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Google Glass Data Visualization and Monitoring for Organs-on-a-Chip and Biomedical Applications

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ABSTRACT

The present scripture represent the master thesis of Fabio Busignani, and it has been carried out at *Khademhosseini Lab* (Cambdridge, MA, USA), Harvard-MIT Health Science and Technology, Brigham and Women's Hospital under the supervision of professor Ali Khademhosseini and Ph.D. Yu Shrike Zhang.
The design which is going to be described, has been inserted inside the context of a five years project (***XCEL*** grant), sponsored by the U.S. Defense Threat Reduction Agency (*DTRA*).

The aim of *XCEL* is to develop a *Body-On-A-Chip* microfluidic platform that is able to simulate multi-tissue interactions under physiological fluid flow conditions.

In this master thesis will focus on designing of a custom user interface on *Google Glass* for simultaneous recording of biosensing data such as temperature, pH, and microscopy images/videos as well as remote control of microfluidic valves and devices. The project involves all the hierarchical layers, starting from the physical one with the circuit in charge to acquire data from bio-sensors and drive the valves, up to the glasswear[1].

In the Introduction chapter, the main keys of the project are presented in detail as well as the final result from a user point of view.
After that a detailed description of each abstraction level which goes to build the entire systems is shown: starting from the bottom (Hardware) reaching the top (Google Glass Application) passing through the Firmware, that runs in an embedded *Linux* platform, and the Software, present on the *PC* and the *Google App Engine*.
The Experiments and Conclusion chapter ends this thesis, showing the obtained results with different experiments.

[1] Google Glass Application

CONTENTS

INTRODUCTION

This master thesis has been carried out at Khademhosseini laboratory, Harvard-MIT Health Science and Technology (Brigham and Women's Hospital), in Cambridge, MA. During my six-months of research I have joined ***XCEL*** grant project, a five years project sponsored by the U.S. Defense Threat Reduction Agency (*DTRA*).

The goal of this project is to develop a system, a microscale bioreactor containg four 3D fully-functional *organs-on-a-chip*.

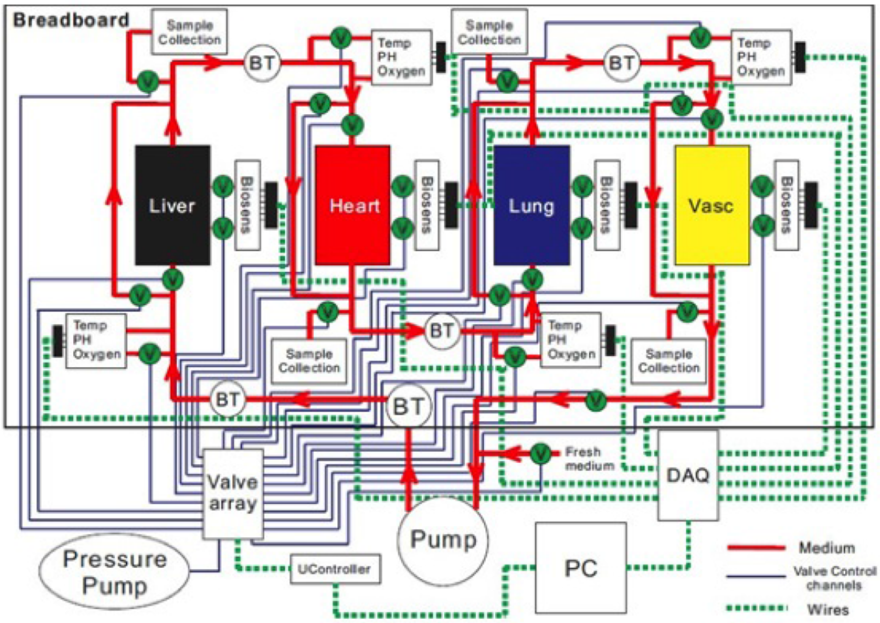


Figure 1: *XCEL* project (*Body-on-a-chip*)

The (Fig.1) shows, in a schematic representation, the design of the entire *XCEL* project. On the breadboard four organs are connected from each others: liver, heart, ling, and vascular system (*Vasc*). The medium used to connect them is using tubing circuit where the media flows. This tubing connections are driven by electrovalves.

My role in this project has been to create a custom user interface on Google Glass for simultaneous recording of biosensing data such as temperature, pH, and microscopy images/videos as well as remote control of the microfluidic valves previously introduced. In summary my aim was to design a Google Glass App for use in organs-on-a-chip platforms.

The *organs-on-a-chip* platforms contain interconnected microfluidic modular components including the bioreactors for hosting biomimicry human organ models, downstream biochemical sensors to continually monitor the levels of biomarkers secreted by the organs, and physical sensors to monitor the physical microenvironment of the circulatory system. Due to their extensive similarity with human organs, these miniature human models are finding widespread applications where the prediction of in vivo responses of the human body is needed, including but not limited to drug screening, basic biomedical studies, and environmental safety assessment. Thus, the *organs-on-a-chip* platforms seek to recapitulate human organ function at micro-scale by integrating microfluidic networks with three-dimensional organ models, which are expected to provide robust and accurate predictions of drug/toxin effects in human bodies. In fulfilling this aim, a set of physical/chemical parameters need to be monitored and stored in order to capture such effects of drug/toxin administered into the system.

By precisely designing the Google Glass App for this organs-on-a-chip platform it allows convenient observation and control of the organ models, biosensors, and the microfluidic circuitry, which has been difficult to achieve previously.

The system designed and described in this thesis is illustrated in (Fig.2).

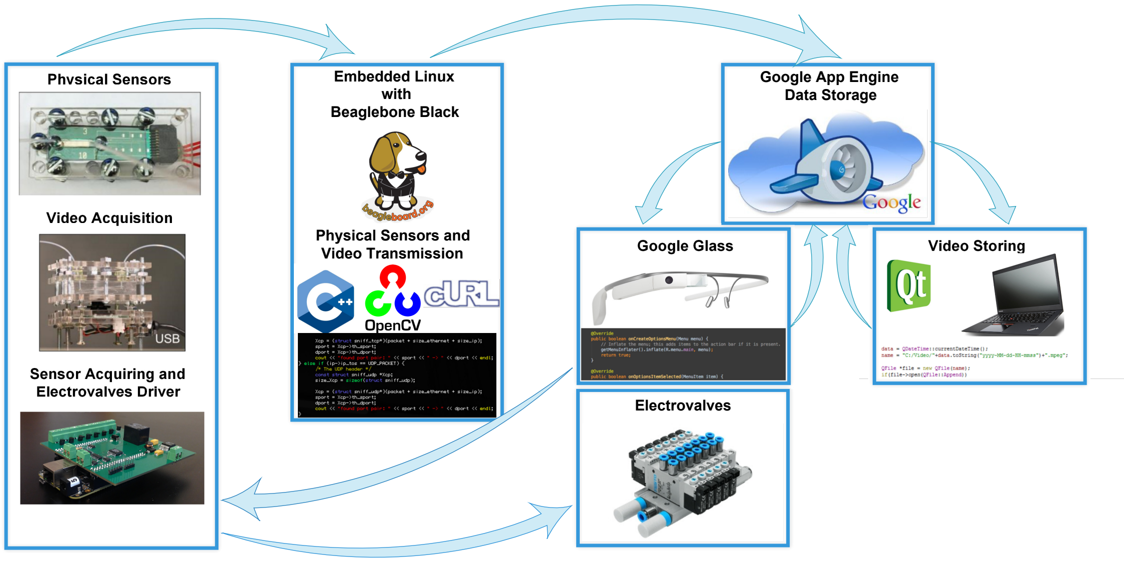


Figure 2: Block diagram of the system

The (Fig.2) shows the principal steps of data transmission from physical and video sensors to the Google Glass via an *Embedded Linux System* performed using the **Beaglebone Black**.
The Beaglebone Black runs processes that are in charged to:

- acquire the sensors value and to store them onto *Google App Engine Data Storage*;
- acquire the video, perform the beating plot, and to store them onto *Google App Engine Data Storage*;
- get from the *Google App Engine Data Storage* the electrovalves status set from the user through the Google Glass and to drive the electrovalves.

The whole designed environment includes a program, written using the framework *Qt*, for storing the recorded video from microscope.

THE GLASSWEAR

The (Fig.3) shows the structure of the Glasswear. From the Home Screen (Fig.3a), using the voice trigger "*Show Measurement*" or tapping on the "*Measurement*" card (Fig.3b) user is allowed to enter in the application (Fig.3c). From this point, tapping and swiping, it's possible to navigate into the glasswear's menu (Fig.3d-h) and choose which card has to be shown. *View PH* (Fig.3i) and *View Temperature* (Fig.3j) cards plot on the card's left side the value of pH and temperature, respectively. While on the right side they show the average value. The microscope's video is shown by tapping on *View Video* (Fig.3k). The *View Beating* card shows the graph of the beating associated to the video.

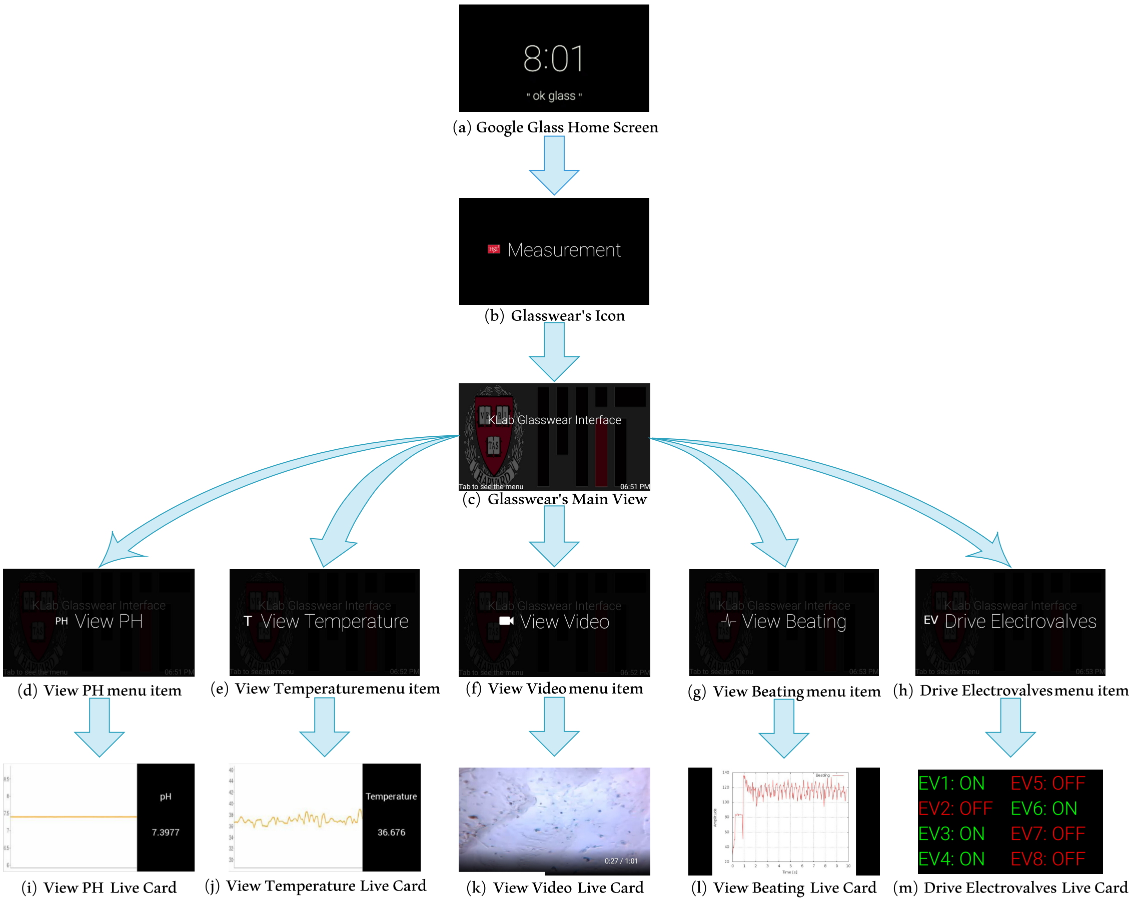


Figure 3: Glasswear's Block Diagram

From the *Drive Electrovalves* card (Fig.3m), the user can set the value of each electrovalve. The main view of this card shows the status of each electrovalve (written in green if it is on and in red if it is off).

(a) Elecrovalves Status View (b) Toggle EV1 menu item (c) Toggled EV1

Figure 4: Drive Electrovalves Steps

The (Fig.4) shows the steps to toggle the status of the first electrovalve:

1. (Fig.4a) shows the initial status of the whole electrovalves (all off);

2. tapping on the card and swiping the user is allowed to change the status of each electrovalve from the menu, as shown in (Fig.4b);

3. after that the electrovalve has been chosen, a toast message pops up (Fig.4c), and the new values of the electrovalves are shown.

To return on the main card of the glassware, the user has to tab on *Back* item (Fig.5) from every menu.

Figure 5: *Back* menu item

To terminate the glassware, from every menu, the user has to swipe up to the final item and tab on *Exit* item (Fig.6).

Figure 6: *Exit* menu item

THE BOARD

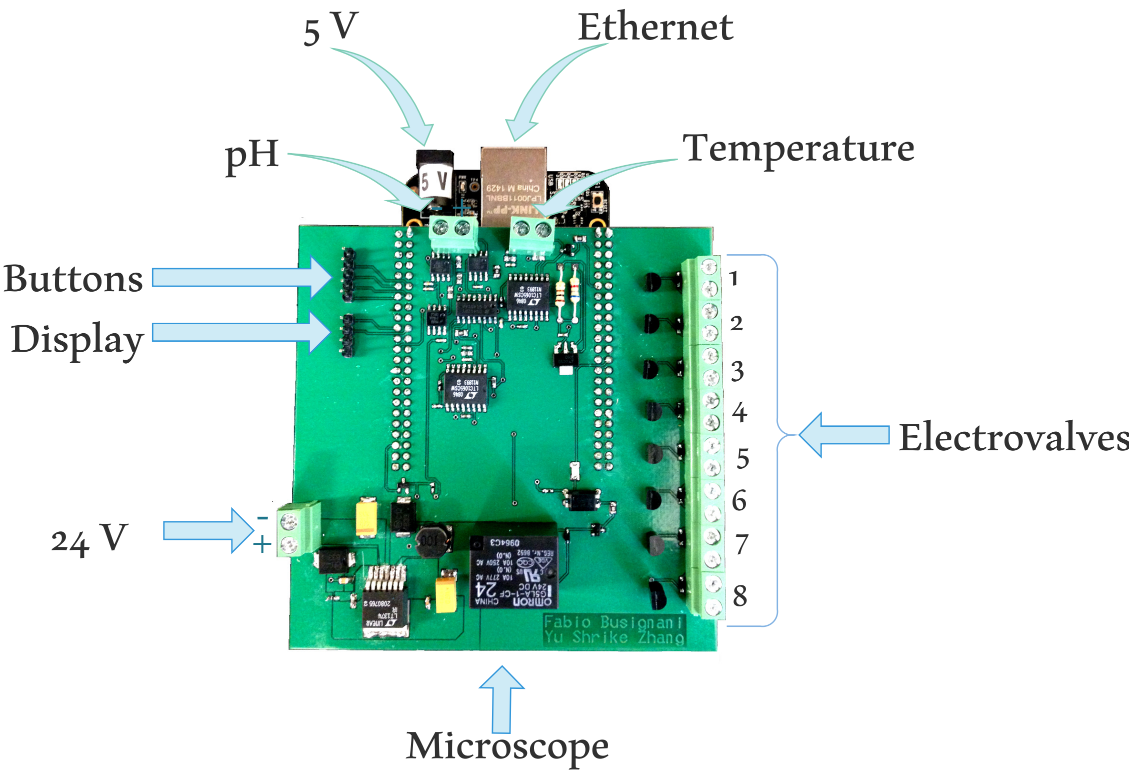


Figure 7: The Board

The (Fig.7) shows the top view of the system board. As can be seen it is composed by different interface and connections:

- 5 *V* power supply, required by the microcomputer on the Baglebone Black and by the conditiong circuits on the *PCB*;
- 24 *V* power supply, required by the electrovalves;
- *Ethernet*, to connect the board to the Internet;
- *USB* connection, for the microscope;
- *pH header*, to connect the pH sensor[2];
- *temperature header*, to connect the temperature sensor;
- *electrovalves header*, made by eight pairs of terminals, ordered as shown in (Fig.7), from the top to the bottom.

The remaining two headers, shown in the top left corner of (Fig.7) are thought for future application. In particular they are going to be useful for all those jobs that don't required the interaction with Google Glass, such as sensors calibration.

[2] **WARNING**: to ensure the correct functionality, user has to pay attention at this connection, since the pH sensor is a passive one, it has a polarity. The positive pin of the sensor has to be connected to the right terminal, looking fro the top (as shown in (Fig.7))

VIDEO STORING

The storing of the microscope video plays an important role of this system. It may be essential to review the recorded video during the experiment and in order to fulfill this aim a *Qt* program has been designed.
We chose *Qt* because in this way the program is available for different operating systems, *Linux*, *Windows*, and *MacOS*.

The program is very easy to use, the user just has to run the executable (Fig.8).

Figure 8: Storing Microscope Video Program's Icon

Once it has been launched, a console is opened (Fig.9). The program checks every 20 seconds if a new video has been uploaded on the server. If so, the new video will be stored inside the computer (directory `C:/Video`) with the current data and hour as name in the following form: $YYYY - MM - DD - HH - mmss$, as shown in (Fig.10).

As shown in (Fig.9) on the console the user can read all the information about what the program is doing.

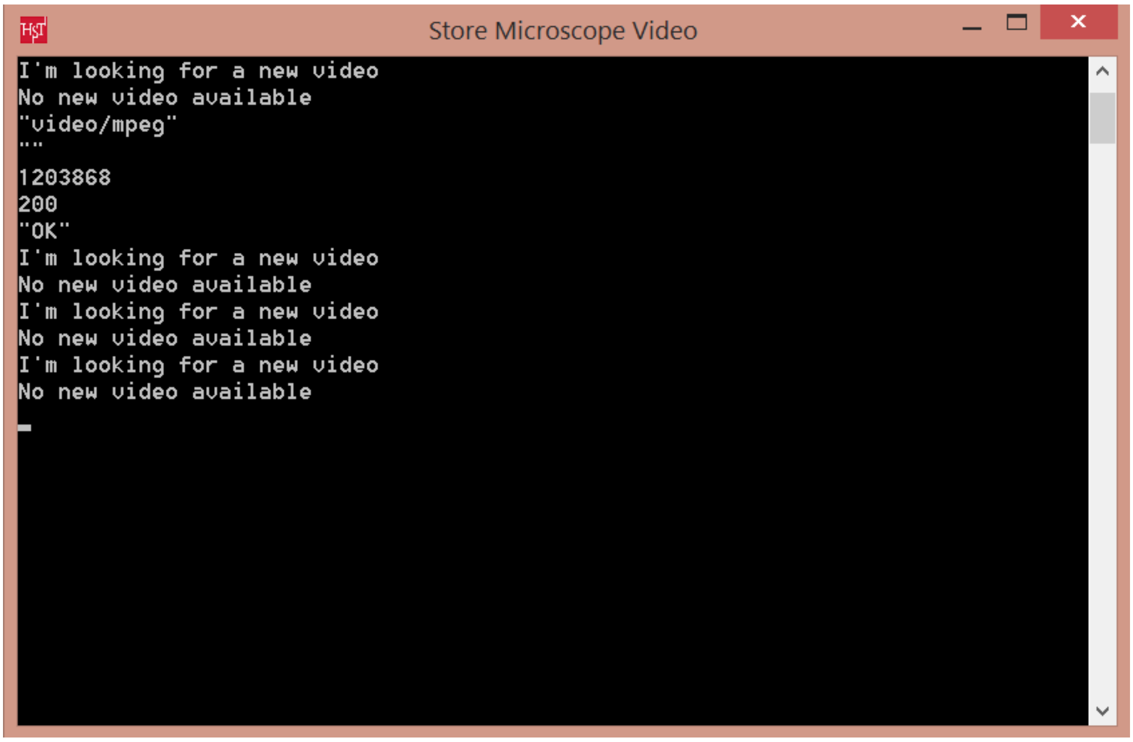


Figure 9: Storing Microscope Video Console

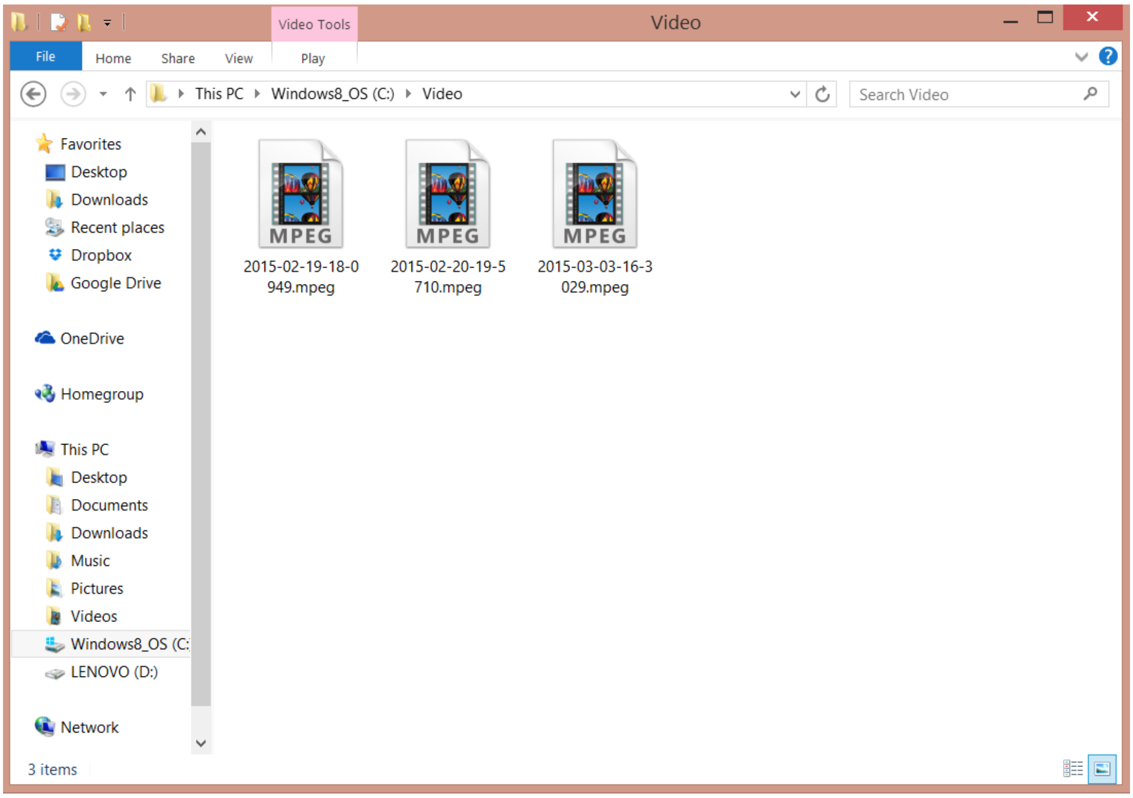


Figure 10: Video Stored in the Folder

Part I

HARDWARE

In this part of the thesis the hardware that has been designed in this system is explained. The design specification for this part are:

- make a sensor conditioning for pH and temperature sensors;
- make a driver for electrovalves which must be able to drives two different kinds of electrovalves, both of them require $80\ mA$ but one type at $24\ V$ while the other one at $12\ V$. To fulfill this aim a *DC-DC* converter has been designed, as well;
- make a *PCB* which supports and connects all the previous components and that is a *capes* for the Beaglebone Black, it has to be wedged on top of it.

1 CONDITIONING CIRCUIT AND ELECTROVALVES DRIVERS

1.1 PH CONDITIONING

1.1.1 The Sensor

A pH sensor is used to measure hydrogen ion activity

1.1.2 The Circuit

As already explained in (Sec.1.1.1), the pH sensor is a passive sensor, which means no excitation source is required because the sensor itself generates its own electrical output signal. In particular any variation of pH in input is transduced in a voltage variation in output.

The pH sensor is also bipolar, this means the voltage output may be both positive and negative, as shown in (Fig.11).

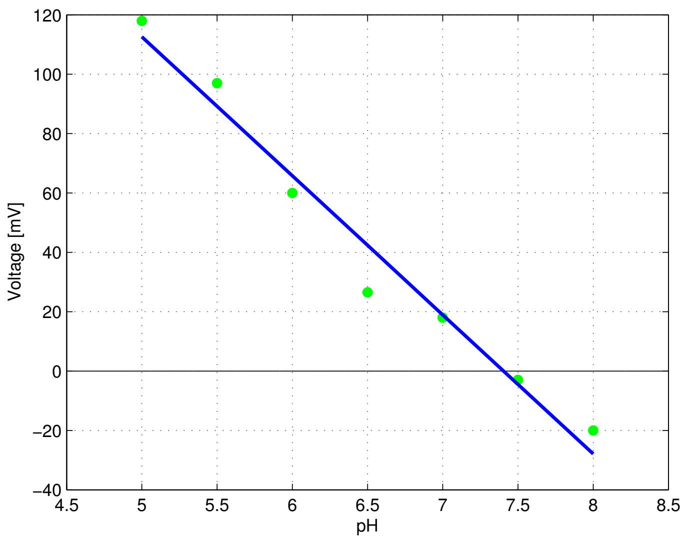


Figure 11: Typical pH-sensor transfer function

Resuming, it produce a voltage output that decreases linearly with pH of the solution being measured. The sensors give a sensitivity which ranges between 50 and 70 mV/pH (it depends from sensor to sensor), this means that, in order to well observe this variation, an amplification stage may be required.

The (Fig.12) shows the adopted solution for conditioning the pH sensor.
Fist of all, since the pH sensor produces a bipolar signal and this application operates on a single voltage supply, the signal has been level shifted. To achieve this first challenge the operation amplifier *U1* forces an off-set of $512\ mV$ to the pH sensor. Indeed, the *LM4140A-1.0* is a high precision low noise *LDO* (Low Drop Out) voltage reference which provides an accurate $1.024\ V$. This voltage has been halved by the $10\ K\Omega$ resistor divider. The *U1* is in voltage follower configuration, thus its output should be equal to the input, and it biases the reference electrode of the pH sensor with $512\ mV$, at low impedance. So, what the part of circuit made by *U1* and *LM4140A-1.0* does is to shift the bipolar pH sensor signal to an unipolar in order to be usable in the single-supply system.

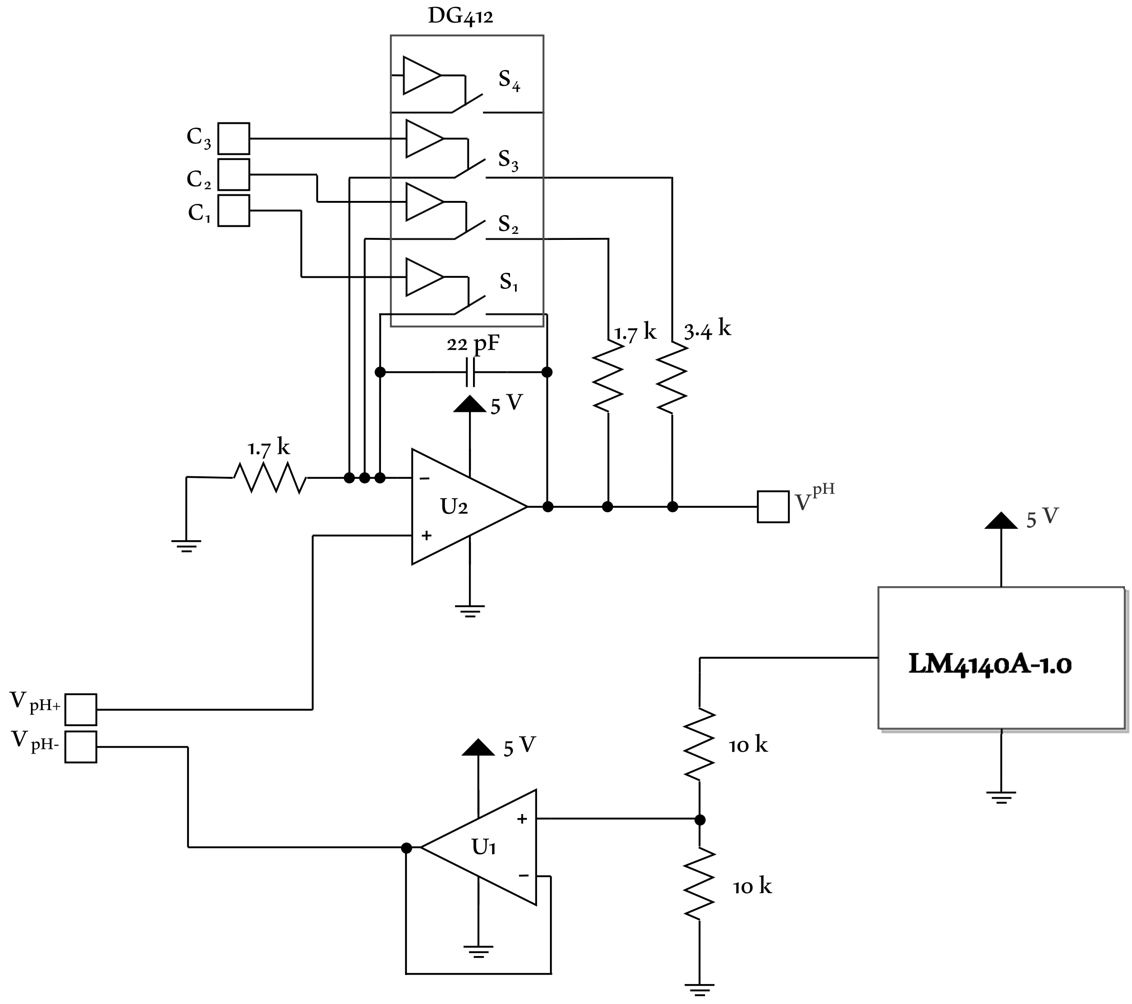


Figure 12: Conditioning circuit for pH sensor

Another challenge is given by the high impedance of the electrode. In fact the output impedance of the pH sensor is higher than $100\ M\Omega$. The circuit in (Fig.13) shows a typical connection of this sensor where the output voltage is given by:

$$V_{out} \simeq V_{in} = V_S - I_{bias} \cdot R_S \tag{1}$$

Thus, in order to reduce the error caused due to amplifier's input bias current a really low input bias current amplifier has to be chosen. For this reason, the *LMP7721* is used, it is has an ultra-low input bias current ($3 \pm 17\ fA$).

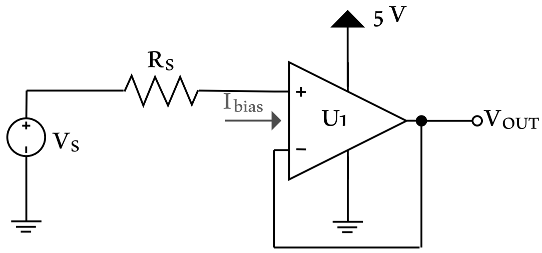


Figure 13: Error caused by Amplifier's Input Bias Current

In (Fig.12) both *U1* an *U2* are *LMP7721*. The second amplifier with the *DG412* represents a simple **PGA** (*Programmable Gain Amplifier*), where the resistors have been chosen to give the following gains:

- 1, when C_1 is asserted and the others are denied;
- 2, when C_2 is asserted and the others are denied;
- 4, when C_3 is asserted and the others are denied.

The feedback capacitor is used to ensure stability and holds the output voltage during the switching times. Indeed, in these slice of time the output node would be floated without the capacitor.
This PGA stage introduces an additional offset error of $75 \pm 470\ fV$, due to the bias current of the operational amplifier and R_{ON} of *DG412* ($25\ \Omega$). That voltage combined with the *LMP7721* offset (which is very higher than the first one) is approximately equal to $26\ \mu V$.

Since the environment in which the circuit is going to be used is a laboratory, so a really noisy place, the conditioning circuit for the sensor has to involve the design of a ***low-pass filter*** in order to reject the noise.

The circuit shown in (Fig.14) is a third order low-pass filter with a *Bessel* response. It has been designed in order to ensure a really flat-response in the pass band.
The parameter of the filter are:

1. *cutoff frequency* (f_c): $26.8\ Hz$, ;
2. *stop band attenuation*: $-28.2\ dB$ at *stop band frequency* (f_s) $60\ Hz$ (the line frequency in USA);
3. *Quality factor* (Q): 0.65;
4. *filter order*: third;
5. *filter response*: Bessel.

It's important that $Q < 0.707$ because otherwise would be some peaking in the filter response. While, in this case, as shown in (Fig.15), roll-off at the cutoff frequency is greater.
This filter also behaves as *anti-aliasing filter*, to prevent the aliasing components from being sampled during the analog to digital conversion.

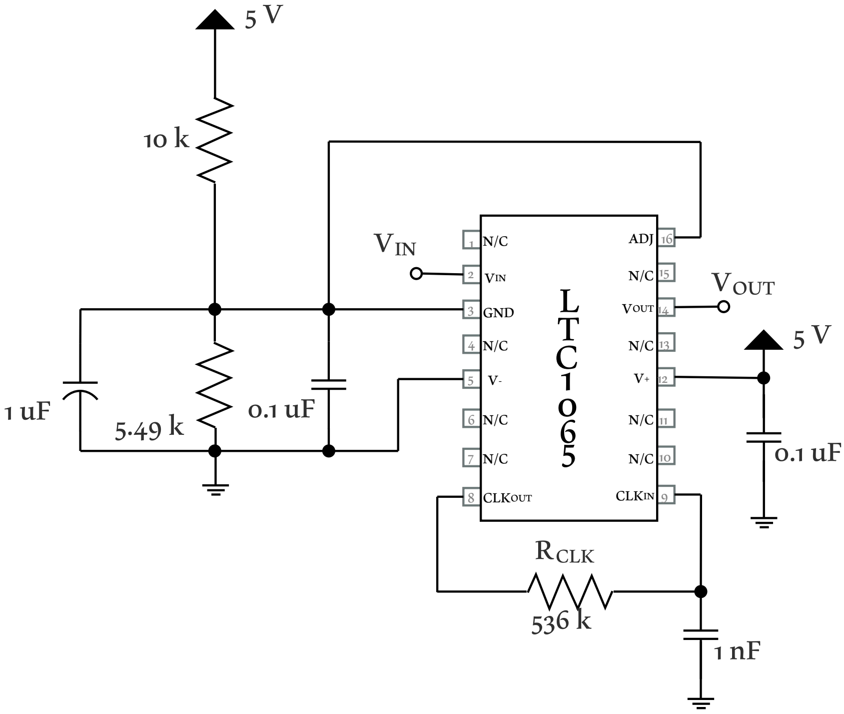


Figure 14: Low-Pass Filter Schematic

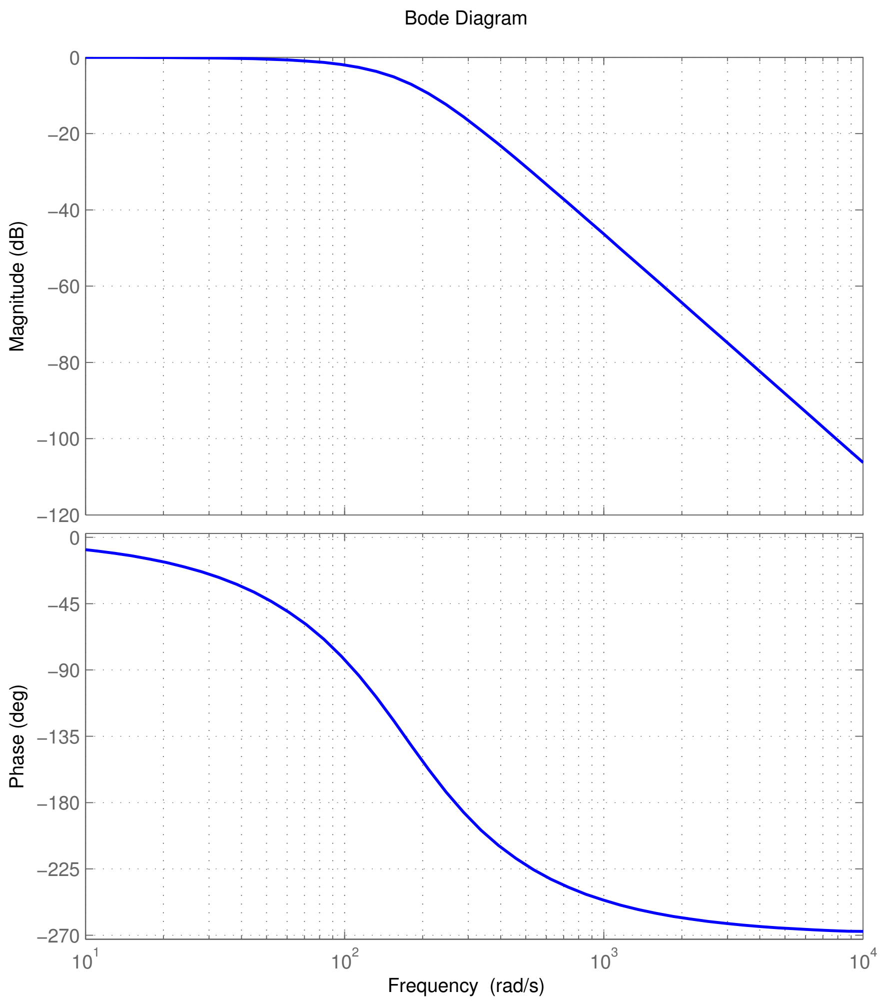


Figure 15: Low-Pass Filter Frequency Response

The output of this filter represent the input signal of the embedded ADC inside the Beaglebone Black.

Connecting together al this part we obtain the circuit in (Fig.16) where we can also see the general purpose input/output pin used to drive the *PGA* and the analog input used for the pH sensor. As it is explained in (Chap.4) `AN_2` is used to let the microcontroller know about the added offset.

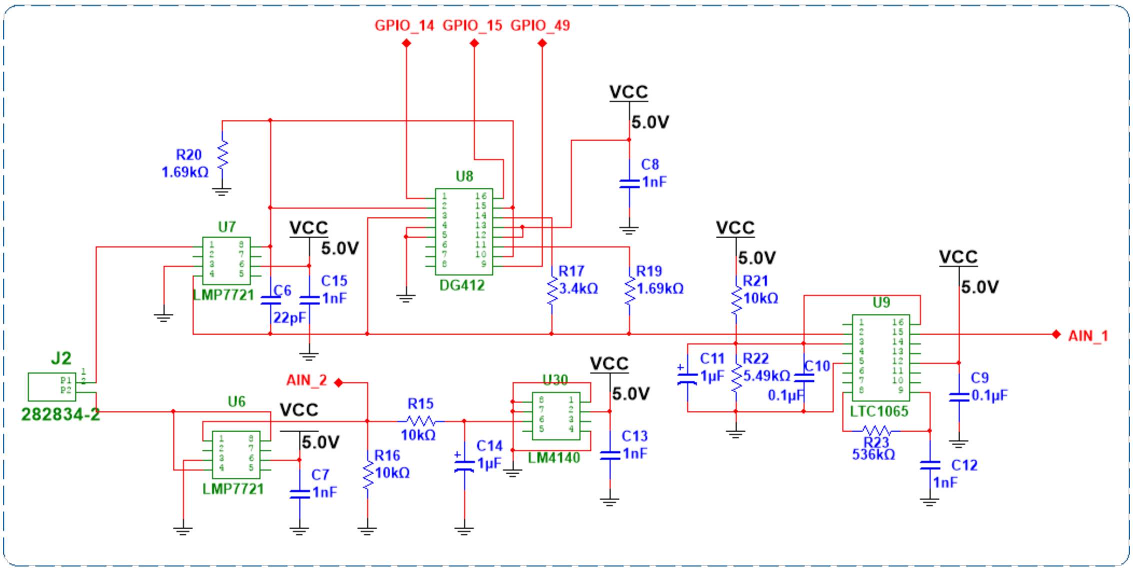


Figure 16: Acquisition Path for pH Sensor

1.2 TEMPERATURE CONDITIONING

1.2.1 The Sensor

1.2.2 The Circuit

As already explained in (Sec.1.2.1), the temperature sensor is a active sensor, which means excitation source is required because the sensor is resistor based so a current must be passed through it. Then, the corresponding voltage has to be measured in order to determine the temperature value.
So, any variation of temperature in input is transduced in a resistance variation in output.

The (Fig.17) shows the adopted solution for conditioning the temperature sensor.
In this connection the temperature sensor is excited by $680\ \mu A$, so the voltage V_T is given by the following equation:

$$V_T = 680\mu \cdot R_T \tag{2}$$

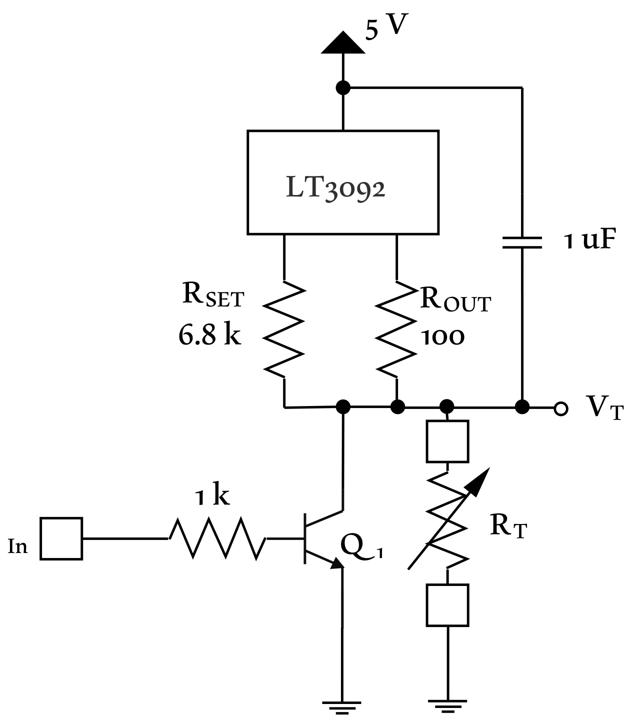


Figure 17: Conditioning Circuit for Temperature Sensor

In order to provide this amount of current a *LT3092* is used. It can supply an output current equal to:

$$I_{OUT} = 10\mu \cdot \frac{R_{SET}}{R_{OUT}} \tag{3}$$

To ensure the stability of the component, a feedback capacitor of $1\ \mu F$ is exploited. The transistor Q_1 is used to avoid the self-heating of the temperature sensor: when the temperature value has to be sampled In is denied, for the remaining time In is asserted, in this way the resistive sensor is by-passed, and the *Joule* effect is avoided.

For the same reason exposed in (Sec.1.1.2), also in this case a filter is needed, and, since the voltage value is almost the same, the used filter is equivalent to the previous on.

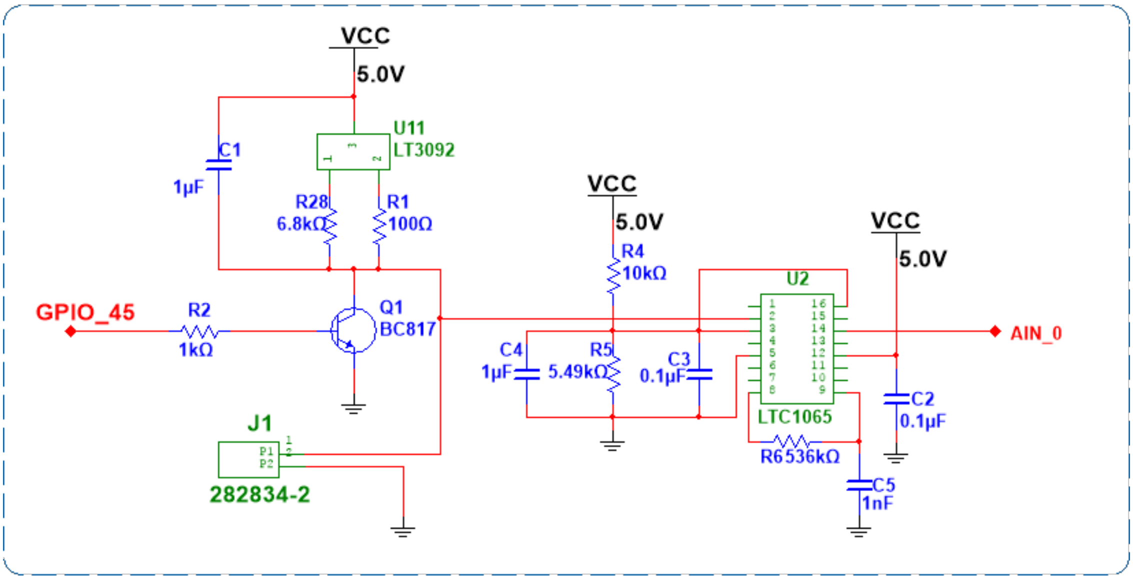


Figure 18: Acquisition Path for pH Sensor

1.3 ELECTROVALVES DRIVER

In order to allow the reverse control, from Google Glass to electrovalves, it is important to design a circuit that has to drive them from digital values provided by the *Beaglebone Black* (0 equal to $0\ V$, 1 equal to $3.3\ V$ and in both cases the maximum suppliable current is only $6\ mA$).

The electrovalves used are FESTO solenoid valves MH1. They require a voltage of $24\ V$ in DC and a current of $80\ mA$.

To fulfill this aim a low-side switch MOS has been used, as shown in (Fig.20).
The *Fairchild Semiconductor BS170 N-Chnnel MOS* has been chosen because of its low price and its capability of supporting a drain-source voltage of up to $60\ V$ and supplying a continuous drain current of up to $500\ mA$.

To protect the *BS170* from reverse inductive current surges due to the solenoid of the electrovalve, a *Vishay Semiconductors 1N4148 Diode* is used. It is able to support a re-

Figure 19: Electrovalves

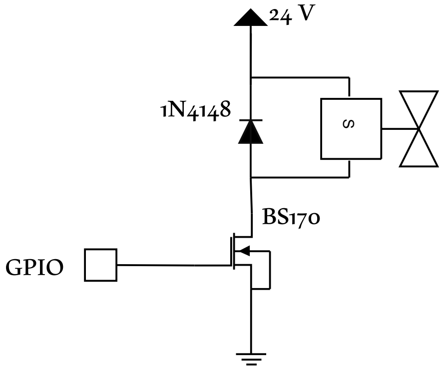


Figure 20: Driver for electrovalves

verse voltage of up to $75\ V$ and a continuous forward current of up to $150\ mA$.

As shown in (Fig.19) the number of electrovalves used is eight, so the previous driver has been replicated in order to obtain the circuit in (Fig.)

1.4 DC-DC CONVERTER

Since this system is supposed to drive different kind of electrovalves, which require a different value of voltage (but not in current) a *DC-DC converter* is used in order to convert the voltage supply from $24\ V$ to $12\ V$.

Using the *LT1374* the circuit in (Fig.22) has been designed, it is a constant frequency (equal to $500\ Hz$), current mode buck converter. It has an embedded clock and two feedback loops to control the duty cycle of power switch.

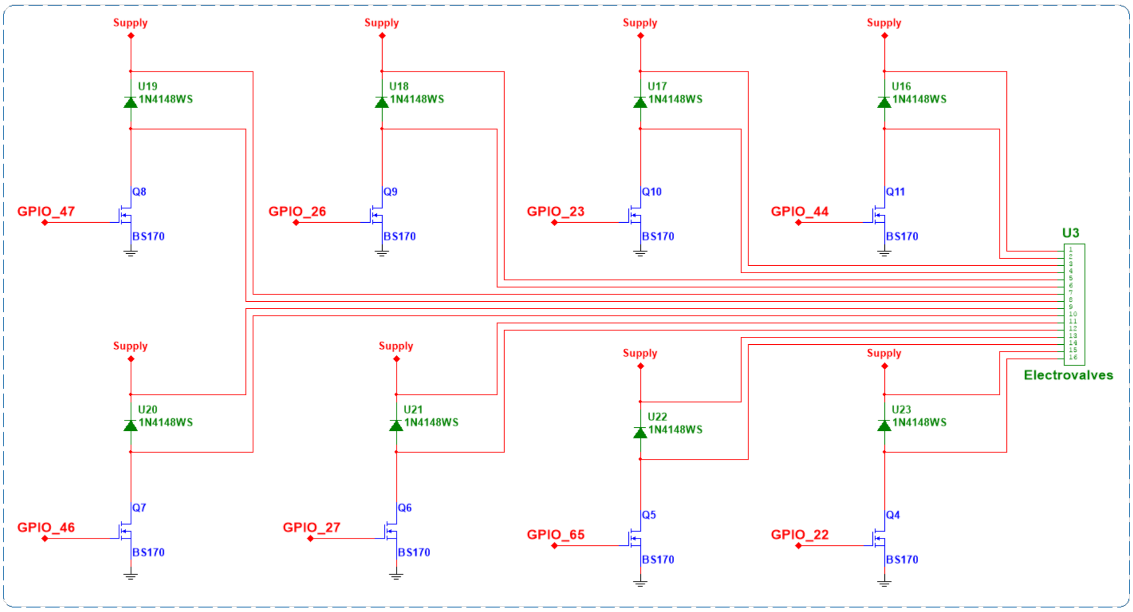


Figure 21: Electrovalves Driver Circuit

Trough a low-side switch, made with the *BS170*, it is possible to shutdown the converter from the software. When the *LT1374* is in shutdown, the supply current is reduced to $20\ \mu A$. As it is explained in (Chap.4) this is used to prevent regulator from operating when $24\ V$ are required.

1.4.1 Components Choice

All the components have been chosen with attention and for some reasons that are going to be explained belong.

FEEDBACK RESISTORS

The main behavior of the feedback pin on the *LT1374* is to set the output voltage, and this deals with selecting the resistors R_1 and R_2. They are related from each others by the following equation:

$$R_1 \quad \frac{R_2 \cdot (V_{OUT} - 2.42)}{2.42} \tag{4}$$

As suggested on datasheet of the component, the resistor between feedback pin and ground is $4.99\ k\Omega$. So, from the (Eq.4) results that the value of R_1 is $19.6\ k\Omega$.

INDUCTOR

The choice of inductor is a trade-off among:

- *physical area*, lower values of inductor mean lower size;

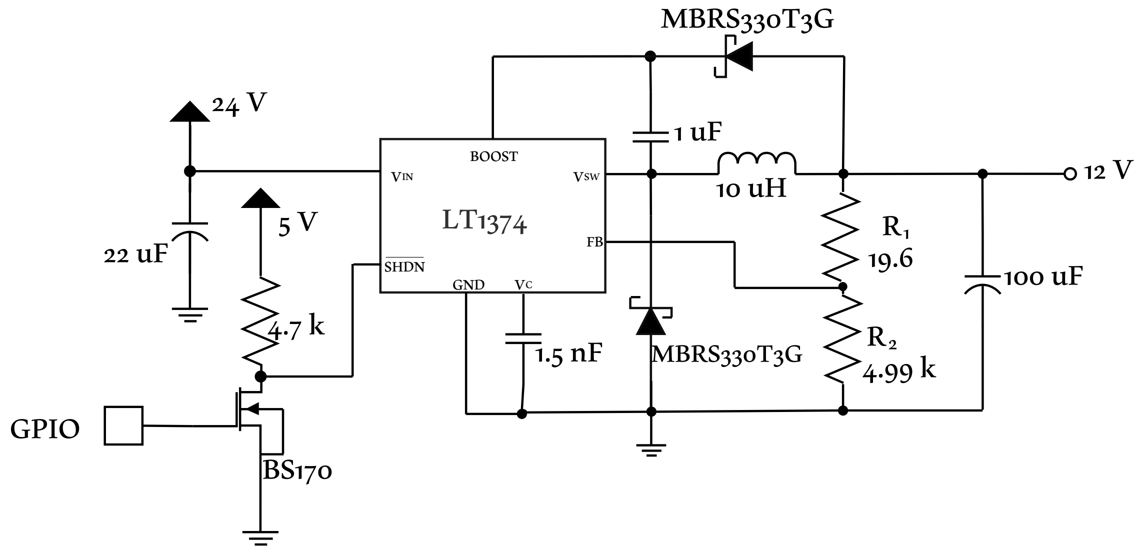


Figure 22: DC-DC circuit

- *output current*, higher values of inductor allow more output current because they reduce peak current ($I_{SW(PEAK)} \propto 1/L$)
- *ripple voltage*, higher values of inductor reduce the output ripple voltage.

A good choice is represented by $10\ \mu H$, with this inductor the maximum current peak (Eq.5) is equal to $1.24\ A$.

$$I_{SW(PEAK)} = I_{OUT} \quad \frac{V_{OUT} \cdot (V_{IN} - V_{OUT})}{2 \cdot f \cdot L \cdot V_{IN}} \tag{5}$$

OUTPUT CAPACITOR

The output capacitor determines the output ripple voltage, for this reason a small *Effective Series Resistance* (ESR) is required.
The frequency operation of *LT1374*, as already said, is equal to $500\ Hz$ and at this frequency any polarized capacitor is essentially resistive. As suggested from datasheet, for typical *LT1374* application the ESR has to range from $0.05\ \Omega$ to $0.2\ \Omega$, for this reason the output capacitor is a *solid tantalum capacitor*. The choice of $100\ \mu F$ is a good trade-off between output ripple voltage and physical area.

SCHOTTKY DIODE

The chosen diode is *On Semiconductor MBR330* because of its capability of supporting a $3\ A$ average forward current and $30\ V$ reverse voltage.
Indeed, the reverse voltage is approximately $12\ V$ (the output voltage), while the average forward current is given by the (Eq.6).

$$I_{D(AVG)} = \frac{I_{OUT} \cdot (V_{IN} - V_{OUT})}{V_{IN}} \tag{6}$$

The (Eq.6) will never yield values higher than $3\ A$, neither in worst-case scenario.

BOOST CAPACITOR

The boost capacitor has been chosen based on the voltage that has to support, which is basically equal to the output voltage ($12\ V$) and the (Eq.7) provided by *LT* on datasheet of the component. In this application result that its minimum value is equal to $1.5\ nF$.

$$C_{MIN} = \frac{(I_{OUT}/50) \cdot (V_{OUT}/V_{IN})}{f \cdot (V_{OUT} - 3)} \tag{7}$$

1.4.2 Relay

Since the electrovalves may need $12\ V$ or $24\ V$ a way to switch between this two voltages supplies is needed. The circuit shown in (Fig.23) has been used for this purpose.
It allows the switching trough the firmware.The circuit uses a optocoupler, the DPC-817C, to isolate the Beaglebone Black to the relay, and prevent in this way that pounces produced by magnetic part of relay reach the general purpose pin of the Beglebone itself. The relay used is the G5LA1CF24DC and, as happened in (Sec.1.3), a diode has been exploited to preserve the transistor used as voltage controlled switch from broking.

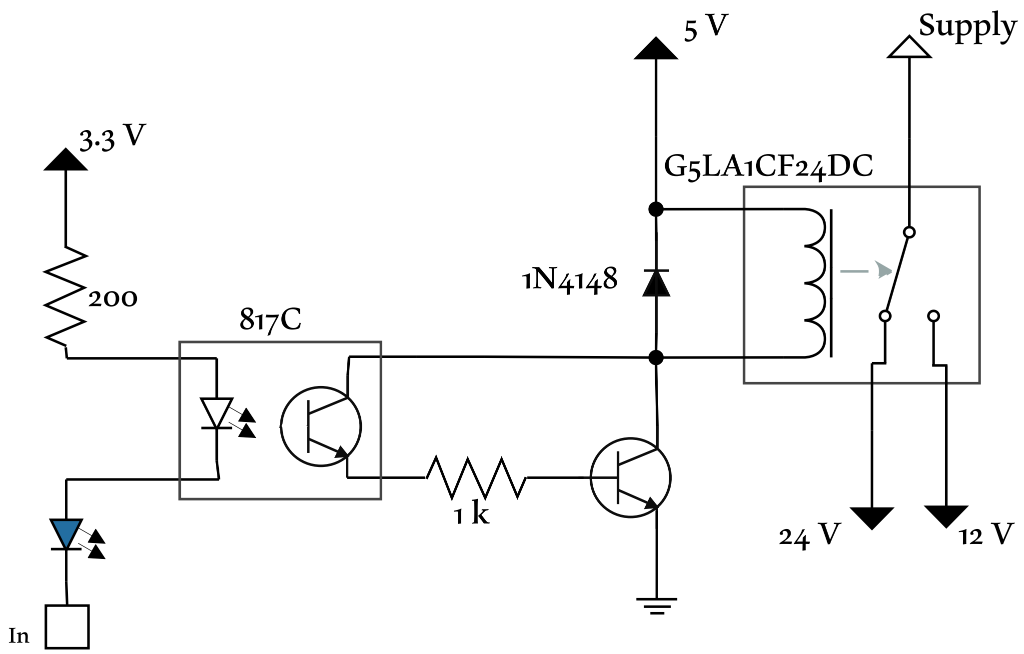


Figure 23: Relay circuit

Summary, in the circuit represented in (Fig.23) the *Supply* is the voltage which is going to be provided to the electrovalves. When the *In* signal is asserted, the relay is in its normal connection, son *Supply* is tied to $24\ V$. On the other hand, when *In* is denied relay is excited and *Supply* is tied to $12\ V$.

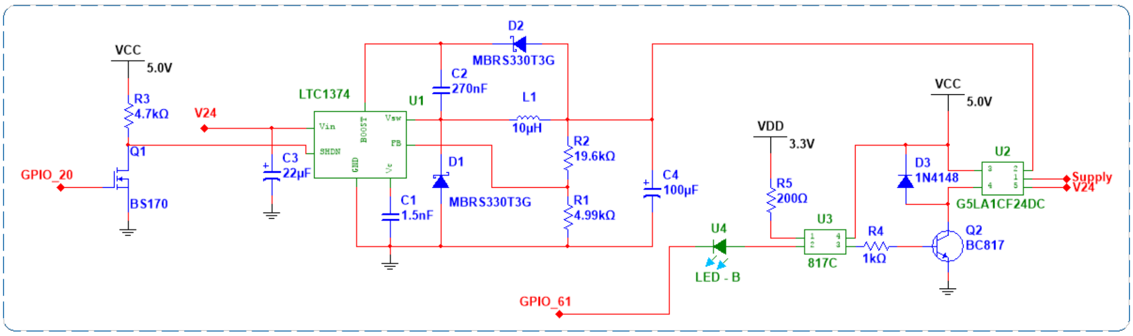


Figure 24: Electrovalves Supply Circuit

The circuit in (Fig.24) shows the connection between *DC-DC* circuit and the switching one, all of this is necessary to correctly supply the different kind of electrovalves.

2 PCB

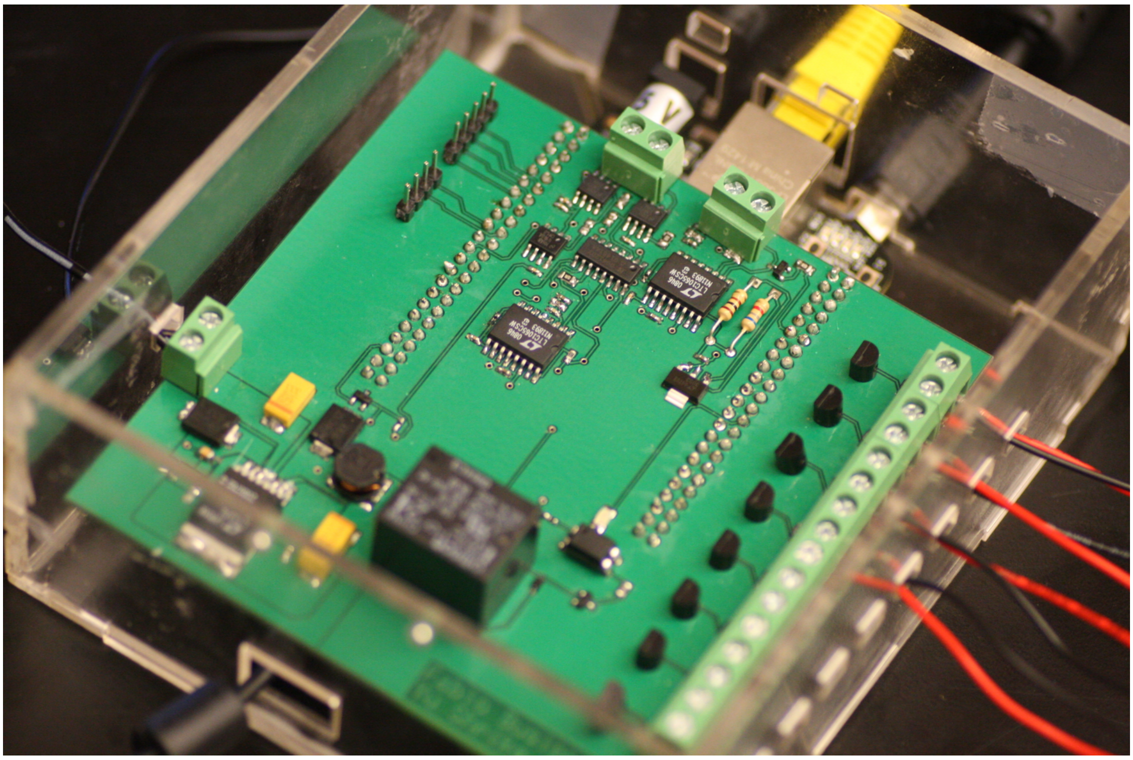


Figure 25: Final system mounted on a PCB

All the hardware and the circuit described so far has been mounted on a Printed Circuit Board (*PCB*) that is supposed to be a *cape* of the Beaglebone Black. This means that the whole physical structure has been made to be attached on the headers of the board. In (Fig.26) all the circuit that has to be made on the *PCB* is shown.

The PCB has been designed in a two-layer board ($100\ x\ 100\ mm$) using the *National Instruments Circuit Design Suite*, in particular *Multisim* to carry out the schematic and *Ultiboard* for what concern the PCB.
The design has followed the guidelines for reduced electromagnetic interface (*EMI*). First of all, since Surface-mount devices (*SMD*) are better than Through-hole components (*THD*) in dealing with RF energy, because of reduced inductances and closer component placements available (Instruments [November 1999]), where there was a choice, *SMD* components have been used.

Particular attention has been paid for the *DC-DC* converter layout, because a wrong *PCB* design for switching power supply often means failure. Moreover, in these terms, what is good for *EMI* is also good in terms of functional stability for the regulator.

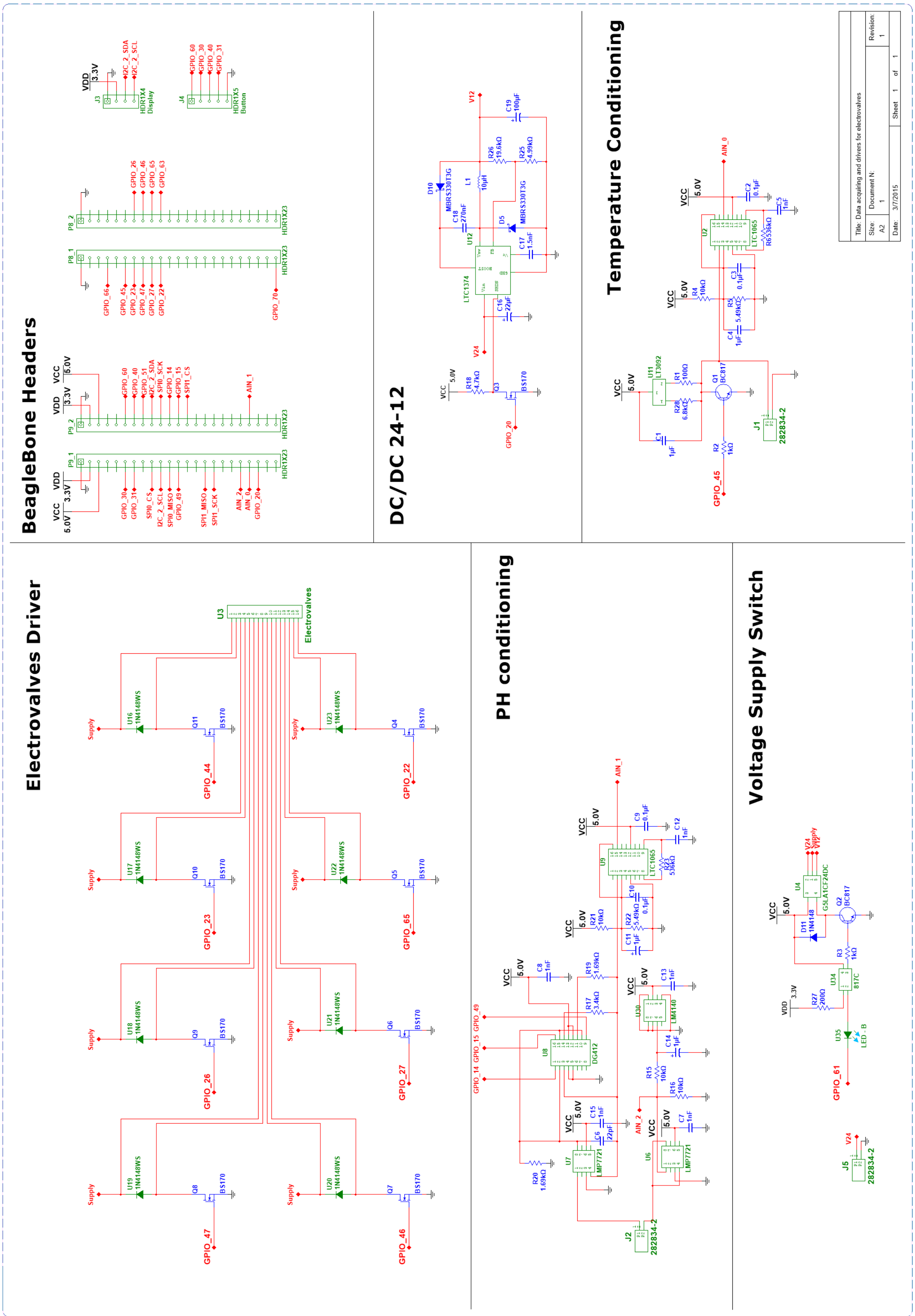


Figure 26: Schematic of Complete Circuit

The circuit in (Fig.27) is schematically a common buck regulator. In that figure, with a blue circle, is highlighted the high speed switching current path: the loop which produces the highest *EMI*. Indeed, in the blue loop flows a fully switched alternated current, and for this reason it is also referred as **hot loop**.

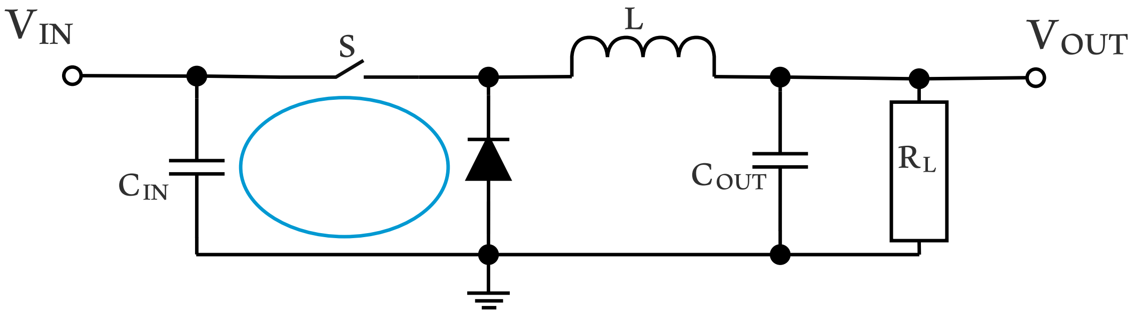


Figure 27: *DC-DC* High Speed Switching Path

In order to ensure clean switching and reduce *EMI* the minimum lead length is required for reducing the radiating effect of the hot loop as much as possible: and so it has been done, as can be seen from (Fig.28).

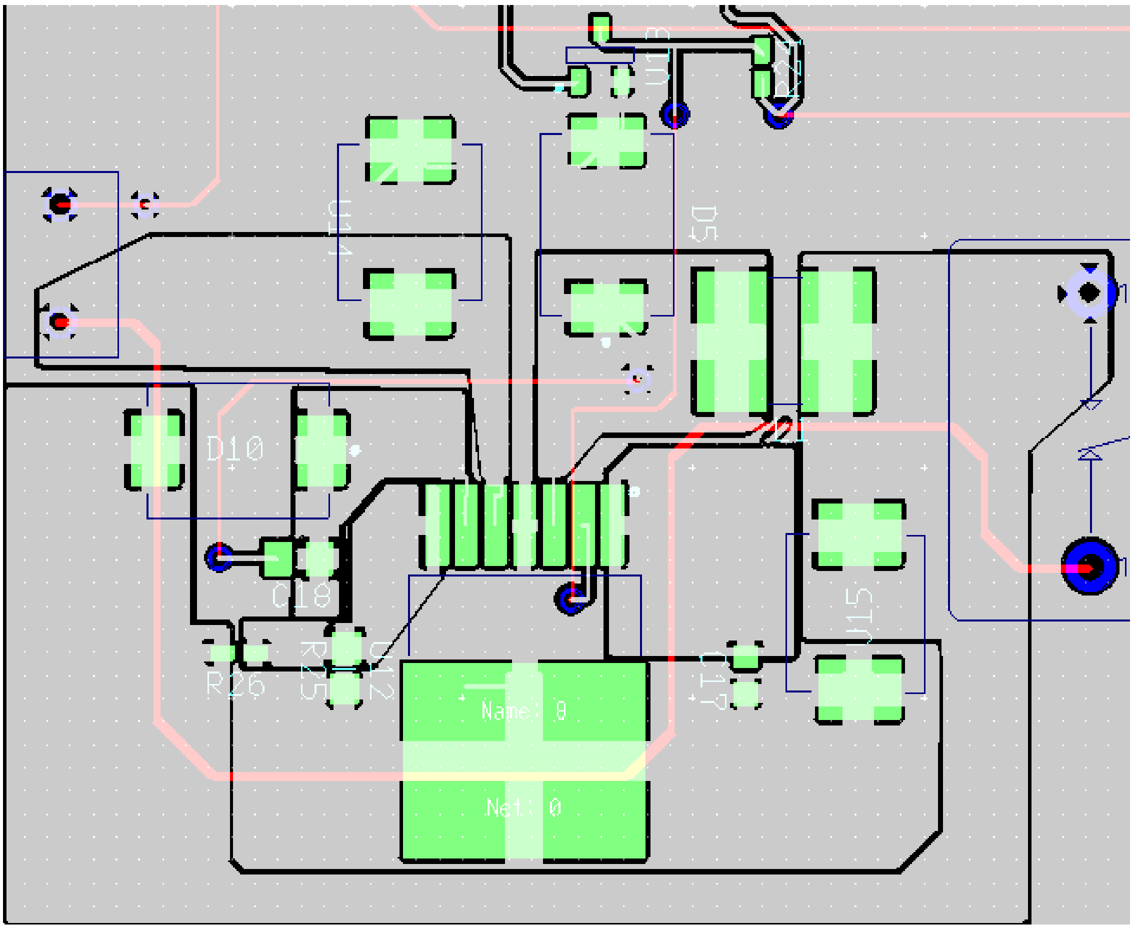


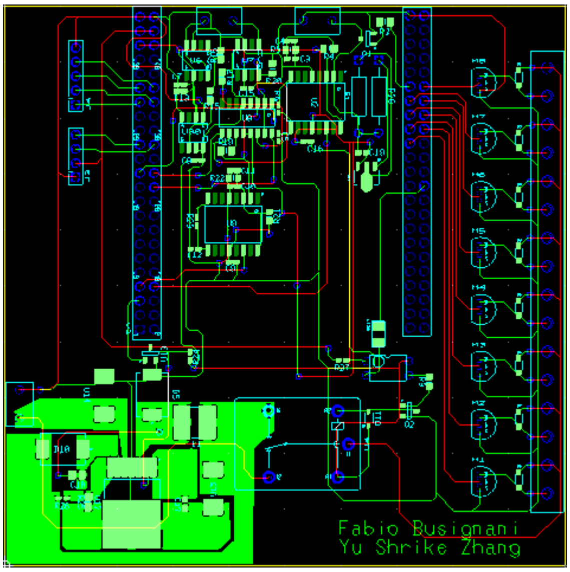
Figure 28: *PCB* Layout of *DC-DC*

In (Fig.28) the *PCB* layout for *DC-DC* converter has been shown, in which we can see that:

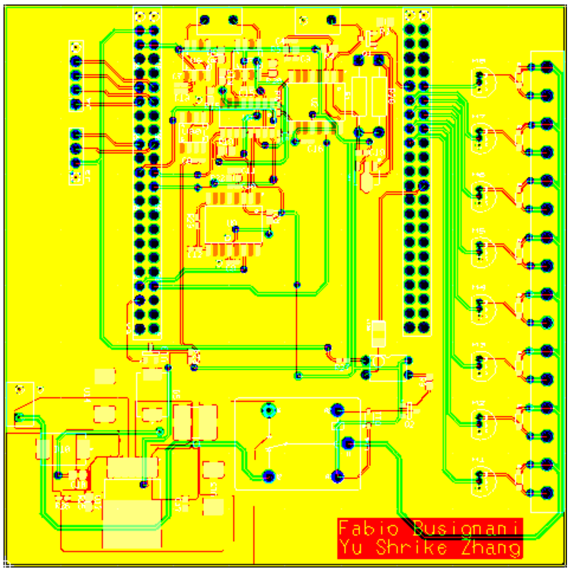
- the magnetic radiation is minimized by keeping by keeping catch diode and the input capacitor leads as short as possible;
- the electric radiation is minimized by reducing the area and length of all traces connected to the switch and boost pins.

Moreover, in order to reduce the noise on the feedback, that is translated in error on output voltage, the switch node and the feedback resistors are kept as far as possible from each others.

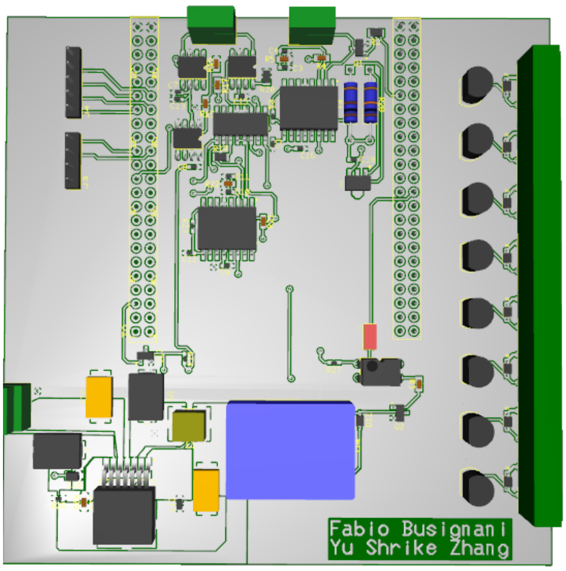
The (Fig.29) shows the *PCB* layout without ground plane (Fig.29a), then with both top and bottom ground plane (Fig.29b) which help with heat dissipation and *EMI* reduction. In (Fig.29c) and (Fig.29d) the 3-D model generated using *Ultiboard* and the final real result are compared.



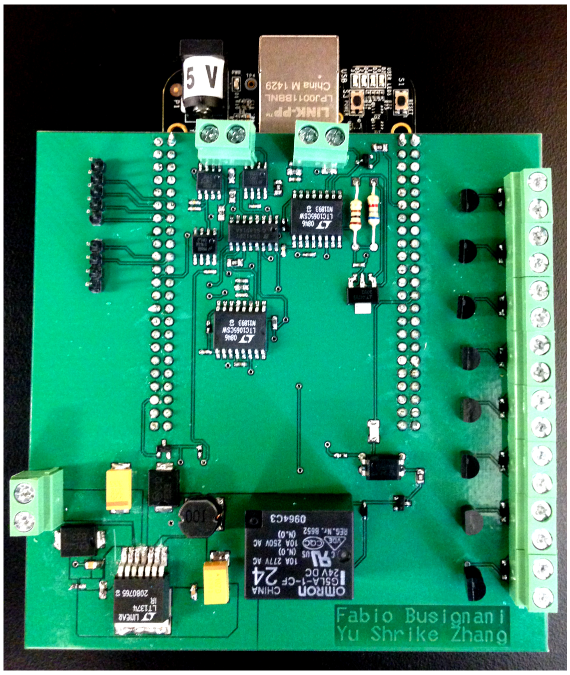
(a) *PCB* Layout Withot Ground Plane



(b) *PCB* Layout With Both Top and Bottom Ground Plane



(c) *PCB* 3-D Model View



(d) *PCB* Real Result

Figure 29: PCB of the System

Part II

FIRMWARE

3 INTRODUCTION

4 EMBEDDED LINUX

Part III

SOFTWARE

5 GOOGLE APP ENGINE

6 | MICROSCOPE VIDEO STORING

Part IV

GOOGLE GLASS APPLICATION

7 INTRODUCTION

7.1 FIRMWARE

7.2 VIDEO STORING SOFTWARE

7.3 GOOGLE APP ENGINE

7.4 GLASSWARE

Part V

CONCLUSION AND APPENDIX

8 | TEST AND PERFORMANCE

A CODE

A.1 FIRMWARE

A.2 VIDEO STORING SOFTWARE

A.3 GOOGLE APP ENGINE

A.4 GLASSWARE

Instruments [September 2008–Revised April 2013]

LIST OF FIGURES

LIST OF TABLES

BIBLIOGRAPHY

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