CELL EXTRACTOR

A.C. GHEORGHE

Valahia University of Targoviste, Faculty of Electrical Engineering, Electronics and Information Technology, Romania
E-mail: gheorghe_andrei89@yahoo.com

Abstract. *The study aims for the development of a system for cellular extraction, developed at the level of an experimental model, with the help of which the user can generate a series of sessions of cellular extraction from the cultures of specific cells. To move to the prototype level, the system that will materialize in an specialized equipment for cell extraction and inter / intra-cell injection needs a developed user interface, so that the equipment as a whole is easy to use by the human operator. The present project provides a viable technical interfacing solution for the above mentioned equipment, using the Raspberry Pi hardware resources and the Python C. software resources. Demonstrating the capability of the Raspberry Pi - Python technical tandem for the biomedical equipment to be built is the essence of this project, and the further development of a specialized user interface is a natural step.*

Keywords: Raspberry Pi, cellular extraction, Python, user interface

1. INTRODUCTION

The field of research in bio-medical sciences involves a series of current working equipment, which allow the operation with the biological material developed in the cell cultures or living tissues. There are a number of specialized companies worldwide that develop and manufacture such equipment. The manipulation of the biological material involves extraction and transport to the operating areas, and this facts requires a technical-scientific approach within them microfluidics domain. The present project presents a system of cell extraction, realized at the experimental model level, with the help of which a series of sessions of cellular extraction from the cultures of specific cells can be generated. To move to the prototype level, the system that will materialize in a specialized equipment for cell extraction and inter / intra-cell injection needs a developed user interface, so that the equipment as a whole is easy to use by the human operator. The main projects provides the development of the hardware equipment and a viable technical interfacing solution for the above mentioned equipment, using the Raspberry Pi hardware resources and Python C. software resources. Further development of a specialized user interface is a natural step.

In this material are presented a series of generalities about the aspects of specialties achieved on the way to the realization of the multifunctional biomedical system, intended for both cell extraction and microfluidic transport of cellular biological material, as well as inter / intra-cellular microinjection. The basic pneumatic support of the system is mentioned, by presenting the main component

that is a part of the technical assembly, the electronic control and control subsystem referring to them, through an electrical scheme based on relays and transistors functionally coordinated by a controller that communicates with the computer. The matter is solved in a simplistic way but with a direct reference to an implemented technical reality, the matter of which has led to the design of the source program developed in the Python C language, a program that is the basis for the effective realization of the alpha variant of the user interface. The claim of achieving the final interface that will be integrated in the prototype biomedical equipment is not issued, but it is a functional application that opened the way to a viable technical solution when I refer to the finalization of the first commercial interface.

1.1 Microfluidics

Microfluidics has been determined as a study of the behavior of fluids (or those inside them), for example, colloids, discrete nanoparticles or individual cells, in channels a couple of micro meters or around microstructures. Although the micro channels may be relatively long (for example, several tens of mm), they are still called micro channels as long as a critical size (e.g, channel width or channel depth or tube radius) is micro-scale. Micro-fluid channels, for example, can be used to transport, guide, mix or manipulate fluids and we can see in Figure 1 a basic microfluidic chip.

Figure 1. Basic microfluidic chip.

1.2 Microinjection

Microinjection is the use of a glass micropipette to inject a liquid substance at a microscopic or granular level. The target is often a living cell, but may also include intercellular space. Microinjection is a simple mechanical

process that usually involves an inverted microscope with a magnification power of about 200x (although sometimes it is done with a 40-50x stereo dissection microscope or a traditional compound microscope with similar power to a model reversed). In Figure 2 we can see the microinjection principle.

Figure 2. Microinjection principle.

1.3 Cell Extraction

Due to cellular heterogeneity, the analysis of endogenous molecules in single cells has a significant interest and has major implications. While micromanipulation or cell sorting followed by cell lysis is already used for subsequent molecular examinations, approaches for direct extraction of live cell content remain a challenging but promising alternative for obtaining non-destructive sampling and preserving the cellular context. This approach has uncovered the ability of cells to withstand the extraction of up to a few picoliters and opens up opportunities for studying cell dynamics and cell-cell communication under physiological conditions at a single cell level. In Figure 3 we have the cell extraction principle.

Figure 3. Cell extraction principle

1.4 Pneumatic Support

The main part of the pneumatic support is a vacuum generator from Festo (Figure 4), the vacuum generator has the next key features: rapid purging of vacuum for safe placement, M12 plug for the central electrical connection, monitoring and visualization of the vacuum pressure via the LCD display that shows the pressure in Bars, QS fitting, fast vacuum build-up with the help of the

integrated solenoid valve for controlling the compressed air supply.

Figure 4. Festo vacuum generator

1.5 Electronic control

The electronic control is a simple design that contains relays and transistors (Figure 5), The schematic shown below is just for the control of the vacuum generator and the valve used to make the extraction process happen, the control is done by the Raspberry Pi board that engages the vacuum generator based on the reading of the vacuum sensor (automatic process), the board also controls the valve via the user interface (manual process).

Figure 5. Electronic control schematic

1.6 Raspberry Pi Development Board

Raspberry Pi (Figure 6) is known as the most accessible programmable computer in the world. Its features and Linux-based open source platform make it versatile, suitable for common applications such as home entertainment, internet browsing, multi-media viewing, but is most commonly used in development applications such as automation, robotics, etc. Its performance is given by a Broadcom BCM2837 64bit Quad Core processor rated at 1.1GHz (1.2GHz - Turbo), 1GB RAM and video processing that has 4 graphics processor, rated at 300MHz offering Full HD 1080p support. In terms of connectivity you will find 1 x HDMI port, 1 x 4-pole connector for analog AV, 4 x USB 2.0 port, 1 x RJ-45 port for LAN, 40 x GPIO pins (Figure 7) for attaching sensors and modules, Micro SD card slot, Micro USB connector for power

supply, CSI connector for connecting Raspberry Pi cameras, DSI connector for display / touch-screen.

Figure 6. Raspberry Pi 3 B+ overall look

Peripherals	GPIO	Particle	Pin #	Pin #	Particle	GPIO	Peripherals
	3.3V		1	X	X	2	5V
I2C	GPIO2	SDA	3	X	X	4	5V
	GPIO3	SCL	5	X	X	6	GND
Digital I/O	GPIO4	DO	7	X	X	8	TX
	GND		9	X	X	10	RX
Digital I/O	GPIO17	D1	11	X	X	12	D9/A0
Digital I/O	GPIO27	D2	13	X	X	14	GND
Digital I/O	GPIO22	D3	15	X	X	16	D10/A1
	3.3V		17	X	X	18	D11/A2
SPI	GPIO10	MOSI	19	X	X	20	GND
	GPIO9	MISO	21	X	X	22	D12/A3
	GPIO11	SCK	23	X	X	24	CE0
	GND		25	X	X	26	CE1
DO NOT USE	ID_SD	DO NOT USE	27	X	X	28	DO NOT USE
Digital I/O	GPIO5	D4	29	X	X	30	GND
Digital I/O	GPIO6	D5	31	X	X	32	D13/A4
PWM 2	GPIO13	D6	33	X	X	34	GND
PWM 2	GPIO19	D7	35	X	X	36	D14/A5
Digital I/O	GPIO26	D8	37	X	X	38	D15/A6
	GND		39	X	X	40	D16/A7

Figure 7. Raspberry Pi 3 GPIO pins datasheet

2. THE PRINCIPAL OF FUNCTIONING

In Figure 8 we have the block diagram of the extraction system, where the purpose of this project was to realize the control interface, the electric block and the valve subsystem. The user enters the data through the interface on the touchscreen display which consists of 3 sliders where the user can set the frequency, the filling factor and the number of pulses. The data is sent to the microcontroller for processing and the microcontroller operates the valve subsystem via an electrical block which is composed of relays and transistors used for signal amplification.

Figure 8. Block diagram

The device has the ability to concentrate the extraction force on a very small area, centered on the cell. This is possible due to a very high microfluidic switching frequency, allowing the use of large depressions on small units of time. In Figure 9 you can see the first version of cell extractor. The applicability of the device is for research in the field of cellular biotechnology (the scope of applicability can be extended to dry tissues in the field of oncology and microinjections). The physical resolution of the device depends on the mechanical constants of the valve type element (these constants differ depending on the requirement of the minimum volume conveyed, so that the elements will differ for nanolitres quantities compared to picolitres going up to femtoliters). The electronics used to make the device are common, but the way it is combined electronically with mechanics has led to obtaining a mechatronic system with high performance for a special equipment in the field of cellular biotechnology research.

Figure 9. Cell extractor v1.0

2.1 Software application

The software application (Figure 10) is made specially for the Raspberry Pi development board, the programming language is Python C and for the user control interface the Tkinter module is used which is the standard Python interface. The control interface of the valve subsystem is composed of 3 slider type buttons that set the frequency, the filling factor and the number of impulses, 2 buttons for start / stop and exit button from the application, to mention that the exit button is present only in the debug version.

Figure 10. User interface

2.2 Cell Extraction

In Figure 11 we can see an adherent cell and the extraction tip placed next to the cell that we want to extract from the cellular culture. Operating the system is easy, once the user has selected a cell, he can place the extraction tip of the machine next to it and choose from the interface the fill factor, frequency and the number of pulses need to gently extract the cell.

Figure 11. Cell extraction adherent cell

After the user chooses the settings for the extraction the cell is gently extracted from the cell culture as we can see in Figure 12.

Figure 12. Cell extracted

3. CONCLUSIONS

The Raspberry Pi 3 minicomputer, in combination with a touchscreen display, is a special hardware support for enhancing a user interface for the equipment that is intended to be used in a field as demanding as that of Biomedical Research. The Python C programming language is one of the most sought after specialists, for its simplicity and functional robustness, which offers programming possibilities for the interconnection of the Raspberry minicomputer with other controllers in the system, in a very viable and stable environment.

The theme of the project, namely to develop through Python C language, is a viable solution for interfacing a biomedical equipment for easy and useful use. It is a good start that opens the way for future efforts with professional results in the field of HMI (Human Machine Interface).

4. REFERENCES

- [1] K. Kearney, W. Freeman, Creative Projects with Raspberry Pi, Raspberry Pi Foundation, 2017.
- [2] E. Matthes, Python Crash Course: A Hands-On, Project-Based Introduction to Programming, No Starch Press, 2015.
- [3] D. Singh, Fundamentals of Optics, PHI Learning Pvt. Ltd, 2015.
- [4] Al Swigart, Automate the Boring Stuff With Python: Practical Programming for Total Beginners, No Starch press, 2017.
- [5] B. Lubanovic, Introducing Python: Modern Computing in Simple Packages, O'Reilly Media Inc., 2015.