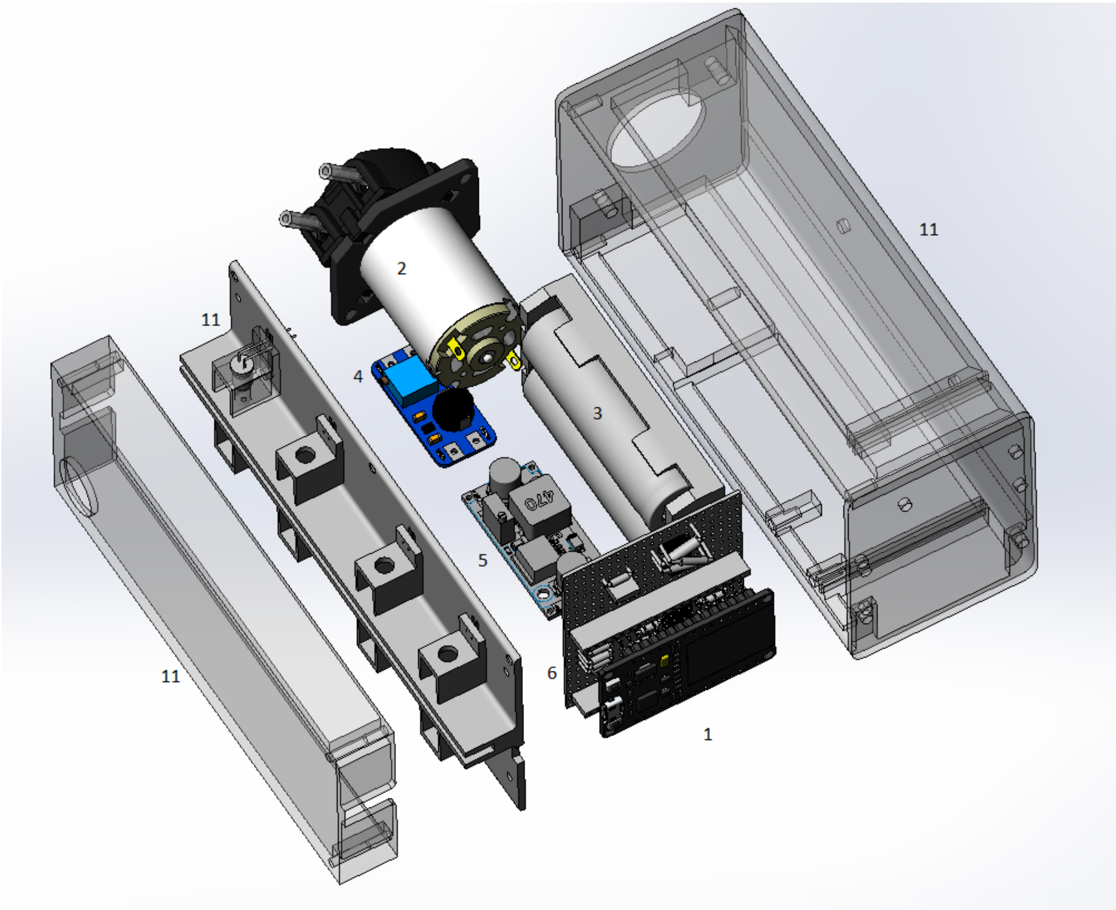

Figure 12. SolidWorks prototype. Shows the enclosure and components used

In the Figure 12 can be seen the hardware layout, how everything should come together. The layout was created with SolidWorks. Because it's hard to print full enclosure then during the design it was considered that each part of the case should be printable. So, the enclosure consisted of multiple parts which were assembled together.

Then, when the assembly started, there were some design errors, but they could be solved by drilling holes in the enclosure and cutting parts out with the knife. The enclosure was printed out of PLA and it was quite soft. So, by designing holes a little bit tighter the bolts threaded themselves inside and fewer nuts were used.

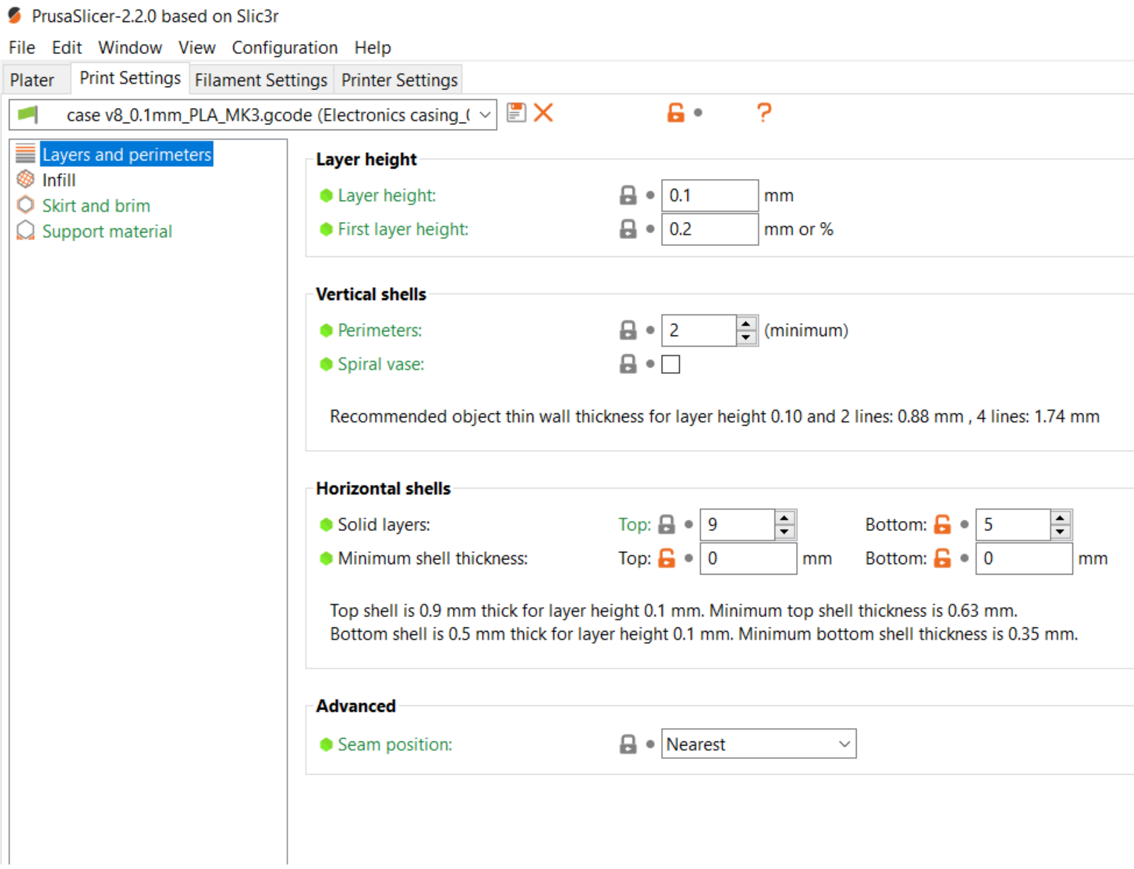

Figure 13. PrusaSlicer printing settings

The printing itself took place in TalTech University and a Prusa i3 MK3 printer was used. It is important to have the correct printing settings otherwise the printing quality and the filament flow is not good and give bad prints or no prints at all. For creation of the printable files PrusaSlicer was used and the settings were imported from a model, which was on the SD card.

In the Figure 13 the printing settings for layers and parameters can be seen. For Infill was used 10% fill density and fill pattern was grid. For top and bottom fill recliner pattern was used. Under the skirt and brim tab the distance from object was 2mm and the prim width was 0. Under support material auto generated supports were selected. In the filament settings tab under filament the diameter for the filament was 1.75mm and density 1.2 g/cm^3. The cost was 24,99€/kg. The temperature for extruder was 215 and bed temperature 60. Cooling was always on. In the printer settings tab under extruder 1 the nozzle diameter was 0.4mm and the retraction length was 0.8mm and lift Z was 0.6mm.

3.1 Electrical circuit diagram

In appendix chapter 9.2 the whole automation drawing is added. A simplified block diagram is as follows:

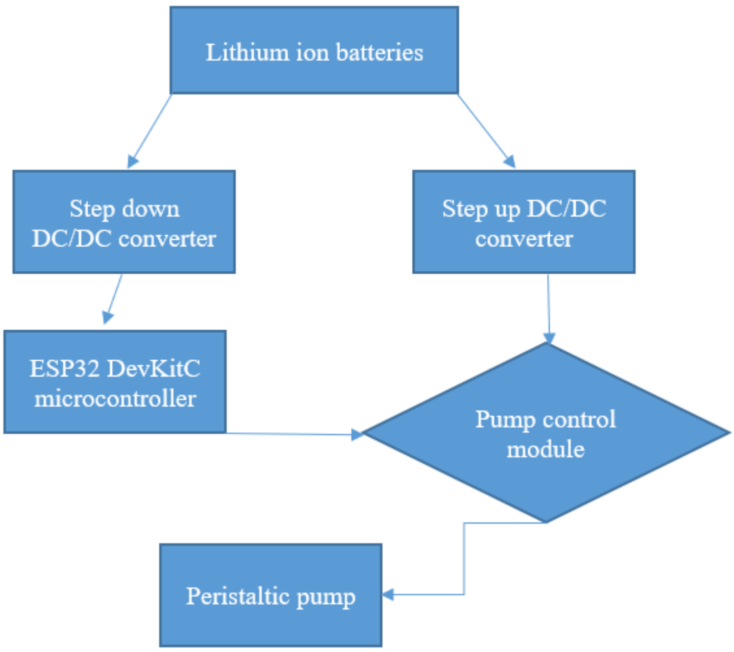

Figure 14. Electrical flow chart, describes power distribution and control

For pump control a MOSFET circuitry with an operational amplifier was designed. In the market DC motor drivers are available as well. Because the plan was to control the pump with pulse width modulation then it was simpler to custom design the circuit. In the end the pump was controlled by the MOSFET with different gate threshold voltages by using the analog output of the microcontroller.

3.2 Power calculations

In the data sheet of ESP32 DevkitC is said that the power supply for ESP32 should apply at least 500mA or more. The LMT2596 DC/DC step down converters efficiency is 92%.

ESP32 power consumption without losses is:

$$P = UI = 3{,}3V * 0{,}5A = 1{,}65W$$

Taking account, the conversion losses then, ESP32 power consumption is:

$$P_{withloss} = P * \frac{100}{ef} = 1{,}65W * \frac{100}{92} = 1{,}75W$$

The LM2577 step up module efficiency varies depending on the load. The worst-case efficiency is 72%. The peristaltic pump current consumption is 300mA on 12V. When not taking into account the pump control module consumption then the peristaltic pump consumes:

$$P = UI = 12V * 0{,}3A = 3{,}6W$$

$$P_{withloss} = P * \frac{100}{ef} = 3{,}6W * \frac{100}{72} = 5W$$

Total consumption is:

$$P_{total} = 1{,}75 + 5 = 6{,}75W$$

Let’s calculate how long the pump can run on the batteries. Lithium-ion battery voltage is 3,7V and the capacity is 3400mAh. Using the batteries in parallel then the capacity is 6800mAh. The power capacity is:

$$P_t = 6{,}8 * 3{,}7 = 25{,}6Wh$$

The pump running time on batteries is:

$$t = \frac{25{,}6}{6{,}75} = 3{,}79h$$

Let’s calculate if there is a heatsink needed for the MOSFET.

For IRF520N on resistance the datasheet says that Rds(ON) = 0,2 Ohm. When the pump consumes Id = 0,3A. Then the power what the MOSFET consumes when it’s on is:

$$Pd = I^2 * R_{ds(ON)} = 0{,}3^2 * 0{,}2 = 0{,}018W$$

The maximum power what the MOSFET can dissipate in the ambient temperature is:

$$P_{jmax} = \frac{T_{jmax} - Ta}{R_{thetaJA}} = \frac{175 - 25}{62} = 2{,}42W$$

Where Tjmax is the maximum operating junction temperature of IRF520N and RthetaJA is the junction to ambient thermal resistance from the data sheet. From the calculation can be seen that no heatsink is needed because calculated Pjmax is higher than Pd.

3.3 Pump simulations

For the simulation a motor equivalent circuit was used.

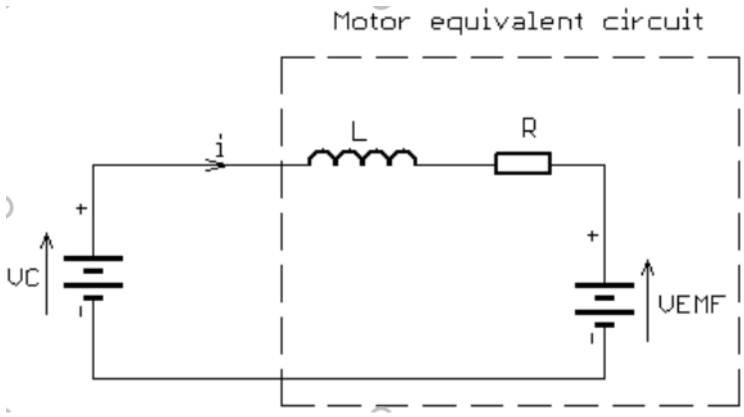

Figure 15. Motor equivalent circuit

In the Figure 15 is a DC motor equivalent circuit diagram.

We know that:

U=12V
I=300mA
R=40 Ohm

For simulating the characteristics when the motor is powered, we need to find out the motor winding inductance. For that there were estimates done.

$$R = Q_{CU} * \frac{I}{A} \rightarrow I = R * A/Q_{Cu}$$

Where QCu is for copper 1,67*10^-8 ohm/m. The formula for inductance is:

$$L = N * \frac{fi}{l}$$

Where N is the number of turns in the coil, fi is the magnetic flux in webers. The flux can be calculated:

$$fi = \frac{NIA}{l}$$

Where l is the length of the wire in the coil in meters.

So, when using the formulas then:

$$L = N^2 * \frac{A}{l} = N^2 * \frac{A}{R * \frac{A}{Q_{Cu}}} = N^2 * \frac{Q_{Cu}}{R}$$

We do not know; how many turns the motor winding has. Let's suppose N=500, then

$$L = 500^2 * 1{,}67 * \frac{10^{-8}}{40} = 10437{,}5 * 10^{-8} = 104{,}4 * 10^{-6} = 104{,}4\ uH$$

The IRF520N MOSFET gate source threshold voltages are from 2V to 4V. With different voltages the MOSFET is letting through different amount of current. Because ESP32 analog output isn't giving out 4V then we can't switch the MOSFET fully open. Therefore, an operational amplifier was used to control the MOSFET.

In Figure 16 can be seen a Multisim diagram. In simulations was used 2N7000G MOSFET which has gate source threshold from 0.8 up to 3V and is a little different from the pumping system.

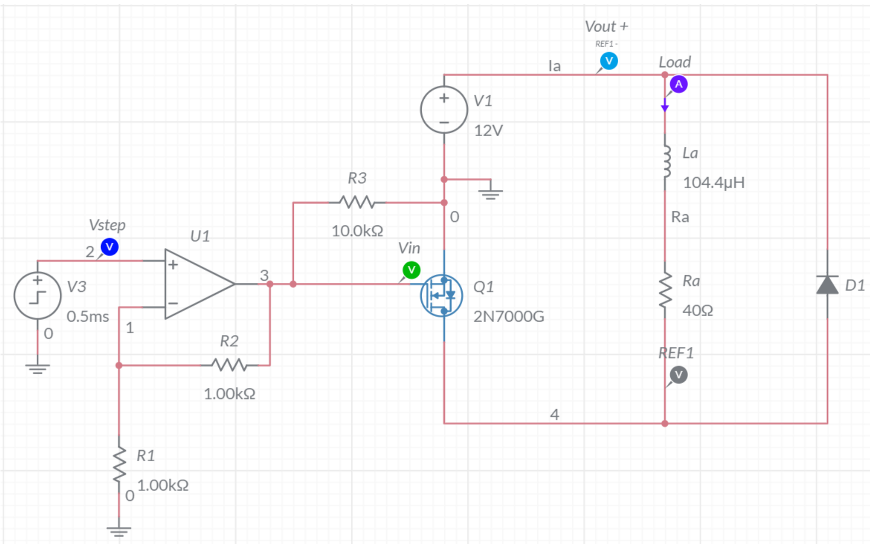

Figure 16. Multisim diagram

The MOSFET was open when Vin is 6V and Vstep is 3V. When Vin was 3volts (Vstep=1,5V) then motor current was 25mA and the voltage 1V.

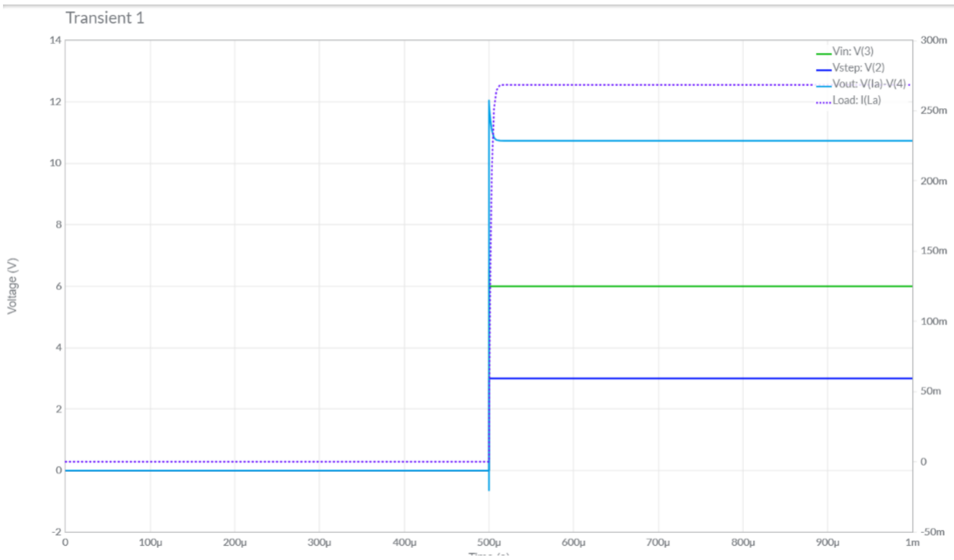

Figure 17. Simulation results

In Figure 17 can be seen that the motor current is approximately 268,46mA and the voltage 10,74V with Vstep 3V. In the simulations the minimum Vstep was 1,2V where motor is running with current 1,23mA. In the application Vstep represents the microcontroller analog output. In the lab experiments the controller was able to control the pump with analog values 1377-3955 which represents voltage control from 1,1V to 3,19V. The simulations where accurate.

3.4 Flow sensor setup

In 2005 N.Nguyen and T.Truong researched the flow rate measurement options in microfluidics using optical sensors.[34] In the setup they recorded the time the liquid travels and calculated the flow rate. They were able to measure flow rates as low as 280 nl/s with an error of 1,37%. In the system was used two detections points consisting of an IR emitter and a phototransistor.

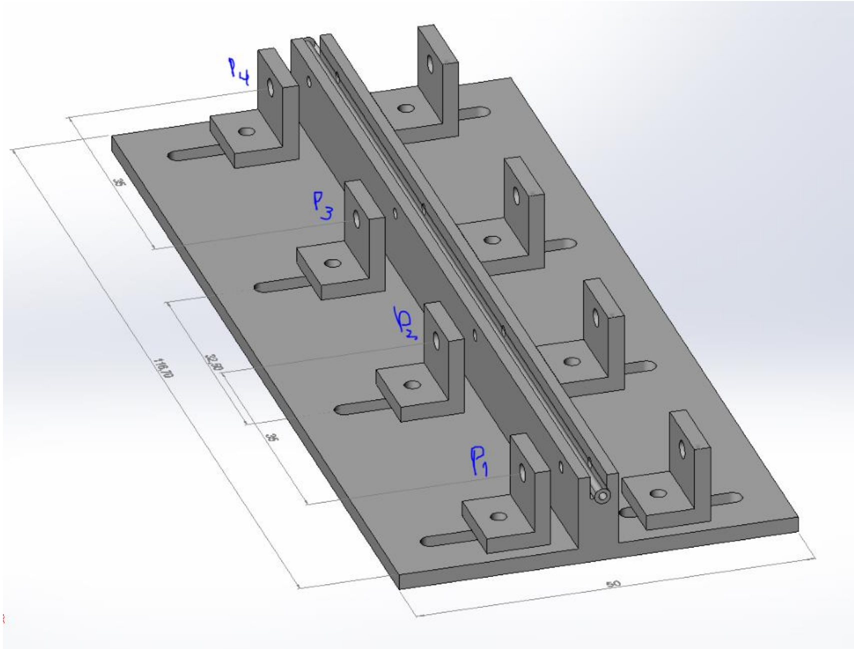

Figure 18. Flow sensor setup.

Measuring flow rate with optical sensors has been done before. Because off the shelf optical sensors are quite cheap then a flow sensor setup was designed instead of buying a commercial one. The cost of the sensor setup was below 10€. Commercially available flow sensors are more than 100€ and they get in touch with the flowing liquid.

In the research paper N.Nguyen and T.Truong used two measurement points for calculating the flow rate. In Figure 18 can be seen that there are 4 measurement points. When the liquid gets to point P_1 then controller takes the first-time stamp. When the liquid gets to point P_2 then the controller takes the 2nd time stamp. Knowing the tube internal diameter and the travel distance then the pumping flow rate can be calculated.

So, for example, when the user set's a flow rate such as 50ml/min and the calculated flow rate deviates from the set point then the PID algorithm is adjusting the pumping speed to have the right flow rate.

The processing speed of ESP32 is 240MHz, which means that the controller checks every 4,17ns if there is liquid detected. So, in point P2 the flow can be regulated almost instantly. When the liquid gets to point P3 then the 3rd time stamp is taken. The flow rate is calculated for P2-P3, which should already be as the user has it set. And for checking purposes was added point P4. Because there are air bubbles in the tubing then P3-P4 calculations can be used for flow rate validation. Ideally the setup should work when there are also air bubbles detected. When air bubble is detected then time stamps are set to zero and if the air bubble travels with constant speed then the flow can be calculated again.

3.5 Pump control flow chart

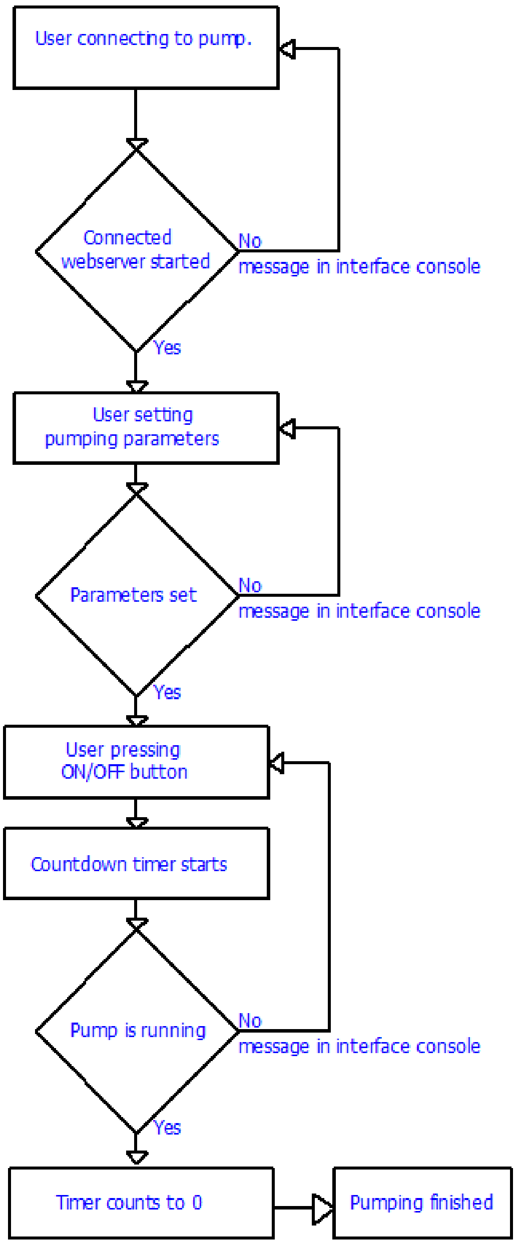

Figure 19. Flow chart

In the Figure 19 is shown a simplified cycle from connecting to pump until finishing the pumping process.

The debugging messages can be seen in the PC browser console. User can skip setting the parameters as well. Then parameters are used which are in the controller. The interface is not checking what parameters are in the memory stored and loads initial parameters. Multiple users can connect to one pump. The parameter updates are not synchronized between the different user interfaces also. So, if one user changed the flow rate then the

2nd user is not seeing it. The user interface is loading initial values. The values in the microcontroller memory might be different.

In the code can be made improvements when the interface is loaded then it loads the values from the controller. When multiple users set parameters then the user interfaces are syncrhonized with each other. Because the interface was out of scope from the thesis then for proof of concept was done with an interface which allows controlling the pumps with minor flaws.

3.6 Communication

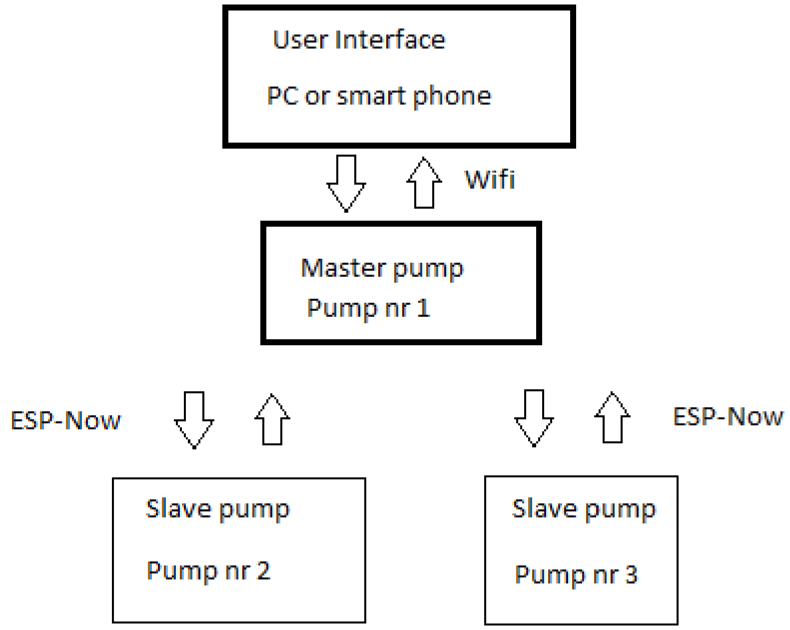

Figure 20. Communication structure. Shows how the master pump and slave pump communicates

From Figure 20 can be seen that the user is controlling the master pump. The master pump is controlling the slave pumps. All the communication is bidirectional. So, the user is getting feedback if the slave pump got connected or the pump turned on.

Communication protocols

The communication between the user and the master pump is done through Wi-Fi. The master pump acts as an access point and users can connect to the pump. When choosing the protocol then it was important that it’s easy to implement and there is ready made libraries for the communication.

For the slave pumps was used Espressif System own protocol ESP-Now, which is meant for transmitting short messages and up to 125m distances between the microcontrollers. For the slave pump was an antenna added to receive the transmitted messages.

3.7 User interface

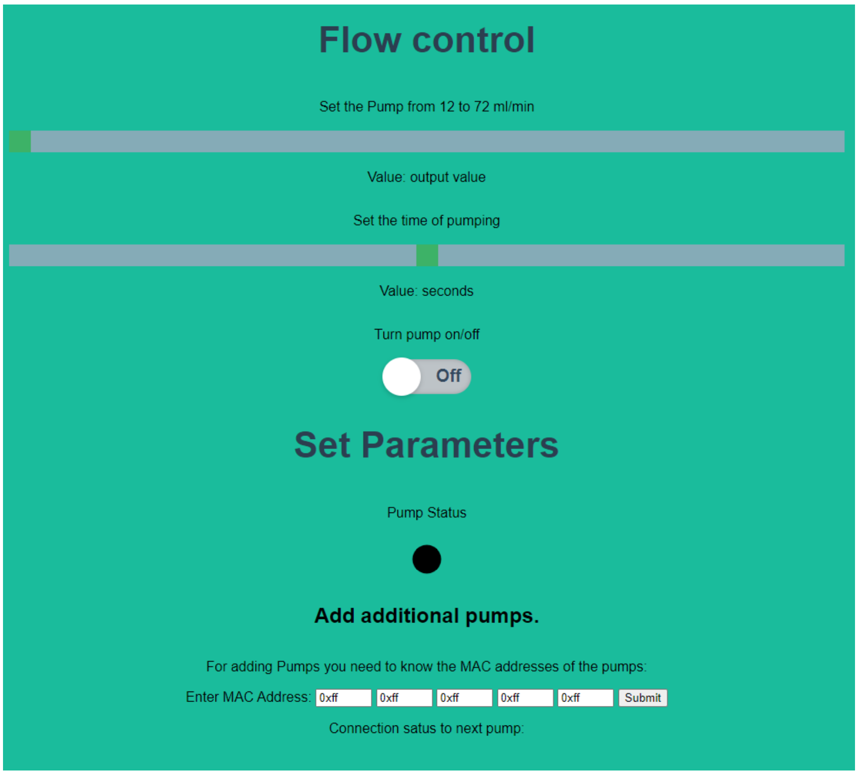

Figure 21. User interface in web browser. In figure control sliders for setting time and flow rate and ON/OFF button. Possibility to add slave pumps.

The user interface was done by using HTML, JavaScript and CSS. In Figure 21 can be seen that the interface has 2 sliders where you can regulate the flow rate and the pumping time. Then it has an on/off button, which starts pumping. After pressing the button then a count down timer is appearing on the interface. When pumping process is interrupted then the indicator turns red and when it's done then it turns green.

There is an option to add pumps by knowing the slave pump MAC address. When the connection is established then the interface is creating similar sliders and buttons for the 2nd pump. Up to 2 pumps can be added and all the pumps can be controlled separately.

For the user to connect to the device it is needed to connect to an AP "SmartFlowController2" and enter password "Taltech2020".

When it’s connected then in a web browser is needed to be opened. In the address bar should be written 192.168.5.1 and the UI will appear. Right now, when the UI is loaded then default slider values are shown. When browser is refreshed then also default slider values are shown. There are cases where in the memory are different values compared what is showed in the interface. So, when a pump is chosen to be controlled and there are multiple users then it’s good to change the slider values before starting the pump to be certain that the pump is having correct flow rate or pumping time.

In the future when the interface is loaded then an implementation of a request to the web server is needed to be written to get the values which are stored in the memory. After values are received, the UI should show already the right slider values.

Another issue what might appear is when there are two users and one is getting disconnected. What will happen then. In a single pump system, when the user gets disconnected then the pump stops. In a system when you have multiple pumps and multiple users, then right now pumps continue working when there is at least one user connected.

4 Experimental analysis

Figure 22. Final assembled pumps.

The pumps were assembled according to the design with minor adjustments. The assembled pumps can be seen in Figure 22. There were some handmade fixes which the design couldn't foresee. Such as some dc/dc converters had different dimensions compared to the specification and couldn't fit into the lot designed and the PCB board was mounted on the front panel instead in the place designed. The pumps were calibrated to get the right flow rates. The electronics of the pumps were tested: the flow sensors, battery, dc/dc converters and the pump.

After that two pumps were used in a real Lab-on-a-Chip application. The application testing was not exactly as expected and there were made simulations and new proposal for future developments.

4.1 Flow sensor test

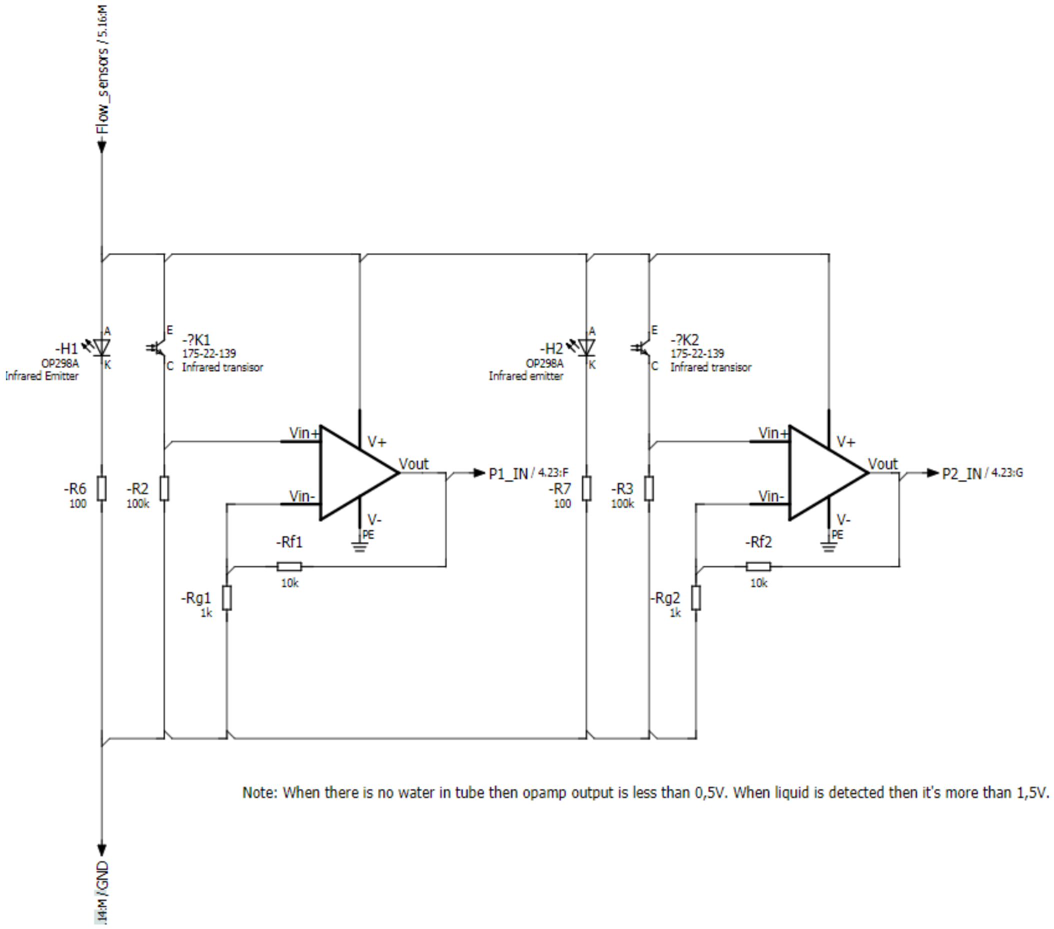

Figure 23. Flow sensor setup.

In Figure 23 can be seen the flow sensor schematic for two detection points, which was removed from the final design. When there was liquid in the tube, then normally the receiver had values higher than 1,5V and when there was no liquid in the tube then the values were less than 0,5V. That can be seen in the table below:

Table 5. Flow sensor measurements.

	P1 receiver	P2 Receiver
Measurement 1 (no water) [V]	0,4	0,44
Measurement 2 (water) [V]	1,69	2,04
Measurement 3 (no water) [V]	0,418	0,427
Measurement 4 (water) [V]	1,69	2,03
Measurement 5 (no water) [V]	0,384	0,932
Measurement 6 (water) [V]	1,69	2

The emitters where having resistors of 24 ohm instead of 100 ohm for having higher detection values when liquid passes the tube.

The flow sensors were removed from the final prototype because the values, which were calculated weren't consistently the same. There was enclosure added for the design because the sensors were sensitive for the ambient light. Even with enclosure the monitoring values weren't always the same. There might have been an error in the code which calculated the values or an error in the setup also. Sometimes the sensors got misaligned and were giving wrong values. All in all, it was possible to detect air bubbles in the tubing. The sensors can be used in bubble detection and for initial flow rate calculation. For constant monitoring they weren't suitable.

4.2 Flow rate calibration

In the user interface the pumping time was set to 10 seconds. The analog output of the microcontroller was increased incrementally. Every time the volume of the pumped liquid was measured with a precise pipette. For each analog value was done 3 measurements. A table was generated where the characteristics of flow rate and analog values where found. The characteristics can be seen in Figure 24. The mean absolute error between the measurements were less than 0,25%.

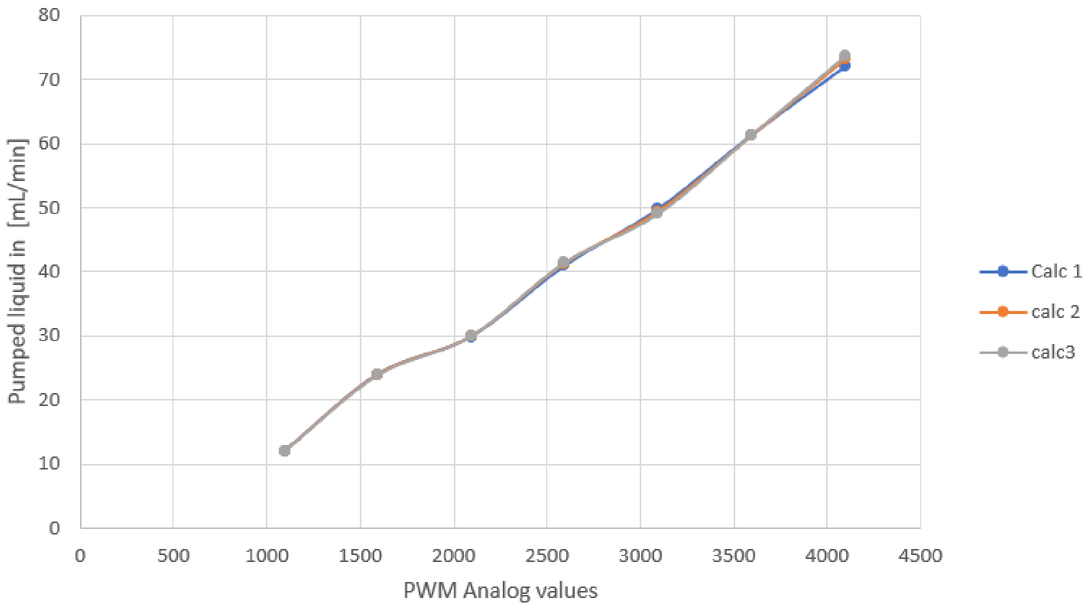

Figure 24. Flow rate vs PWM analog values

There was calculated the deviation for the expected volume of liquid compared to the actually pumped volume. That can be seen in the Table 6.

Table 6. Deviation of the expected pumped flow rate and volume.

Flow rate [ml/min]	Volume 10s pumped [ml]	Expected pumped volume[ml]	Analog values	Deviation
12	2	2	1096	0
18	2,8	3	1348	0,2
24	3,8	4	1603	0,2
30	5,2	5	2100	-0,2
36	6,1	6	2365	-0,1
42	7,4	7	2643	-0,4
48	8,7	8	3010	-0,7
54	9,5	9	3289	-0,5
60	10,5	10	3541	-0,5
66	11,5	11	3797	-0,5
72	12	12	4055	0

Because the curve is not completely linear and the deviation when pumping with different flow rates is not the same then in the UI there was made a function with 6 different sections to have as precise characteristics curve as possible and a pumping flow rate which user expects to have.

When the calibration was done then the pump is pumping exactly the same amount of liquid which was measured with the precise pipette. The calibration was done for one of the pumps. The 2nd pump is having the same calibration values. The pumped volume was measured for the 2nd pump as well and it had good enough precision so there was no need for another calibration process.

4.3 Battery lifetime test

The pump was set to run on the max flow rate. In the interface the timer was updated to 18000 seconds which represents 5 hours. Pump should be able to run for 3,79h. During the endurance test pump stopped 3 times, because Wi-Fi got disconnected. Each time pump was running approximately ten minutes. Exact test results can be seen in the Table 7. A total run time of half an hour was achieved.

Table 7. Endurance test results

Measurement	flow rate [ml/min]	runtime until stop [min]
1	72	10
2	72	13
3	72	8

When the lithium-ion batteries are fully charged then their voltage is 4,19 or 4,2V. As the pump runs then the voltage drops gradually. Pump is not able to run after the battery voltage is 4V even though there is still battery capacity left. The batteries should be able to last until the voltage drops to 3,7 or 3,6V.

The problem is that the DC converters don't adjust their outputs and the controller is not getting enough power. Firstly, the Wi-Fi gets disconnected because the ESP32 chip doesn't get enough current. When Wi-Fi disconnects then the pump stops automatically.

In the future there should be implemented battery management system which is automatically adjusting the correct voltages according to battery voltage to increase the run time.

4.4 Droplet generation experiment

The experiment was done in TalTech Microfluidics institute laboratory. The idea of the experiment was to use the pumps and then the chips to generate droplets. Different chip layouts where tested. Can be seen in Figure 25, Figure 26, Figure 27.

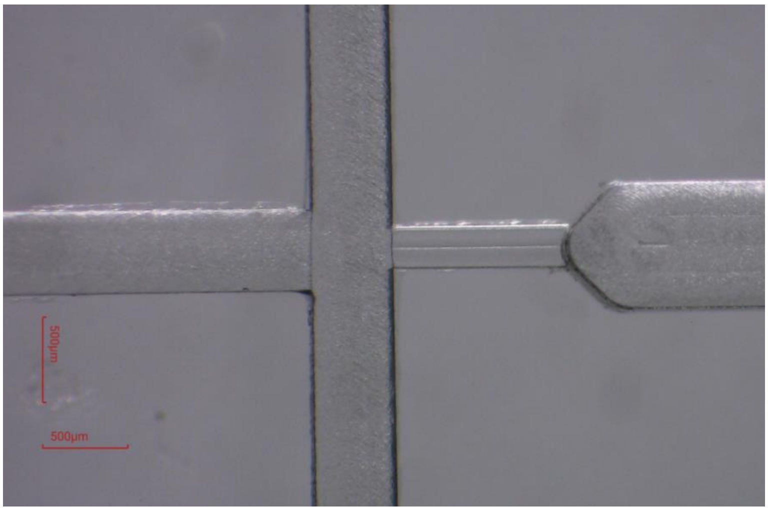

Figure 25. Cross flow chip

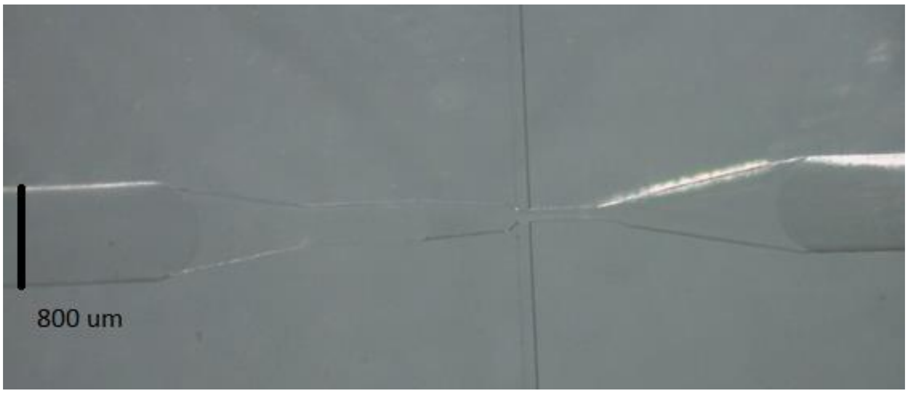

Figure 26. Cross flow chip layout

Figure 27. T-cross flow chip layout (droplets generated with reference KF technology syringe pumps)

In Figure 28 the lab setup can be seen. One pump was pumping oil. And then 2nd pump was pumping red color water. Under the microscope was the chip for observing how the droplets are generating. The output of the chip was collected in a reservoir.

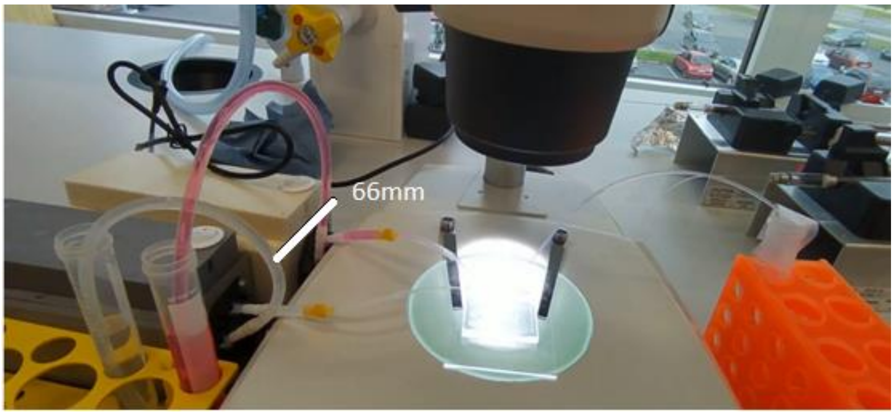

Figure 28. Lab setup

In Figure 23 can be seen the droplets generated by a reference pump from KF Technology. KF Technology used syringe pumps and the flow rates were 170 ul/min for oil and 70ul/min for water.

The pumps which were designed aren't able to generate such low flow rates. The lowest flow rate is 12ml/min and the highest which can be used is 72ml/min. During the experiment for pumping water the flow rates where varied from 12-20 ml/min for water and for oil where varied from 12-24ml/min.

Because the flow rates were much higher then under microscope was difficult to see if droplets were generated or not. Probably high-speed camera is needed and slowing down the recording to be certain that droplets are generated. Only moment when it was visible that there are droplets in the chip channel was when the pumps stopped running and when the pumps decelerated then they generated droplets. The generated droplets can be seen in Figure 29.

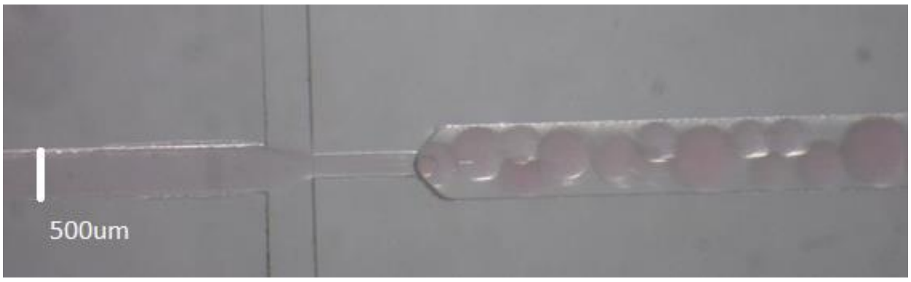

Figure 29. Generated droplets (two-phase emulsion) using the peristaltic pump developed in this thesis

4.5 Optimization of microfluidic droplet generator chip geometry

There was done additional simulations in COMSOL to research why the lab experiment was not giving the results as expected. For simulation was used a PC in TalTech University where was installed COMSOL Multiphysics 5.4 research version. PC itself had Intel XEON 2,4 GHz processor and was running 64-bit Windows 10. A model from scratch was built and the same chip layouts where tested with the same flow rates which were used during the lab experiment. It was found out that with this kind of chip sizes and with milliliter flow rate range it is not possible to generate droplets. The chips were generated droplets in microliter flow rate range.

Creating a model

In COMSOL interface from model wizard was created a two-phase laminar flow model. Under geometry same chip layout was designed as in Figure 29.

Two global parameters were defined. The water and oil flow rate. Can be seen in figure below:

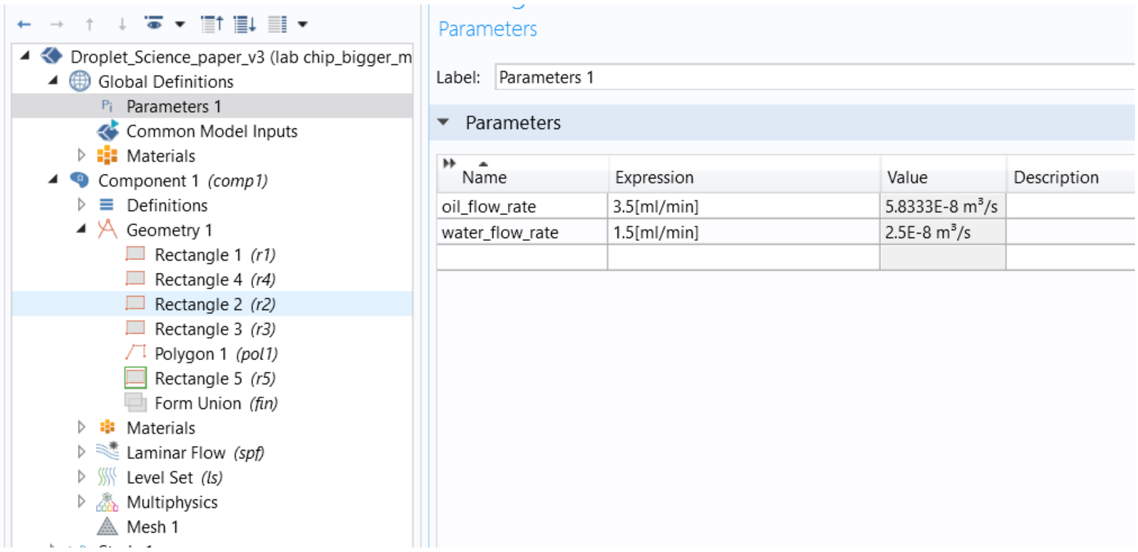

Figure 30. Global parameters

The material simulation parameters for oil and water can be seen in Figure 31, Figure 32.

	Property	Variable	Value	Unit	Property group
✓	Dynamic viscosity	mu	eta(T)	Pa·s	Basic
✓	Density	rho	rho(T)	kg/m³	Basic
	Coefficient of thermal expansion	alpha_iso ; alphaii = alpha_iso, alphaij = 0	alpha_p(T)	1/K	Basic
	Bulk viscosity	muB	muB(T)	Pa·s	Basic
	Ratio of specific heats	gamma	gamma_w(T)	1	Basic
	Electrical conductivity	sigma_iso ; sigmaii = sigma_iso, sigmaij = 0	5.5e-6[S/m]	S/m	Basic
	Heat capacity at constant pressure	Cp	Cp(T)	J/(kg·K)	Basic
	Thermal conductivity	k_iso ; kii = k_iso, kij = 0	k(T)	W/(m·K)	Basic
	Speed of sound	c	cs(T)	m/s	Basic

Figure 31. Water characteristics

	Property	Variable	Value	Unit	Property group
✓	Dynamic viscosity	mu	4.1[cP]	Pa·s	Basic
✓	Density	rho	1855	kg/m³	Basic

Figure 32. FC-40 oil characteristics

The inlets, outlet and domain characterization can be seen in Figure 33. Fluid 1 is FC-40 domain and Fluid 2 is water domain. The wetted parameter under multiphysics module is defined in Figure 34. The domains were defined from material. Can be seen in Figure 35 The mesh was defined as finer and under study was done phase initialization and time dependent study. Study parameters can be seen in Figure 36.

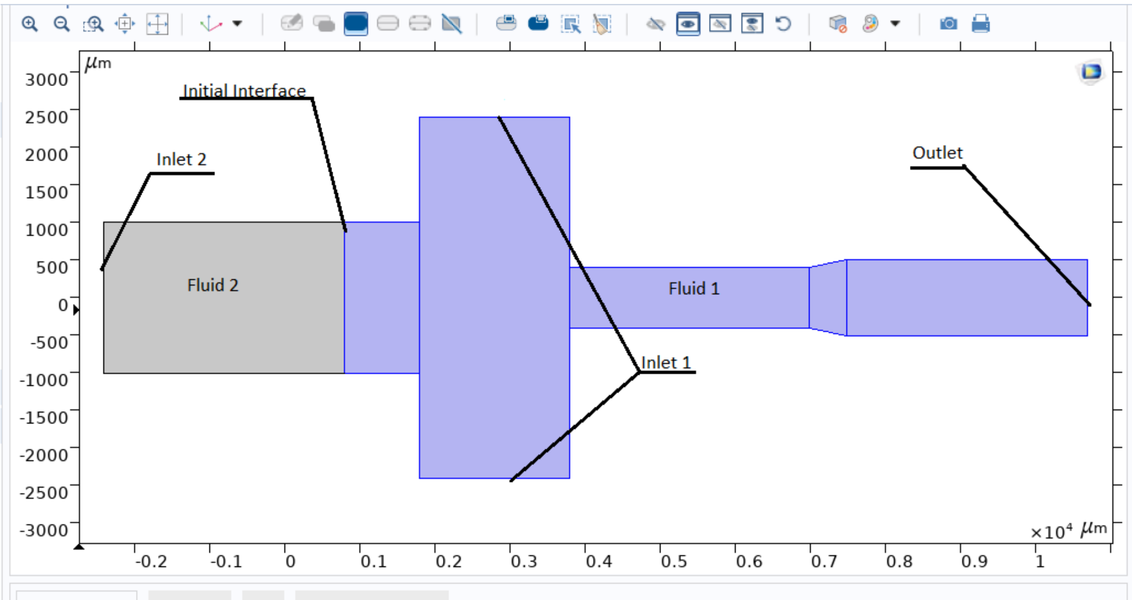

Figure 33. Inlets, outlet and domain characteriziation

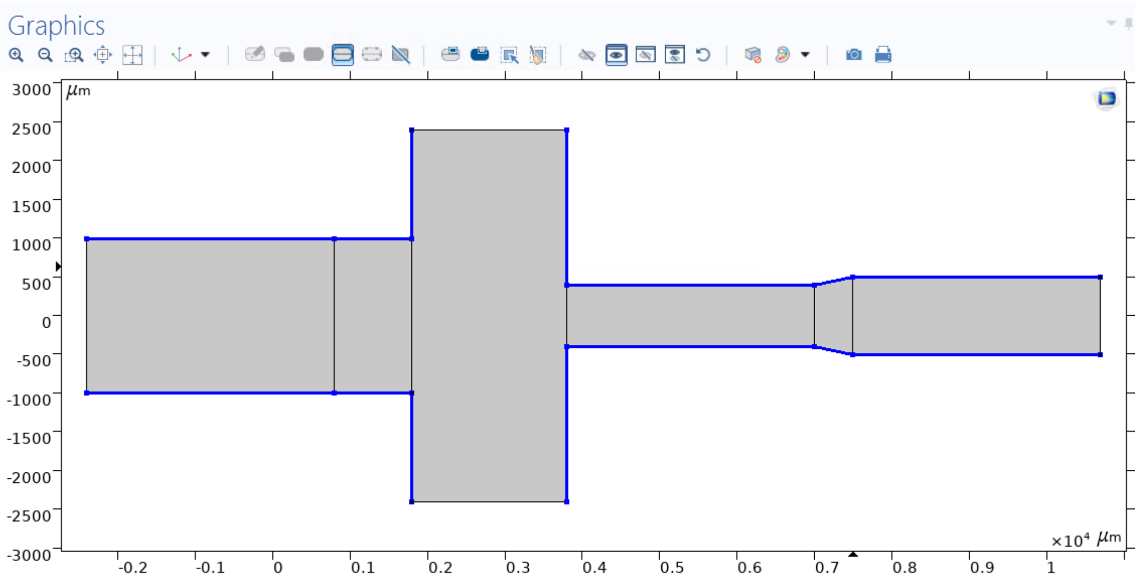

Figure 34. Defined wettted wall.

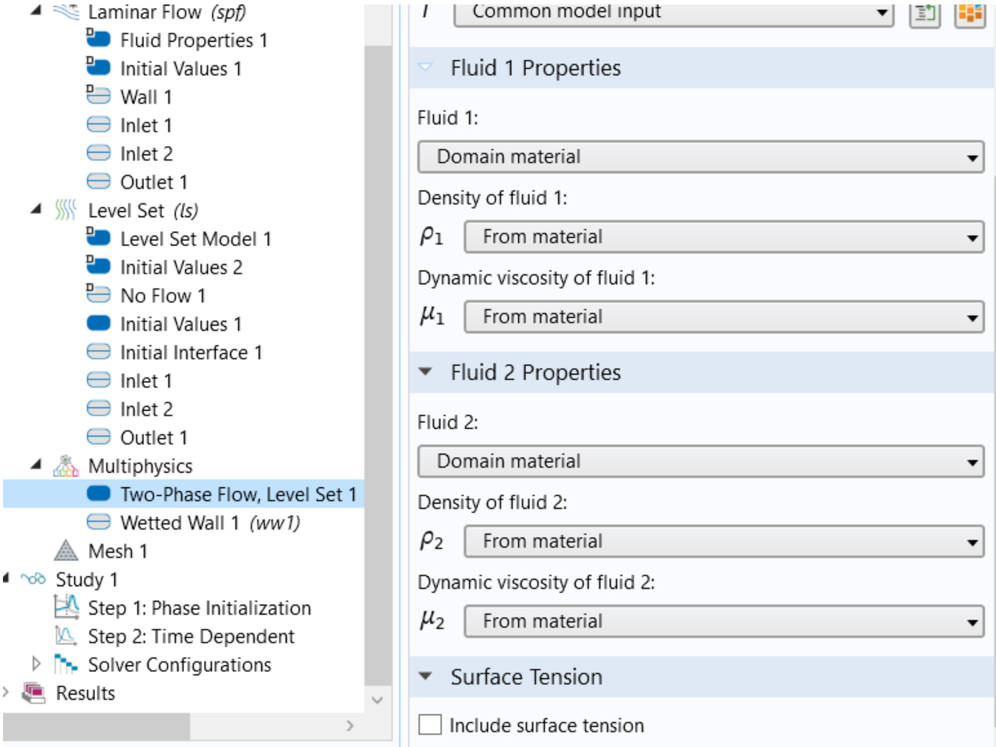

Figure 35. Fluid properties definition

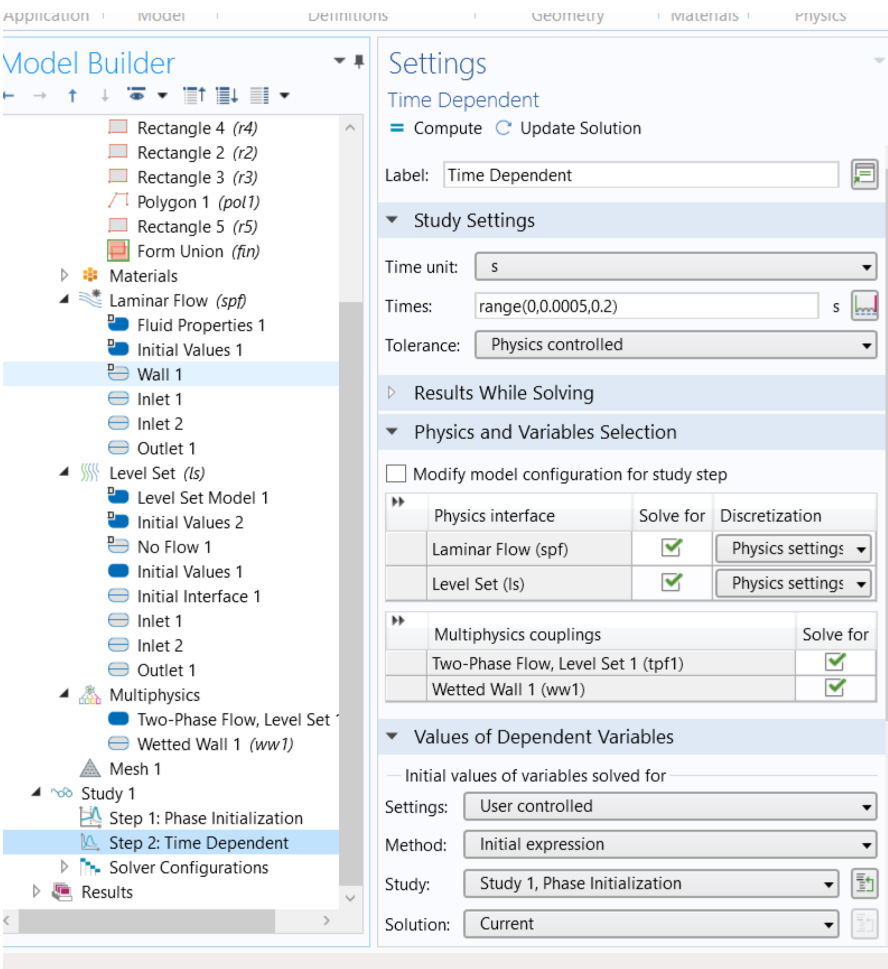

Figure 36. Study paramters

Simulation process

Initially the geometry from Figure 29 was taken and the chip layout and the size was increased proportionally until the chip didn't generate anymore droplets. Can be seen in Figure 37.

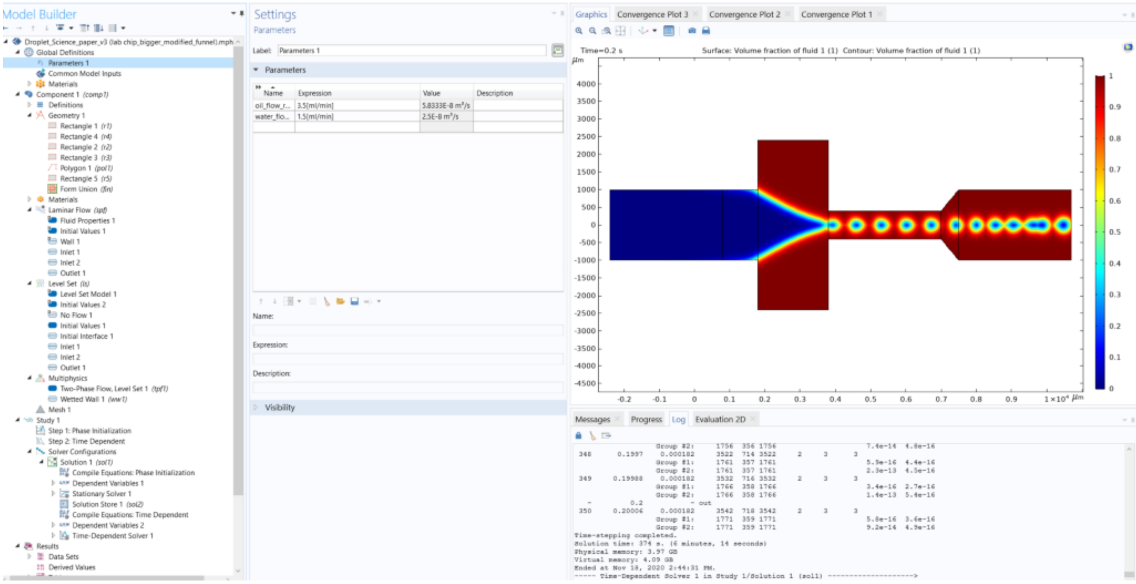

Figure 37. The biggest chip size when it generated droplets.

Because in the wider channel got couple droplets merged (Figure 37) then the channel was made narrower.

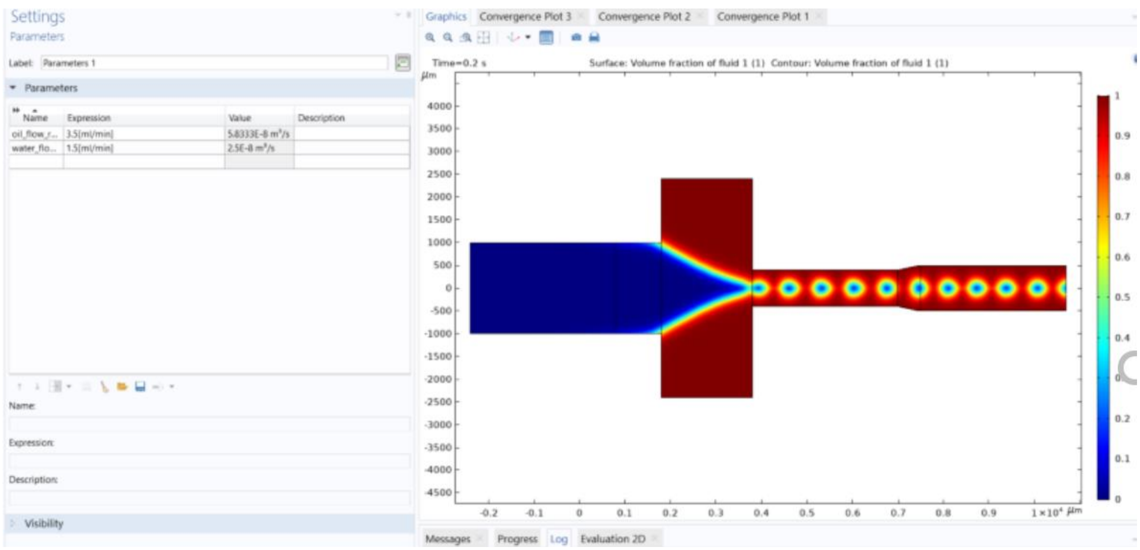

Figure 38. COMSOL chip geometry

In the Figure 38 the final chip geometry can be seen, which is generating droplets. The chip is generating droplets when oil flow rate is 3,5ml/min and water flow rate is

1,5ml/min. The input channels are 2mm wide and then the output is narrower and then getting larger.
Two of the chip layouts where printed out for future developments. The printed chip can be seen in the Figure 39.
For example, it is possible to exchange tubing of the peristaltic pump to get lower flow rates or to change the peristaltic pump head which is already having smaller tubing. Right now, a peristaltic pump was used which had tubing ID 3mm. That was way too large. For example, tubing with ID 1mm would generate flow rates up to 14ml/min and the pump could be regulated to have lower flow rates. When the tubing is changed then the pump needs to be calibrated again and new lab experiments made.

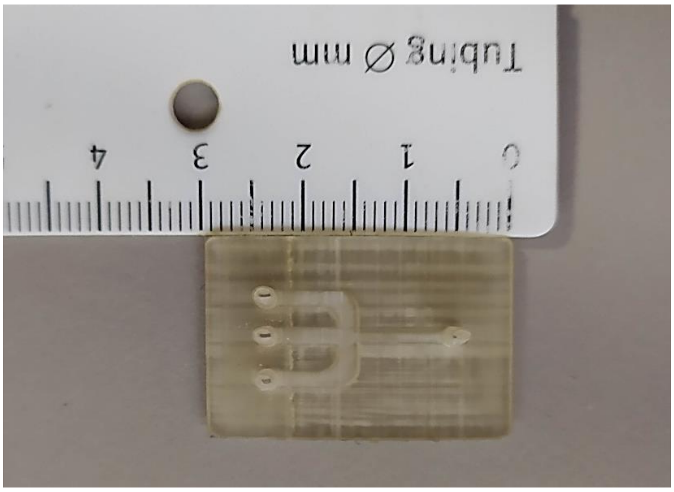

Figure 39. Optimized chip for higher flow rates up to 3,5ml/min

5 Future developments

5.1 BMS for having longer run time

Right now, when the pump is running then the battery voltage and current are not monitored. BMS (battery management system) is a complicated process and it is not easy to implement. As described in the article [33], where is talked about the lithium-ion battery SOC estimation and management then even nowadays there are a lot of challenges. It's an electrochemical process and the battery aging is also influencing the charge and capacity of the battery. Even with proper models it's a difficult task to implement.

For this task it is needed to design the electronics in a new way. Right now, the DC converters are manually adjusted to have correct output voltages. How it should be designed or what kind of hardware is needed to implement it is another topic to be researched.

5.2 Decreasing the flow rate and dead volume

For getting lower flow rates it is needed to change the peristaltic pump head or the tubing of the peristaltic pump. For example Baoding Shenzhen Precision Pump[14] is having pumps with different tubing up to ID 1mm. With this tubing it is possible to receive 14ml/min flow rate. When we take account that the Adafruit pump with 3mm tubing is be able to generate up to 110ml/min flow rate then it was possible to go as low as 12ml/min. Considering that then it sized down to an 11% flow rate level. 11% of 14ml/min would be 1,54ml/min flow rate, which would be the maximum flow rate for pumping water.

Dolomite is also offering a peristaltic pump which is able to pump in a microliter range[35]. Because this pump is 3V then the pump control module should be overviewed. The 12V DC/DC converter might be regulated down to a 3V one, but still the module needs to be tested. Because the mechanics are totally different then a new design needs to be done.

The dead volume is the liquid which is in the tubing. The longer and wider are the tubing's the more fluid is used in the LoC system. Because the reagents are expensive and the chips, they don't need so much fluid to work then reduction in dead volume is needed. The tubing in the system should be as short as possible. By reduction of tube diameter, a reduction in dead volume is also happening.

5.3 Software

Flow rate according the liquid viscosity

The pump was calibrated according to water viscosity. Different calibration tests should be done to get the flow rates for different liquids. In the user interface should be possible to set the liquid viscosity as well.

Adding feedback sensors

In the initial design there were IR sensors to detect the liquid. It was possible to have some bubble detection and initial flow rate calculation, but for constant monitoring it was not suitable and the sensors where removed from the design.

In the American Control Conference paper [4] was used a pressure sensor by Honeywell and PID control. In this way instead of having pre-calibrated values for viscosities the system would automatically adjust for different fluid viscosities. It would increase the product cost and complexity, but the pump would be more reliable in different working situations.

A standard middleware for communication.

When we are talking about the OSI model then right now in the system the lower layers such as physical, data link and network layers are done with the open-source libraries which were available and are commonly used for ESP32 chips. When we are looking into the higher layers then the API is having the minimum requirements for user interaction and minimum flexibility.

In the system the communication between the UI and webserver is implemented in a message centric way. Each message should be managed and interpreted and getting the messages are by request. This involves the UI when different users are connected.

Right now, when there are two users connected to one pump then when one is changing slider values then the 2nd user slider values are not updated and the user does not know what values are inside the pump.

Slave and master pump

In the future development it would be good that one pump could act as a master or a slave. Right now, the code is static and when you have a master pump then it can’t act as a slave. The same with slave pumps. Mainly the problem with the slave pump is that it can’t be controlled as a stand-alone device.

6 Conclusion

The goal of the thesis was to develop a low-cost, portable, open-source flow regulation system for Lab-On-a-Chip applications.

A pumping system consisting of a peristaltic pump, DC/DC converters, lithium-ion batteries, microcontroller and a 3D printed enclosure were designed. The chosen hardware was tested. The calculations showed that the pumping system can run on battery for 3,79h. Because DC/DC converters didn’t adjust output voltages according to the lithium-ion battery voltage drop then lower run time was achieved. Otherwise, the pump control module was working as expected and it was possible to control the pump with a smart phone.

Performance-wise the flow rates were between 12ml/min-72ml/min. The total runtime on battery at maximum flow rate was half an hour. The user could connect to the pump by using a laptop or a smartphone. A multi-pump system was developed where the user could add up to two slave pumps. The designed pumps were tested for generating droplets in Lab-On-a-Chip applications. In conclusion, the system could be a viable product for some applications, where it is needed to have a milliliter range flow rate.

In the thesis a chip layout was designed, which can be used for 1,5ml/min up to 3,5ml/min flow rates, but still for the pump to work as a droplet generator modification in the pump design are needed to be made.

In the thesis future development directions were given, which can be done to have a better product such as having a BMS and modifying the tubing or having a different peristaltic pumping head with smaller tubing to enable working in the <10ml/min flow range.

Given the initial design requirements with milliliter range flow rates, the pump is working as expected. Even though the control of the pump flow rate was not as wide as expected due to the limitations in electronics and mechanics.

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8 Appendix

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8.2 Appendix 2 Automation drawing

The Automation drawing was created with EPLAN Electric P8 2.6 at JOT Eesti OÜ.

Automation drawing

Smart flow controller

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Title page / cover sheet:

Drawn	Date	Last modification		Reference
GROSMAR	16.12.2019	GROSMAR	16.12.2019	Pumping system
Check	Date	Sheet 1/9	Drawing no. Taltech001	Revision 9
Approved	Date			

Revision overview

Revision	Date	Creator	Revision description
9	19.10.2020	GROSMAR	Simplified circuit.
8	27.08.2020	GROSMAR	Corrected schematic.
7	12.08.2020	GROSMAR	Added ON-OFF pushbutton circuit.
6	07.07.2020	GROSMAR	Removing Opamps
5	25.06.2020	GROSMAR	Removed 2 sensors and added ON/OFF switch. Removed LED indicators.
4	09.03.2020	GROSMAR	Added opamp
3	31.01.2020	GROSMAR	Added 12 Ohm resistors.
2	22.01.2020	GROSMAR	Added flow sensor setup.
1	20.01.2020	GROSMAR	MOSFET source connected to ground and drain through motor to voltage source.
0	10.10.2013	kralgot	initial drawing

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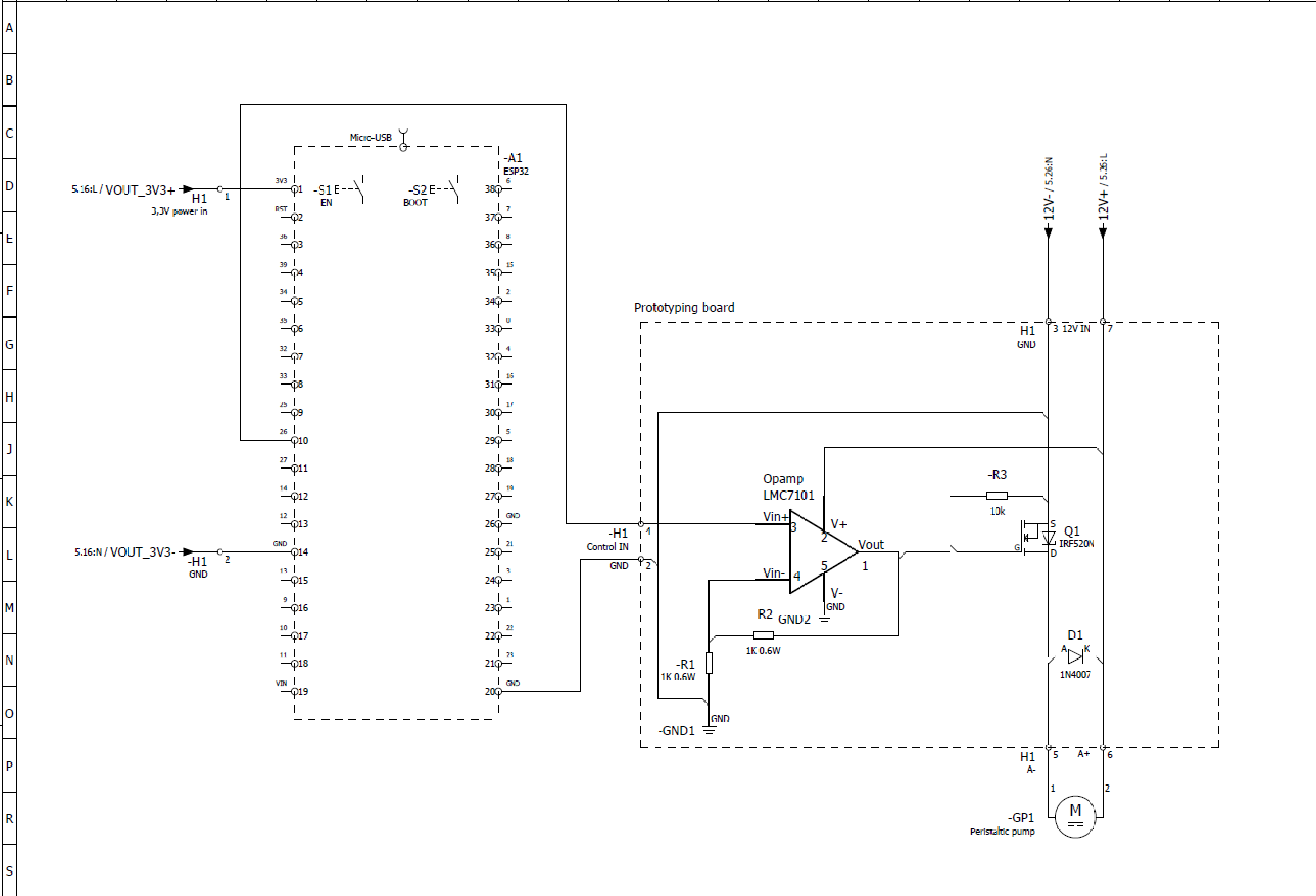
DRAWING INDEX

Revision 7 12.08.2020

Revision 8 27.08.2020 Corrected schematic.

Revision 9 19.10.2020 Simplified the circuit.

Revision 9 19.10.2020



Drawn GROSMAR	Date 27.11.2019	Last modification GROSMAR	19.10.2020	Reference Pumping system	
Check	Date	Sheet 4/9	Drawing no. Taltech001		Revision 9
Approved GROSMAR	Date 19.10.2020				

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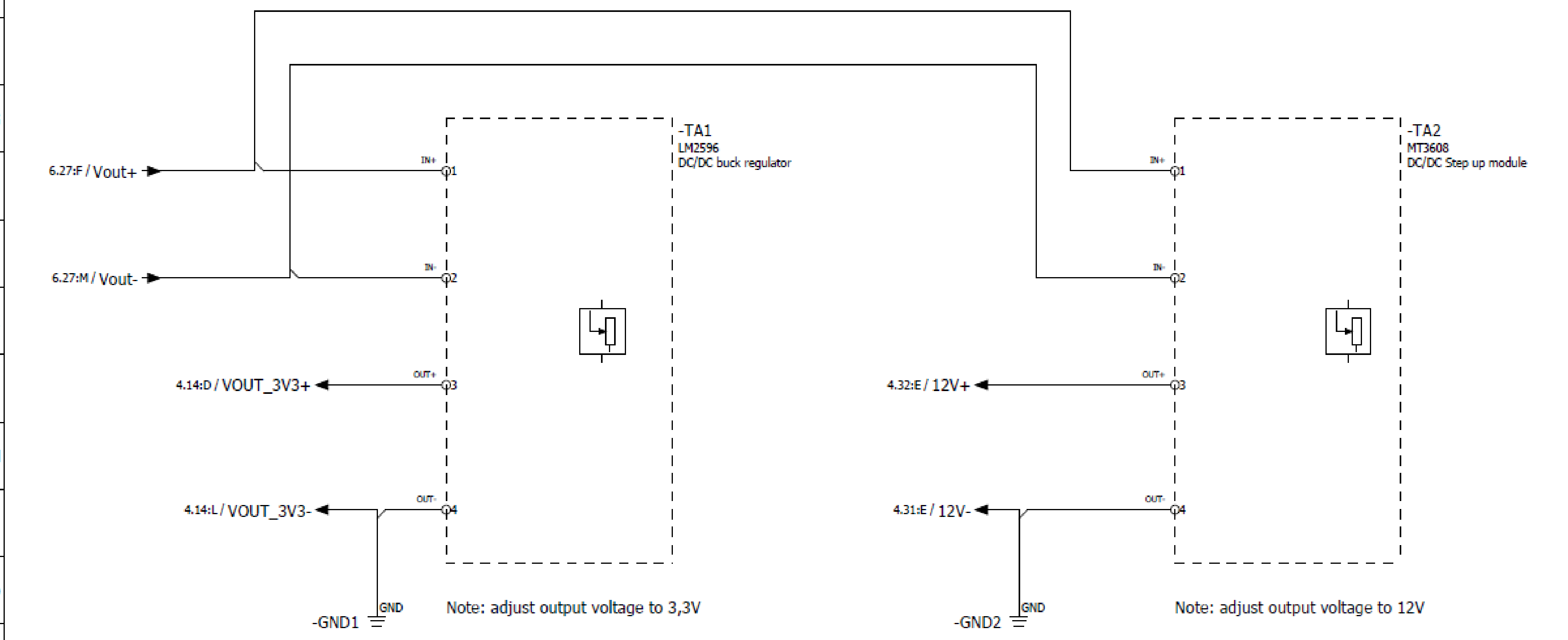
Main drawing



Date	Revision	Description
22.01.2020	Revision 2	Added flow sensors
06.03.2020	Revision 4	Added 10k resistor.
25.06.2020	Revision 5	Removed 2 sensors and added on/off switch.
12.08.2020	Revision 7	

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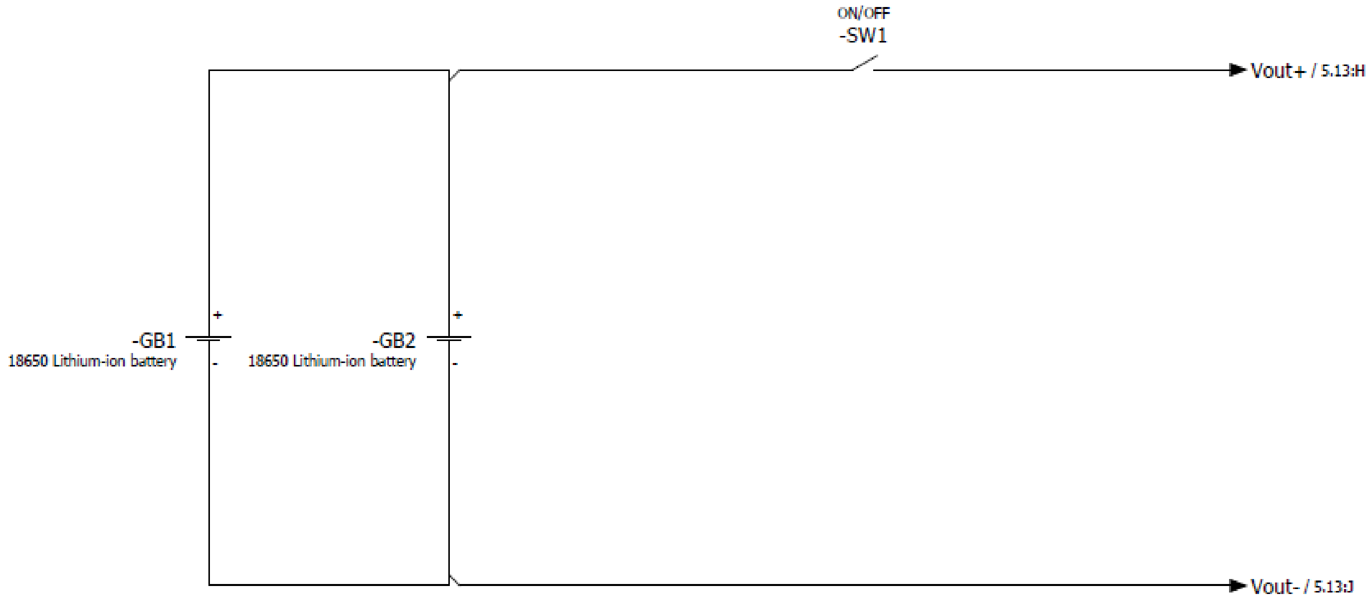
DC power conversion

Drawn GROSMAR	Date 27.11.2019	Last modification GROSMAR 19.10.2020	Reference Pumping system
Check	Date	Sheet 5/9	Drawing no. Taltech001
Approved GROSMAR	Date 12.08.2020		Revision 9



Revision 11.08.2020 New page created
Revision 7 12.08.2020
Revision 7 12.08.2020
Revision 9 19.10.2020 Simplified the circuit.

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ON-OFF Button

Drawn: GROSMAR	Date: 11.08.2020	Last modification: GROSMAR 19.10.2020	Reference: Pumping system
Check	Date	Sheet: 6/9	Drawing no.: Taltech001 — Revision: 9
Approved: GROSMAR	Date: 19.10.2020		

Terminal diagram

JOTE_TD_5_24_TCP

=HLF+-H1

External targets | Internal targets

Target designation	Wiring	Jumper	Saddle jumpers	Part	Jumper	Wiring	Target designation
-TA1:3			1				-A1:1
-GND1:GND			2				-A1:14
-Q1:S			3				-GND2:GND
-A1:10			4				
-GP1:1			5				-D1:A
-GP1:2			6				-D1:K
			7				-TA2:3

Revision | Revision | 19.10.2020 | Revision | New page created | 19.10.2020 | Revision 9 | Simplified the circuit.

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Terminal diagram : =HLF+-H1

Drawn	Date	Last modification		Reference
GROSMAR	19.10.2020	GROSMAR	19.10.2020	Pumping system
Check	Date	Sheet 7/9	Drawing no. Taltech001	Revision 9
Approved GROSMAR	Date 19.10.2020			

COMPONENT LIST

JOT_PL10_dyn

PART	COMPONENT NR.	JOT CODE	PCS	PAGE-PATH	TYPE	MANUFACTURER
Microcontroller	=HLF-A1	SX018433	1	&=HLF+/4.16:C	Espressif Systems ESP32	Espressif Systems
DIODE	=HLF-D1	1N4007-1	1	&=HLF+/4.32:N	1N4007	
Li-ion Battery 18650 3.6V 3350 mAh 1.5C 4.9A LG	=HLF-GB1	SX018387	1	&=HLF+/6.15:J	LG Chem INR18650F1L li-ion battery	LG Chem
Li-ion Battery 18650 3.6V 3350 mAh 1.5C 4.9A LG	=HLF-GB2	SX018387	1	&=HLF+/6.18:J	LG Chem INR18650F1L li-ion battery	LG Chem
Peristaltic pump	=HLF-GP1	SX018437	1	&=HLF+/4.31:R	Adafruit 12V peristaltic pump	
Power MOSFET	=HLF-Q1	SX018436	1	&=HLF+/4.31:L	International rectifier IRF520N	International rectifier
Resistor	=HLF-R1	2200013278-0	1	&=HLF+/4.24:N	1K 0.6W 1%	
Resistor	=HLF-R2	2200013278-0	1	&=HLF+/4.25:N	1K 0.6W 1%	
Resistor 10K, 0,5W, 1%	=HLF-R3	SX007623	1	&=HLF+/4.30:K	multicomp MF50 10K	
DC/DC buck regulator	=HLF-TA1	SX018434	1	&=HLF+/5.17:G	LM2596 supply module	
DC/DC converter step up	=HLF-TA2	SX018435	1	&=HLF+/5.29:G	MT3608 step up module	

Revision 9 — 19.10.2020 — Simplified the circuit.
Revision — 19.10.2020 — New page created
Revision
Revision

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Parts list : SX018433 - SX018435

Drawn	Date	Last modification		Reference
GROSMAR	19.10.2020	GROSMAR	19.10.2020	Pumping system
Check	Date	Sheet 8/9	Drawing no. Taltech001	Revision 9
Approved GROSMAR	Date 19.10.2020	+++		

Bill of Material

JOT_PLG_CL

JOT CODE	PART	TYPE	Qty.	Unit	MANUFACTURER
1N4007-1	DIODE	1N4007	1	pcs	
2200013278-0	Resistor	1K 0.6W 1%	2	pcs	
SX007623	Resistor 10K, 0,5W, 1%	multicomp MF50 10K	1	pcs	
SX018387	Li-ion Battery 18650 3.6V 3350 mAh 1.5C 4.9A LG	LG Chem INR18650F1L li-ion battery	2	pcs	LG Chem
SX018433	Microcontroller	Espressif Systems ESP32	1	pcs	Espressif Systems
SX018434	DC/DC buck regulator	LM2596 supply module	1	pcs	
SX018435	DC/DC converter step up	MT3608 step up module	1	pcs	
SX018436	Power MOSFET	International rectifier IRF520N	1	pcs	International rectifier
SX018437	Peristaltic pump	Adafruit 12V peristaltic pump	1	pcs	