# AUTOMATIC AND NON-INVASIVE CONTINUOUS GLUCOSE MONITORING IN PAEDIATRIC PATIENTS

Roberto Franchini

Researcher, Institute of Clinical Physiology, National Research Council, Lecce Italy

**Abstract**

*Glycated haemoglobin does not allow you to highlight the effects that food choices, physical activity and medications have on your glycaemic control day by day. The best way to monitor and keep track of the immediate effects that these have on your blood sugar levels is self-monitoring, therefore the use of a glucometer. Thanks to this tool you have the possibility to promptly receive information that helps you to intervene in the most appropriate way, bringing or keeping your blood sugar levels as close as possible to the reference values indicated by your doctor. Currently, blood glucose meters are used to measure and control blood glucose. Diabetes is a fairly complex disease and it is important for those who suffer from it to check their blood sugar (blood sugar) periodically throughout the day to prevent dangerous complications. Many children newly diagnosed with diabetes and their families may face unique challenges when dealing with the everyday management of diabetes, including treatments, adapting to dietary changes, and the routine monitoring of blood glucose. Many questions may also arise when selecting a blood glucose meter for paediatric patients. With current blood glucose meters, even with multiple daily self-tests, high and low blood glucose levels may not be detected. Key factors that may be considered when selecting a meter include accuracy of the meter; size of the meter; small sample size required for testing; ease of use and easy-to-follow testing procedure; ability for alternate testing sites; quick testing time and availability of results; ease of portability to allow testing at school and during leisure time; easyto- read numbers on display; memory options; cost of meter and supplies. In this study we will show a new automatic portable, non-invasive device and painless for the daily continuous monitoring (24 hours a day) of blood glucose in paediatric patients.*

**Keywords**

*Glucose, glucometer, diabetes,blood glucose monitoring, Arduino, non-invasive examination.*

## 1. INTRODUCTION

Glucose is the main source of energy for the cells in our bodies and the only short-term energy source for the brain and nervous system. For this reason, a constant supply of ready-to-use glucose is required and an almost constant blood glucose level is maintained.

During digestion, the carbohydrates consumed with the meal are broken down into glucose and other nutrients and absorbed by the digestive system. From here, they pass into the blood and circulate throughout the body. Normally, blood sugar rises slightly after a meal and, in response to this phenomenon, the pancreas releases insulin (hypoglycemic hormone) into the blood. The amount of insulin released is proportional to the size and content of the meal. Insulin contributes to the entry of glucose into the body's cells, where it is converted into energy [1]. When glucose enters cells and is broken down (metabolized), its levels in the blood are lowered and the pancreas reduces the release of insulin.

DOI : 10.5121/hiij.2023.12401 

If this regulatory mechanism involving insulin and blood glucose is working properly, blood sugar remains fairly stable. Conversely, if this regulation is altered, blood sugar increases, the body tries to restore balance by increasing insulin production.

Diabetes is the most common disease that results from the imbalance between glucose levels and insulin levels. Type 1 diabetes is a worldwide chronic disease caused by a disorder of glucose metabolism affecting nearly millions adults, as well as increasing in children under the age of 18 [1]. Type 1 diabetes occurs when the body is unable to produce insulin to lower blood sugar. Usually in type 1 diabetes, the insulin-producing cells (beta cells of the pancreas) are destroyed by the body's immune system (autoimmunity phenomenon)[1]. Type 2 diabetes, on the other hand, results from the combination of insulin resistance (reduced cell response to the action of insulin) and insufficient insulin production [2].

Diabetics who are given insulin to control their blood glucose levels must have their blood glucose selfmonitoring several times a day. Normally, this involves the use of a glucometer that allows the measurement of blood sugar on a drop of capillary blood obtained through a lancing needle and deposited on a stick. Based on this blood glucose, the insulin dose is adjusted [3].

While glycaemic monitoring is a practice for adults, it is different for children. In paediatric patients, monitoring should be done periodically by parents. Additionally, preschool and school-age children may not be able to identify and self-report hypoglycaemic episodes. Safe management of paediatric patients can often require more frequent blood glucose tests, particularly if a child has not eaten well [4]. This type of monitoring, in addition to predicting many finger pricks, provides only the instantaneous blood glucose value at the time of the test, and does not allow a continuous measurement of blood glucose, nor does it give information on the trend of blood glucose and on the up and down variations the bass [3][5].

Finally, parents reported on their child's sleep disturbances as a result of nighttime blood glucose monitoring [1].

However, sensors for self-monitoring of blood glucose have recently been launched on the market, which adopt the innovative Flash Glucose Monitoring (FGM) system[5].

It is a blood glucose measurement system that is innovative precisely because it detects the amount of blood glucose without the need to use disposable strips and without parents wake their child [1][5].

In this paper we will show a new automatic device wearable for continuous glucose monitoring system (CGMS). The system is a daily continuous monitoring (24 hours a day) of blood glucose in a non-invasive, without experiencing any discomfort and painless way. The developed device uses the non-invasive sensor of the commercial FGM FreeStyle Libre system.

FreeStyle Libre is composed by a Sensor and a device reader. Blood glucose detection occurs only when the device reader is manually passed over the sensor. This is a limit because it doesn't permit a continue control.

In this study it has been replaced the device reader of FreeStyle Libre with a more innovative, automatic and smart central unit based on Arduino LilyPad board used to capture the sensor data, analyse them and transmit them to an android smartphone, where an app shows the results on a special GUI. This means that the limits imposed by the FGM FreeStyleLibre system have been exceeded, in fact, it is not necessary to manually scan the sensor with the reader, since the platform proposed in this paper does it automatically every minute by sending the glucose value to the parent smartphone with a sonor alarm if the glycaemic value is height. The most important feature is that in this way there is an automatic and continuous control during all day and especially during the night hours.

## 2. Other Studies

In literature are present a number of articles about the EMG signal processing and classification techniques focused on gait cycle.

In Inyoung Lee et al. [6] present a review of CGMS status

M. Baghelani, et. al. in [7] reports a highly sensitive, noninvasive sensor for real-time glucose monitoring from interstitial fluid. The structure is comprised of a chip-less tag sensor which may be taped over the patient's skin and a reader, that can be embedded in a smartwatch.

X.Jin et al in [8] summarized some of the most advanced progress made in CGM biosensing. They focused on three main applications of AI algorithms in diabetes management: closed-loop control algorithms, glucose predictions, and calibrations.

F. Urbano et al. in [9] show as In recent decades,the development of automated insulin delivery (AID) systems improved the metabolic control and the quality of life of type 1 diabetes patients. Continuous subcutaneous insulin infusion (CSII) combined with continuous glucose monitoring (CGM) devices connected to smartphones represent a good therapeutic option, especially in young children.

## 3. Materials and Methods

### 3.1.System Design

FreeStyleLibre use a NFC electronic module that attaches to patient arm constantly reads the glucose reading and stores it in ram. A watch battery supplies power it lasts about 2 weeks before it starts to read inaccurate readings and needs replacing, but it must be read manually using the NFC device in the back of a normal mobile phone. What in this study was done is build a small wearable device, strapped or stuck on, that uses NFC connection to interrogate the glucose reading, every 5 minutes and transmit it via Bluetooth to a nearby device, like a smartphone or smart watch . So the user has a device which they can set high or low level alarms, that way they will never have hypos again as the alert will go off and give them a chance to get glucose before its too late.

The protocol for NFC is 15693 at 13.56mhz. The idea was to insert the BM 019 NFC module, the Bluetooth HM-17 card to transmit the glucose reading to the mobile device, the lithium battery and the battery charger module into an Arduino LilyPad armband according to the diagram in fig. 1. In this way the Arduino LilyPad board transforms the FGM Libre system into a real wearable continuous glucose monitoring system (CGMS).

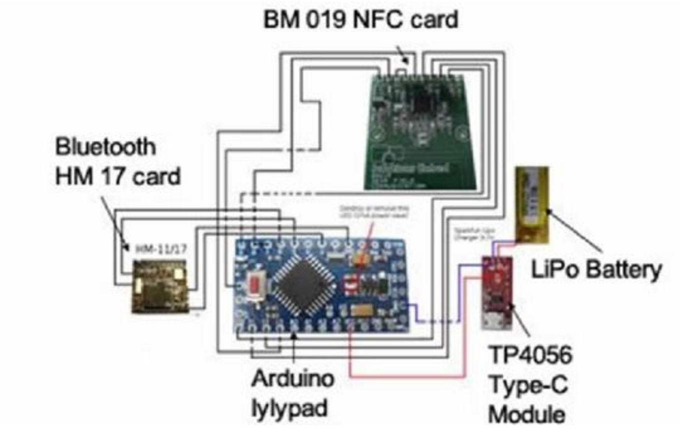


Fig.1. Construction scheme

### 3.2. FGM FreeStyleLibre sensor

FreeStyle Libre is precisely a blood glucose selfmonitoring system (FGM). It is a medical device, which allows us to have:

- a comfortable and painless blood sugar reading,
- that saves us in the long run,
- which gives us a complete daily glycemic profile without having to prick your finger.

In childs with militant diabetes, the FreeStyle Libre system measures the glucose levels of the interstitial fluid.

Therefore, it does not work as a real “classic” glucose meter, as the glucose level is assessed on the fluid that surrounds the cells of the body which acts as a means of transporting glucose and other substances.

FreeStyle Libre is composed by a Sensor (Fig. 2) and a device reader. Blood glucose detection occurs only when the device reader is manually passed over the sensor. In this study we have used only the sensor.

Fig.2. FreeStyleLibre sensor

### 3.3.LilyPad

LilyPad (Fig. 3), Arduino family of boards is especially designed for wearable applications. This board is one of the most popular boards for beginner level projects of Arduino and one of the most important reasons is its spacious layout. It is based on ATMega328 microcontroller. Pin identification is much easier in this board. When it comes to stitching, it has more space for that without the fear of accidently colliding with other pins on board If we talk about built in battery then it’s easy and convenient to select LiPo battery. We can choose any LiPo battery that suits best for our project run time. The best thing about this battery is that we can easily recharge it just by plugging our board into USB port of our computer or by simply using a 5 V wall charger.

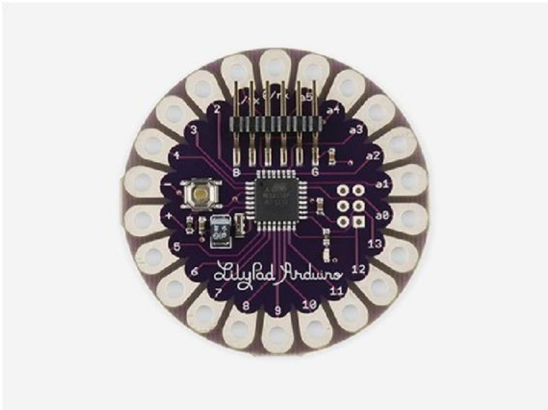


Fig.3. Arduino LilyPad

## 4. DISCUSSION

In this article we want to use the Arduino Lyllipad board to transform the FGM Libre system into a real wearable continuous glucose monitoring system (CGMS). In fact, the system will be "sewn" on a band that will be worn on the arm. This way there will be no problem or bother for the wearer. Furthermore, this means that there is no need to manually scan the sensor with the reader, but the monitoring will be done automatically every 5 minutes.

Arduino LilyPad will send the glycaemic value via Bluetooth to an ANDROID phone on which the xDrip+ software has been installed (Fig 4). It can send blood glucose vaguest o your smartwatch or via Nightscout in the cloud.

The app on the MASTER phone records the glycaemic data and sends them back to the FOLLOWER phones and then to the smartwatch. The initial pairing between the MASTER and FOLLOWER phone takes place very quickly through the QR code issued by the MASTER phone. Everything is simple and automatic.

The most important feature of this project is having a night monitor, wearable like a simple shirt or headband.


Fig.4. xDrip+ software

Alarms can be entered on the software when certain glycaemic thresholds are exceeded, in order to alert the user if he is in danger of hyperglycaemia or hypoglycaemia. Furthermore, you can also enter numbers to call to send an automatic text message in critical cases.

That means that you don't have to manually scan the sensor with the reader. The automatic control glucose system do this for you every 5 minutes. It sends the glucose value to your smartphone which must have the xDrip app installed. xDrip is really a great and matured app for Android. It can send the glucose values to your smartwatch or via Nightscout into the cloud. The most important feature is to having a night guard.

The System is a portable home-built device which receives wireless signals from a commercial continuous G4 glucose sensor worn on the body. It transmits these over the phone network to a private or cloud internet server. It does not work with the later G5 and G6 transmitters.

The system is primarily designed to allow parents and carers to be able to monitor the blood sugar of a diabetic child even if they are a long distance away, for example, carried in the pocket of a school bag. The real-time blood sugar information would be available on the parent’s mobile phone potentially many miles away.

Sophisticated forward prediction and anomaly detection systems, linked with internet connectivity, make it possible to provide alerts and computer based analysis intelligently. This can minimize “alarm fatigue” and reduce the mental burden of constantly tracking blood sugars.
The system was tested on a sample of 70 subjects aged between 5 and 13. The results of the blood sugar values was compared with a manual standard commercial glucometer (One Touch Verio Reflect by LifeScan) and with the CGM Free StyleLibre device in the range between 40 to 500 mg/dL glucose values. The table I resume the values of accuracy, sensitivity and specificity comparated with te system in object.

Table – 1

| Range between 40 to 500 mg/dL glucose | | | |
|---|---|---|---|
| **Product** | **Accuracy** | **Sensitivity** | **Specificity** |
| CGM Free StyleLibre | 100% | 100% | 100% |
| One Touch Verio Reflect | 92,5% | 90,1% | 89,7% |

The calculated blood sugar values show hight values of accuracy, sensitivity and specificity with the gold standard glucometer One Touch Verio Reflect, with the difference that the gold standard had to be consulted manually and was invasive (prick your finger to extract the drop of blood), while the system designed which is the subject of my manuscript monitored the blood sugar level continuously, in real time, non invasive and completely automatically.

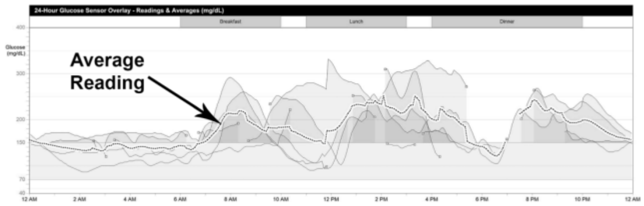


Fig 5 shows the summary graph of automatic system of an 11-year-old female with type 1 diabete. His glycated hemoglobin (HbA1c) value was 7.4%. He was not aware of any particular problems with blood sugar control and the standard commercial glucometer (gold standard for the tests) showed that most of the manual glucose readings were within the target range.

Examination of summary data from our automated CGM system demonstrated stable overnight glucose levels (Fig. 6, Summary Graph and Panel A), but examination of trend graphs from the automated CGM system studied in this paper revealed revealed a pattern of postprandial hyperglycemia (Fig. 6, Panels B, C, and D). The data provided an opportunity for further improvement of glycemic control in this motivated and adherent patient and allowed her doctor to help her correlate elevated postprandial glucose levels with specific foods and the timing of insulin doses.

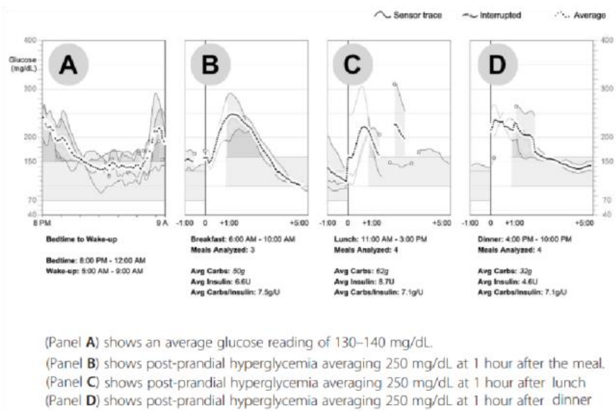


Fig.6. CGM Automatic system summary graph. Specific time periods are summarized in "trend graphs." Overnight (Panel A) shows an average glucose reading of 130–140 mg/dL. After breakfast (Panel B) shows post-prandial hyperglycemia averaging 250 mg/dL at 1 hour after the meal. Similar post-prandial hyperglycemia (Panel C) and after dinner (Panel D).

Fig.7 shows a retrospective CGM summary graph of automatic system from a 12-year-old female with type 1 diabete for 2 years, who received approximately 1 unit/kg/day of short-acting product insulin via microinfusor. The summary graph of the automatic CGM system of the previous 3 days asymptomatic and undetected hypoglycemia during the night levels between 60 and 80 mg/dl and low blood glucose levels levels starting 1–2 hours after evening exercise (Fig. 6). This data was confirmed by mesurements effectuated with the gold standard commercial glucometer One Touch Verio Reflect.

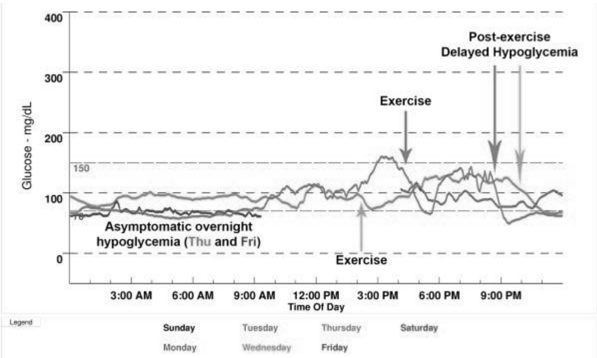


Fig.7. CGM Automatic system summary graph. Asymptomatic hypoglycemia was identified overnight (Thursday and Friday evenings from 11pm to 8am). Delayed hypoglycemia was also observed after exercise in the early evening, where glucose levels fell rapidly between 9 and 10 pm (Wednesday and Thursday evenings, arrows).

Although commercial CGM devices are not sensitive enough to serve as a diagnostic tool for hypoglycemia [1011]. In this study it was demonstrated that the system object of the paper is sensitive enough to evaluate drops in blood glucose levels (under 70mg/dl) and with appropriate alarms on the device it can be a tool useful for evaluating dietary patterns and making changes that may reduce the severity of hypoglycemia.

Just about anything is possible once we have open interoperation of the glucose sensor data. Currently there is active testing of systems which produce alerts based on sensor heuristics and probability tuned predictions of what is likely to be occurring at a given moment. Machine learning systems which can interpolate a lifetime of blood glucose data, detect anomalies and escalate alerts as needed.

These may range from a simple ambient lighting change indicating a blood sugar prediction right up to an emergency call out to friends and family if the diabetic becomes unresponsive.

## 5. Conclusions

This document introduces a new methodology to monitoring the glycaemia in the human blood using the FGM FreeStyleLibre sensor and an wearable automatic system based on Arduino. This device transform the FGM FreeStyleLibre in an automatic CGMS that monitoring the glycaemia of the patient constantly during all day.

Continuous glucose monitoring (CGM) can provide an adequate assessment of the glycaemic profile; however the current indication for the use and benefit of CGM does not include the population with type 2 diabetes on intensive insulin therapy due to the scarcity of published data in this population.

Blood glucose monitoring with the CGM system presented in this paper is particularly useful when dealing with paediatric patients, since it is a totally non-invasive wearable device. It also gives the possibility of monitoring data in real time on mobile devices. The system is primarily designed to allow parents and guardians to be able to monitor the blood sugar of a diabetic child even if he is a long distance away. Real-time blood sugar information would be available on parents' cell phones, potentially many miles away.

This study showed a series of advantages for families and pediatric patients suffering from glycemic disorders: pain relief, better management of hypoglycemia and hyperglycemia , greater control over diet and social life, reduction of worries at school and at night. Cost [12], concerns related to the accuracy, and reliability of measurements for the relationship between glycemic control and hypoglycemia[13-15] have all emerged as barriers to the use of any CGM system[16]. The most important issue was the economic burden of a CGM system [12]. The system proposed here minimizes the costs given the use of open source software and hardware devices such as Arduino make this system a low cost medical device. Subsequent studies are necessary to increase the sample number of patients and verify the already good accuracy, including the population with type 2 diabetes.

## REFERENCES


[1] M. Sinisterra, S. Hamburger, C. Tully, E. Hamburger, S. Jaser, R. Streisand, “Young Children with Type 1 Diabetes: Sleep, Health-Related Quality of Life, and Continuous Glucose Monitor Use” DIABETES TECHNOLOGY & THERAPEUTICS Vol 22(8), pp. 639-642, 2020 doi: 10.1089/dia.2019.0437

[2] B.H. McAdams and A.A. Rizvi, “An Overview of Insulin Pumps and Glucose Sensors for the Generalist” Interdisciplinary Materials vol. 5(5), pp. 1-17, 2016 doi:10.3390/jcm5010005.

[3] G. Li and D. Wen, “Wearable biochemical sensors for human health monitoring: sensing materials and manufacturing technologies.” J Mater Chem B vol. 8(16), pp. 3423-3436, 2020 doi: 10.1039/c9tb02474c.

[4] J.E. Shaw, R.A. Sicree, P.Z. Zimmet, “Global estimates of the prevalence of diabetes for 2010 and 2030”, Diabetes Res Clin Pract, vol. 87(1), pp. 4-14, 2010.

[5] M. Castellana , C. Parisi, S. Di Molfetta, L. Di Gioia, A. Natalicchio, S. Perrini , A. Cignarelli, L. Laviola, F. Giorgino, “Efficacy and safety of flash glucose monitoring in patients with type 1 and type 2 diabetes: a systematic review and meta-analysis” BMJ Open Diab Res Care. Vol 2020(8), pp. 1-10 doi: 10.1136/bmjdrc-2019-001092.

[6] l. Lee , D. Probst , D. Klonoff , K. Sode. “Continuous glucose monitoring systems - Current status and future perspectives of the flagship technologies in biosensor research.” Biosensors and Bioelectronics. Vol. 181(1), pp.1-19, June 2021.

[7] M. Baghelani, Z. Abbasi, M. Daneshmand, P. E. Light. “Non-invasive continuous-time glucose monitoring system using a chipless printable sensor based on split ring microwave resonators.” Nature Scientific Reports Vol. 10(12980), pp. 1-15, July 2020.

[8] X. Jin, A. Cai, T. Xu, X. Zhang “Artificial intelligence biosensors for continuous glucose monitoring” Interdisciplinary Materials Vol. 2023(2), pp. 290-307, Nov. 2022.

[9] F. Urbano, I. Farella , G. Brunetti, M.F. Faienza Pediatric Type 1 Diabetes: Mechanisms and Impact of Technologies on Comorbidities and Life Expectancy. Int. J. Mol. Sci. Vol. 24(15), pp. 1-26, 2023 doi:https://doi.org/10.3390/ijms241511980

[10] T. Battelino, R.M. Bergenstal. Continuous glucose monitoring– derived data report-simply a better management tool. Diabetes Care. Vol. 43(10), pp. 2327-2329, 2020

[11] T. Battelino, T. Danne, R.M. Bergenstal, S.A. Amiel, R. Beck, T. Biester, et al. Clinical targets for continuous glucose monitoring data interpretation: recommendations from the international consensus on time in range. Diabetes Care. Vol. 42(8), pp. 1593- 1603, 2019

[12] O. Onisie, H. Crocket, M. de Bock. The CGM grey market: a reflection of global access inequity. Lancet Diabetes Endocrinol. Vol 7(11), pp. 823-825, 2019

[13] N. Oliver, M. Gimenez, P. Calhoun, N. Cohen, V. Moscardo, N. Hermanns, et al. Continuous glucose monitoring in people with type 1 diabetes on multipledose injection therapy: the relationship between glycemic control and hypoglycemia. Diabetes Care. Vol. 43(1), pp. 53-58, 2020

[14] F. Amaro,M.A. Saltarelli,M. Primavera,M. Cerruto,S. Tumini. Continuous Glucose Monitoring (CGM) and Metabolic Control in a Cohort of Patients with Type 1 Diabetes and Coeliac Disease. Endocrines Vol. 4(3), pp. 595-606, 2023 doi: https://doi.org/10.3390/endocrines4030042

[15] E. Teo, N. Hassan, W. Tam, S. Koh. Effectiveness of continuous glucose monitoring in maintaining glycaemic control among people with type 1 diabetes mellitus: a systematic review of randomised controlled trials and meta-analysis. Diabetologia Vol 65, pp. 604–619, 2022 doi: https://doi.org/10.1007/s00125-021-05648-4

[16] M.A. Burckhardt, L. Fried, K. Bebbington, M. Hancock, J.A. Nicholas, A. Roberts A, et al. Use of remote monitoring with continuous glucose monitoring in young children with type 1 diabetes: the parents' perspective. Diabet Med. Vol. 36(11), pp. 1453-1459, 2019


## AUTHOR

**Franchini Roberto**. was born in Lecce, Italy, in 1972. He graduated with a Degree in informatic engineering from the University of Lecce, Italy, in 2001, with a thesis on satellite networks.

Since 2006, he has been with the Institute of Clinical Physiology of National Research Council, Division of Biomedical Engineering Science and Technology. He is author and coauthor of several research papers. His main research interest is in the development of new algorithms for automatic and semiautomatic image segmentation and signal processing.

He is expert in projects with Arduino..