

CHAPTER FOUR

SYSTEM IMPLEMENTATIONS

4.1 INTRODUCTION

The former two chapters describe in detail different ways of implementing solutions in terms of energy or data, relevant to implantable Microsystems but without entering into system level issues. This chapter describes the system level design and implementation. Showing real use to the solutions described earlier.

The scope of implementation is defined mainly by a European project named ITUBR, led by the CNM-Barcelona. The goal was to develop an implantable wireless device capable of sensing and transmitting remotely biological data. A big portion of this chapter is dedicated to explain the system design details as well as final implementation including in-vivo telemetered data of the system. In addition to that, two more sections follows: the first one describes the design and partial implementation of an implantable battery operated device interfacing to a chemical sensor and the second one describes the design of a chip intended to be used as a general purpose telemetry solution that can be part of any wireless RF powered implant.

4.2 PRESSURE SENSOR-ITUBR DEMONSTRATOR

The biomedical community is becoming more and more aware of the needs of a proper energy and data interface of the new variety of electronic implants with the external world in order to avoid numerous problems like infections, unreliability, aesthetics, etc.. Therefore the European Union understanding these needs granted a project called ITUBR.

4.2.1 Project framework

First a brief description of the project follows. The CNM-GAB was granted by the European Community as the leader of an ESPRIT-INCO project named ITUBR² which stands for Implantable Telemetric Unit for Biomedical Research. The rest of the partners of the consortium were:

CCC: Pacemaker company (Uruguay)

CINVESTAV: Centro de Investigacion y estudios avanzados (Mexico)

ULA: Universidad de Los Andes (Colombia)

UCL: Universite Catholique de Louvain (Belgium)

The main goal of the ITUBR project was to develop an implantable device suitable for a variety of biomedical applications able to receive power (batteryless) and information (wireless) from an external unit. In particular two well-defined applications were targeted. One involving muscular (EMG) recording within a prosthesis control

² ITUBR: project #950917 granted from 01/96 to 01/98

system and the second one involving blood pressure monitoring within a hemosubstitutes evaluation project.

In terms of what is relevant to the following thesis, this chapter shows the efforts done by the PhD candidate in terms of system level design (architecture, telemetry protocols,..), ASIC integration, final system assembly and hybrid prototyping. Even though big pieces of the development have already being shown in chapter two and three, this section outlines system level information including results of in-vitro and finally in-vivo recording, which was ultimately the goal of the project and of the PhD candidate work.

4.2.2 System design and development

4.2.2.1 System Architecture

Picture 4-1 shows a block diagram of the whole ITUBR system including internal and external units:

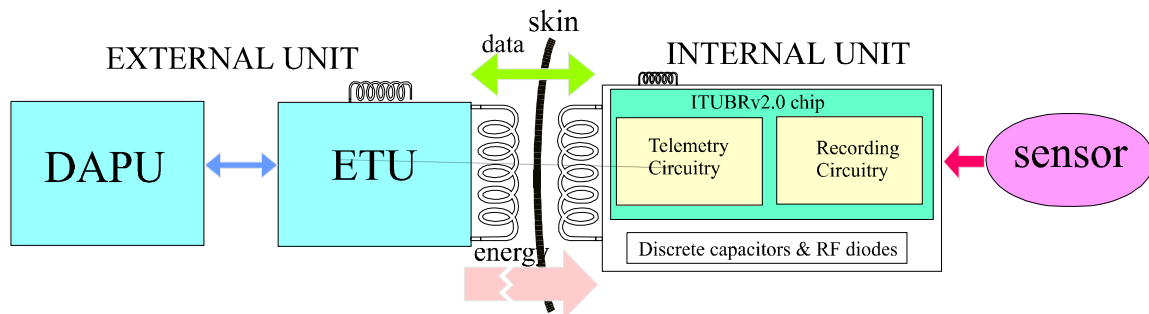


Figure 4-1. ITUBR block diagram

The external unit contains two parts:

- *ETU*: External Telemetry Unit, located just bellow the skin and containing the magnetic transmitter as well as the telemetry circuits.
- *DAPU*: Data Acquisition and Processing Unit, which was essentially an FPGA and a PC interfacing through optic fiber with the ETU.

The implant contained also two parts:

- *Electronic implant*: Internal Telemetry Unit (ITU) plus additional recording circuits or conditioning circuits (CC)
- *Sensor*: in the one application (hemosubstitute) was a pressure sensor and in the other two EMG electrodes.

The most relevant features of the implant were its miniaturization, the absence of any sort of battery (powered from an external magnetic field) and its bi-directional wireless communication capabilities. In order to achieve very small sizes (and also small power consumption) the architecture of the implant followed a system-on-chip (SoC) approach. The circuits already shown in chapter two (RF power) and chapter three (telemetry) were integrated with sensing circuits in a single chip. The final hybrid using chip-on-board (COB) technology was assembled using a small number of passive of-the-shelf components.

4.2.2.2 ASIC design

As mentioned before, due to the need of miniaturization the system level design of the whole implant was based in a SoC approach. The chip was partitioned in three major areas:

- (1) Application independent circuits including RF-power and telemetry
- (2) Application dependent recording circuits (so called CC)
- (3) Control Unit

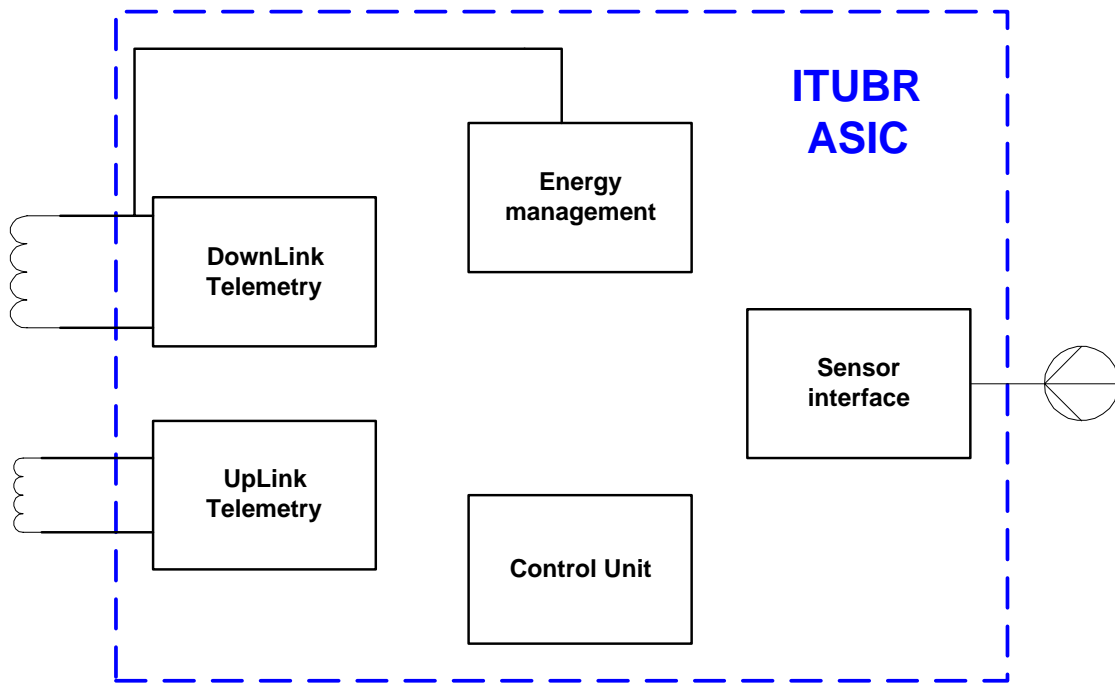


Figure 4-2. ITUBR Implant block diagram

The first and third parts were fully designed up to layout level by the Ph.D candidate. A group at the UCL-Belgium designed the second one (CC), which is the analog sensor interface. The power management and communication circuits in the ITU have already been presented in chapters two (section 2.4) and in chapter three (3.2.1.1. and 3.2.2.) respectively. In this section the digital interface of the telemetry with the analog front-end including the control unit will be presented.

4.2.2.2.1 Telemetry protocol

The communication protocol between the external unit (ETU) and the implant (ITU+CC) can be depicted by the flow-chart figure 4-3:

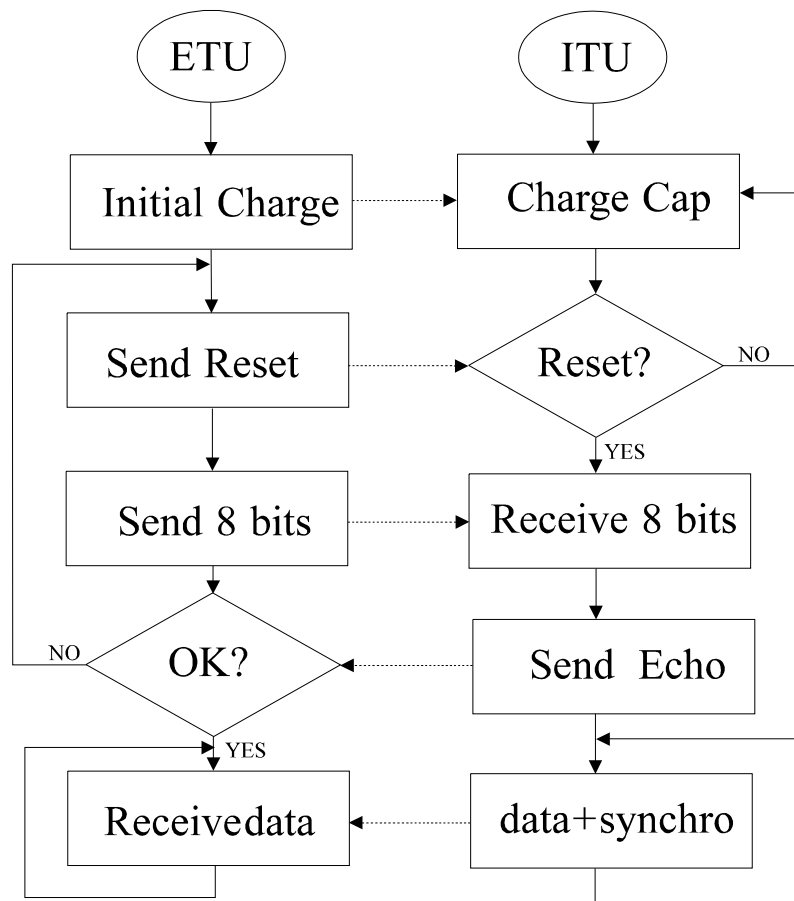


Figure 4-3. Communication protocol between ETU and ITU

Data flow is mainly from the internal to the external unit. The communication protocol behaves as shown in the diagram above: the internal unit stands-by until receiving an asynchronous reset signal. Then the internal unit decodes the next incoming eight bits, send them as an echo frame (to assure a very low BER) and afterwards starts to send indefinitely the recorded data including a synchronization byte every 8 bytes. According to the established protocol this unit provides to CC: (1) the input data properly decoded, (2) the reset signal, (3) the base-clock, (4) a four times faster clock and (5) a ready signal for starting the analog-to-digital conversion. In it's turn the CC send: (1) the digitized-recorded data for being sent to the outside and (2) the synchronization-frame time-interval.

4.2.2.2.2 Communication Protocol between ITU and CC

Within the chip as mentioned before there is an application independent circuit that interfaces the external world (ITU) and an application dependent circuit that interface the sensors (CC). This section shows the communication protocol between ITU and CC within the IC.

The protocol established involves five lines. Three coming from ITU to CC and two coming from CC to ITU, as shown in figure 4-4.

The lines are:

line 1 : reset

line 2 : data for selecting the channels

line 5 : ready signal

line 3 : data to be sent

line 4 : line for the synchronization signal

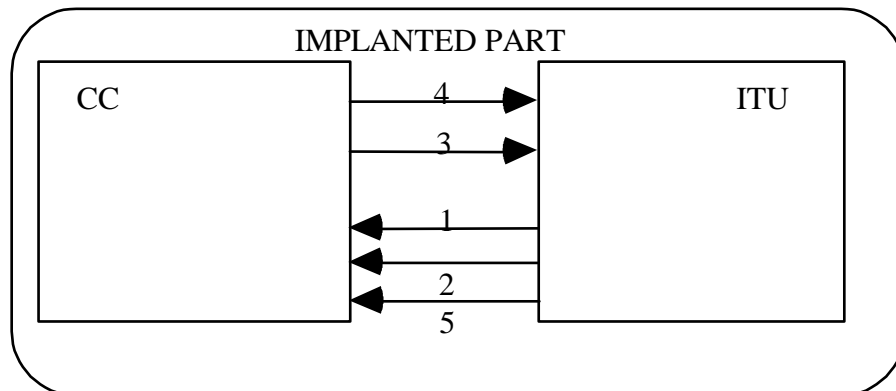


Figure 4-4. Lines exchange between CC and ITU

i). Transfer from ITU to CC

When data is transferred from External (outside the body) to CC, ITU provides signals to CC as following (see figure 4-4): the reset line (line 2) is set to ON : reset all registers in CC and initialises the control unit. During the two following clock cycles, line 1 (data_in) gives one bit per electrode channel to enable/disable each channel.

The code is:

data_in is OFF : related channel is not selected
data_in is ON : related channel is selected
(ON = 5V OFF=0V)

As reset is set to OFF, no change occurs in the CC and all selected channels are taken one by one for data transmission. If only one channel is selected, this channel is taken all the time, no time is lost between two transmissions of data frames (one frame=8 bits + 1 bit parity).

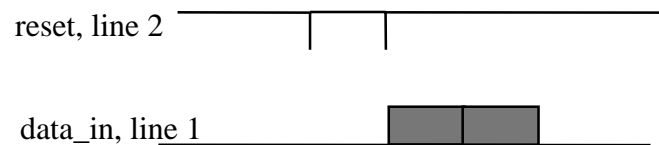


Figure 4-5. Protocol ITU to CC

The last line, line 5, is a « ready signal », which is set to ON when ITU is ready to transmit the first data coming from CC.

ii). Transfer from CC to ITU

When data is going to be transmitted, set_transfer (line 4) is set to ON during 9 clock cycles (the frame duration). Thereafter, data_out sends data at each clock cycle from data sampling, 8 bits data + 1 bit parity.

Set_transfer is needed as synchronisation signal by ITU. Following this synchronisation, 8 data frames are given on line 3. If only one channel is selected, these 8 frames are data from this channel, if two channels are selected, frames are one time for one and one time for the other (see figure 4-6).

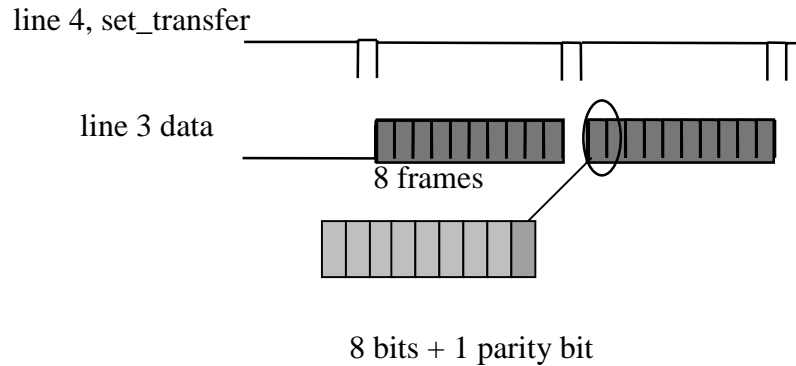


Figure 4-6. Protocol CC to ITU

4.2.2.2.3 Control Unit

As depicted in figure 4-2 the main blocks of the implant (except the sensor interface) are:

- energy receiver (see chapter two, section 2.4)
- data receiver (see chapter three, Downlink section 3.2.1.1.2)
- data transmitter (see chapter three, Uplink section 3.2.2.2.1)
- control unit in charge of the proper interface to the external unit (4.2.1.1) and to the sensor circuit (4.2.1.2).

Figure 4-7 shows a block diagram of the control unit. According to the established protocol this unit will provide to CC (1) the input data properly decoded, (2) the reset signal, (3) the clock (CK), (4) a four times faster clock (4CK) and finally (5) the voltage and current references (analog and digital 5V supply, a 2.5V reference voltage and some

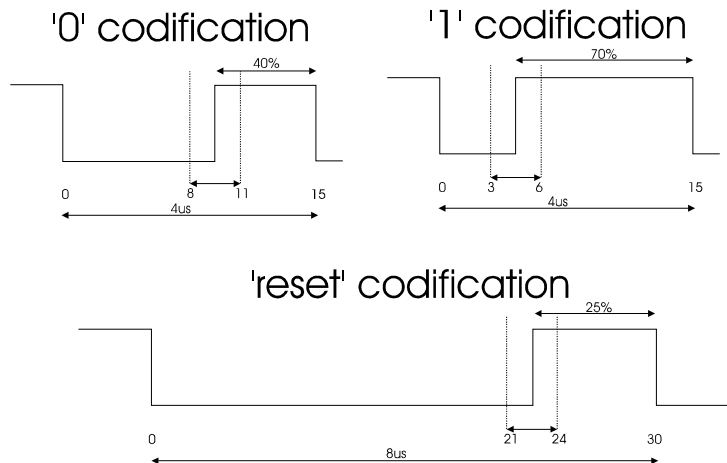


Figure 4-8. Codification in ETU to ITU transmission

4.2.2.2.3.2 Synchronization adapter

The ETU to ITU transmission is totally asynchronous and can be achieved for a wide range of bit rates. The input data carries itself the clock that serially loads the information into a shift register (figure 4-9). After that, a parallel load to a ITU clocked circuit adapts the coming data to the proper internal clock.

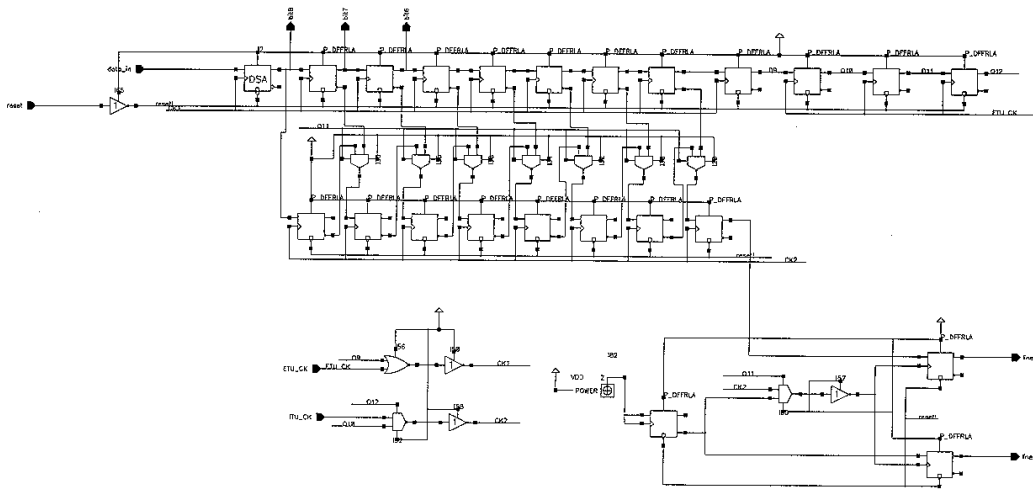


Figure 4-9. Schematic representation of the Synchronization adapter circuit

Two input lines (reset and data_in) clocked at the ETU to ITU transmission bit rate are converted to other two lines clocked at 468 kHz (or 234kHz), that is the internal

unit clock. Line 1 gives the reset signal to CC, and line 2 not only sends the selected channels information to CC but also serves the 8 bits for transmitting the echo frame.

4.2.2.2.3.3 Clock generator

All the internal unit is synchronized by a clock generated internally. The basic synchronization signal is a 30 MHz square-wave signal, produced by a seven-stage resettable CMOS ring oscillator. This frequency also defines the carrier for the ITU to ETU transmission. Therefore the LO of the telemetry is also used as the timing reference of the device.

A six-stages clock divider has been included to provide the required clock signals to the whole circuit, hence obtaining the 2-submultiples of 30MHz down to 234kHz.

The system clock is defined by Bit 6 of the input byte. There are two options: if Bit6='0' then CK is 468kHz else 234kHz.

4.2.2.2.3.4 Coder

The ITU to ETU transmission sends three symbols as mentioned in 4.2.1.1: (1) digital '0', (2) digital '1' and (3) synchronization frame. The bit rate will be 468kHz or 234kHz and the synchronization frame will take 9 bits time. For codifying the digital and synchronization information coming from the CC (and initially from the synchronization adapter for echoing) two counters clocked at 7.5MHz and at 3.75MHz are required. '0' is 33% and '1' is 66% of duty cycle, and the synchronization signal takes the 9 bits (byte) time with a 25% of duty cycle.

The output of this block goes directly to the PSK modulator, to modulate the 30MHz signal for transmitting to the ETU (outside the body) through the coil driver.

4.2.2.3 ASIC implementation

This section shows the technology selection rational used in this project as well as the physical synthesis (macro-cell P&R, digital automatic P&R, and pad placement) performed by the candidate to obtain the final ASIC.

4.2.2.3.1 Technology selection

Due to the requirements of high voltage (induced voltage can easily go beyond 10V), an Europractice-supported HV technology was used. Named HBIMOS, it is a MIETEC 2.4um BiCMOS technology that not only permits high input voltages up to 50V but also includes additional features like bipolar devices and zener diodes.

4.2.2.3.2 Physical synthesis

A single ITUBR-ASIC containing the circuitry required for two sensory applications (pressure sensor and EMG) was fabricated in order to reduce foundry costs. The ASIC can be programmed to be used for each one of the applications by properly bonding two different sets of pads in the hybrid (see next section). The floor-plan, placement and routing was performed using CADENCE tools. The digital circuit was designed in a gate level and then was automatically placed and routed. The analog macro-cells were manually placed and routed. Final core-pad routing was done manually. Figure 4-10 shows a microphotograph of the final ASIC.

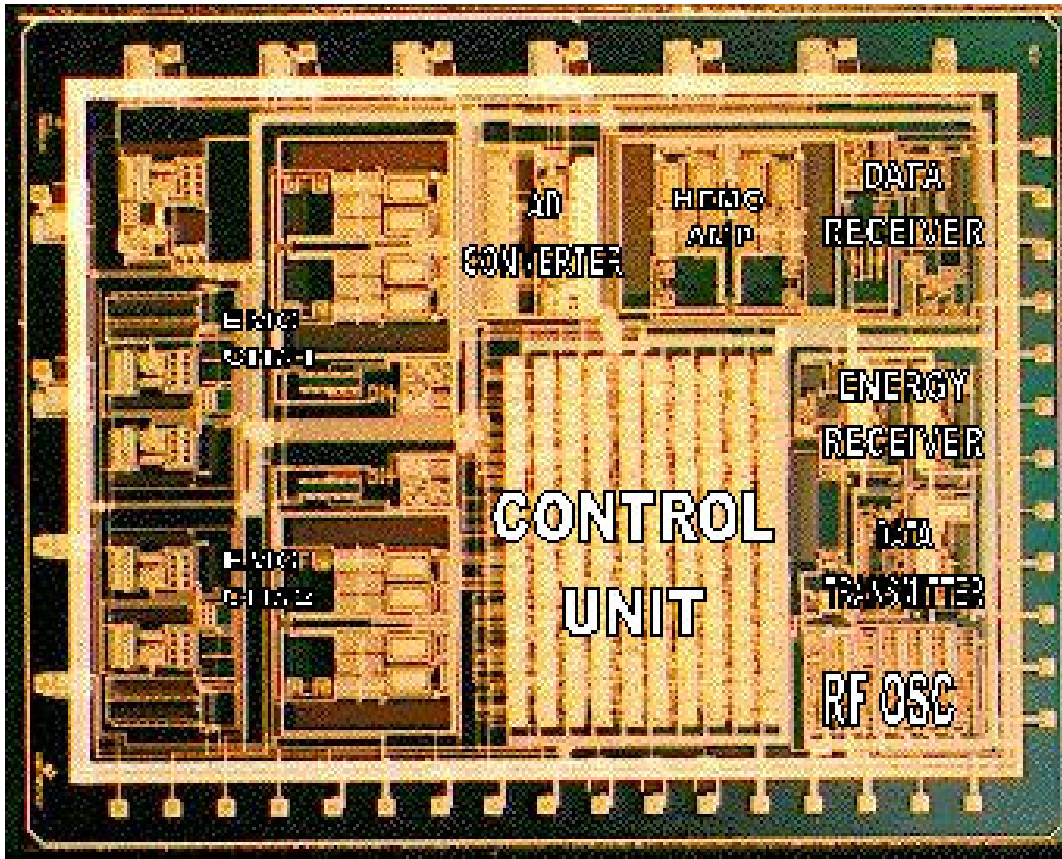


Figure 4-10. ITUBR ASIC microphotograph

All high frequency circuits (RFOSC and DATA TRANSMITTER) were physically located in the lower left corner of the chip (see photograph) with guard ring minimizing the substrate cross-talk to the other end of the chip where sensitive recording amplifiers are located. Also in order to reduce digital noise, the placement of the control unit was done in such a way that only low frequency gates were located in the proximity of recording circuits.

The die size was $5.4 \times 6.4 \text{mm}^2$ with 40 pads: 13 power pads, 4 analog test pads, 8 analog input pads, 1 analog output pad, 3 digital input pads, 8 I/O digital pads and 3 digital output pads.

4.2.2.4 Hybrid

The ITUBR-hybrid manufacturing was subcontracted to SIMESA³ and developed in collaboration with the CNM. In order to obtain a small size system, a double side PCB using chip-on-board and SMD technology was used. The hybrid contains the ITUBR-ASIC, which is the core of the system, plus additional discrete circuitry. The components are:

- fast-switching diode-bridge
- five SMD capacitors (one of them a trimming cap)
- One receiver and one transmitter coil
- ITUBR-ASIC

A layout of the PCB is showed in figure 4-11.

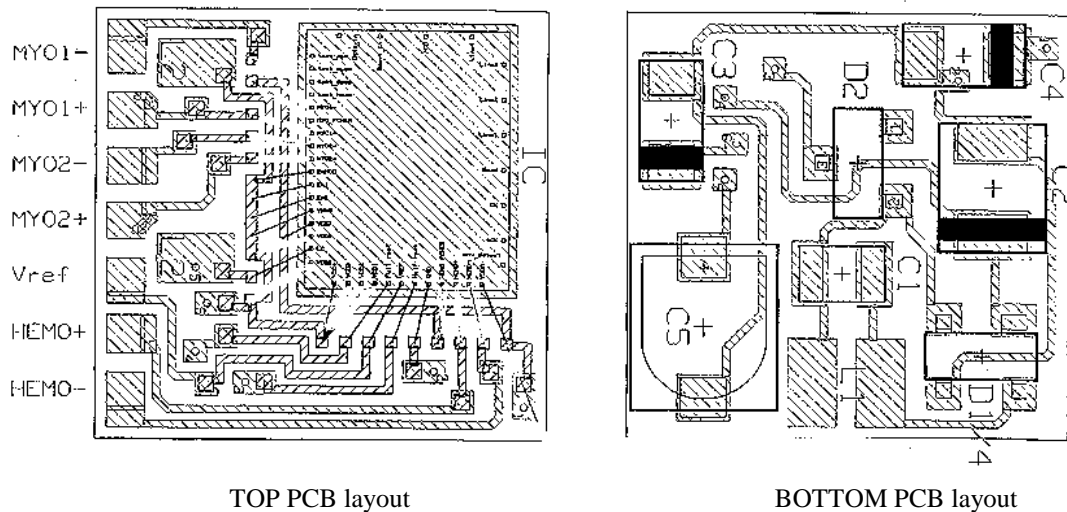


Figure 4-11. Layout of the PCB

³ SIMESA S.A. is a private held Spanish company devoted to electronics manufacturing

In order to simplify the design, the SMD components have been placed in one side (bottom), and the ASIC in the other (top). The 10mm diameter energy receiver coil is placed in the top side over the chip. In order to minimize the cost of fabrication, a single PCB design compatible with the two sensing applications has been used.

Figure 4-12 shows a microphotograph of both sides of the hybrid board. In the TOP side the ASIC (covered by dark epoxy), a capacitor and the connectors-pads are placed. In the BOTTOM side the rest of SMD components are located. Overall size is 11x11x3 mm³.

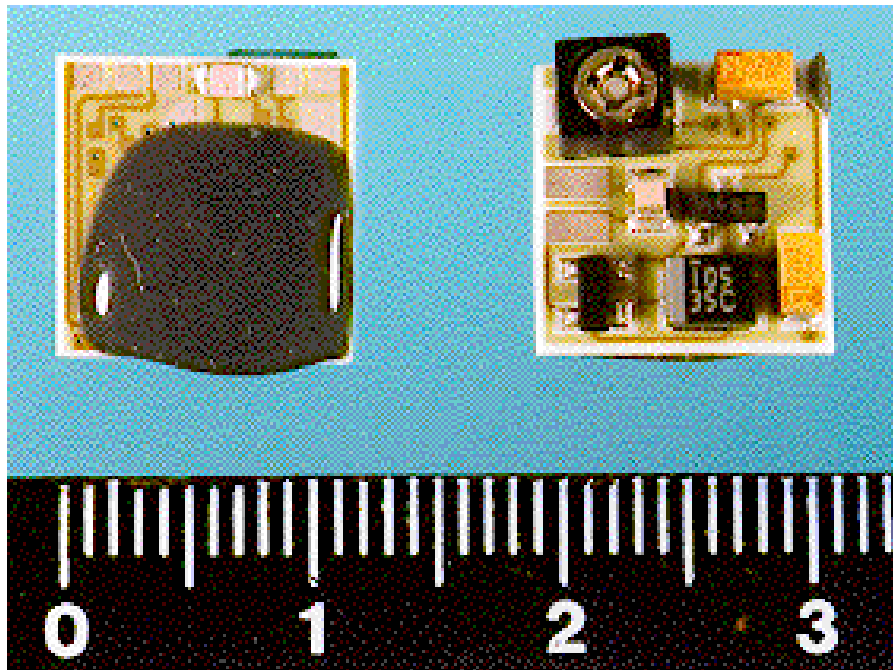


Figure 4-12. Hybrid microphotograph (distances in centimeters)

During the fabrication process a problem related to the epoxy used to cover the die delayed the whole development. An epoxy with too reduced viscosity produced problems with reliability. The consequence was the breakage of cables bonded from the PCB to the chip. A new set of ITUBR devices were built by SIMESA with an epoxy with higher viscosity offering much better yields.

4.2.2.5 Packaging

The hybrid was finally put into a bio-compatible sealed package. The material used was a mixture of resin epoxy Hysol C8-W795 (90%) and of Hardener Hysol H-W796, both fabricated by Dexter Electronics, Medical division. A photograph of the implantable device is shown in figure 4-13.

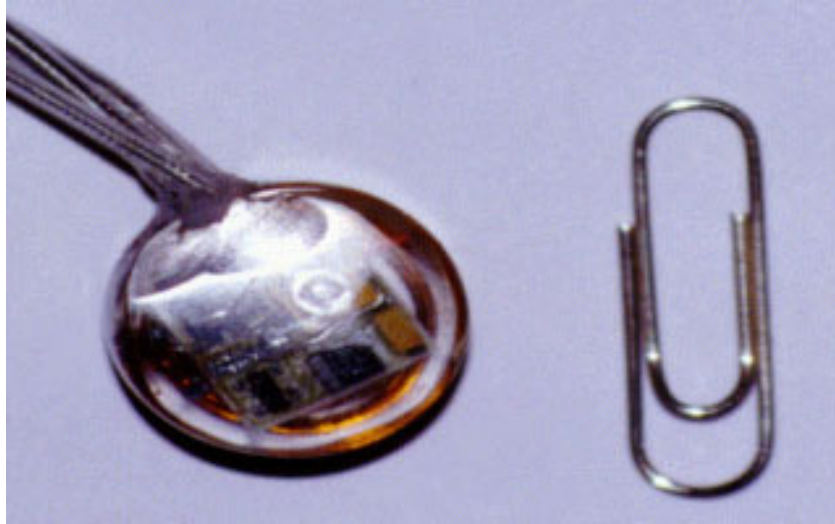


Figure 4-13. ITUBR device ready to be implanted

The package has a cylindrical shape with the corners slightly rounded. It has a diameter of 19mm and a height of 12mm (around 3.4 cm³). The distance between the implanted coils and the package surface is less than 2mm.

Silicone rubber cavities acting as molds were done using a bronze polished mail plug. Filling up these cavities one can obtain the epoxy resin cylinders. These cylinders are hollowed leaving only the lateral walls and one of its bases. The thickness of the cylinder wall is about 1,5mm. Over the same lateral wall small holes were done in order to permit cables to go out to the sensors. Then a hybrid plus the coils and the cables going through the small holes were placed inside each cylinder. Finally the whole cylinder was filled-in with epoxy, it was left to forge and later on it was polished. All the forged steps were done in a nitrogen environment.

4.2.3 Results

In order to use the device in a real application some preliminary “in-vitro” tests were performed to validate the system. Once accomplished successfully the “in-vitro” test, the next phase was to prove that we could sense, process and send via telemetry biological data. The mainstream of results are related to the pressure sensor application, with the animal experiment carried out in collaboration with the ULA-Bogota.

4.2.3.1 Complete system assembly

The final ITUBR system was comprised by the implant side (with the epoxy-packaged electronics with a feed-through interfacing with the sensor) and the external part (with a portable receiver/transmitter connected through fiber optic to an FPGA connected to a PC). Figure 4-14 shows the implant and the portable external unit (figure 4-14).



Figure 4-14. Implant and the external portable unit

The external box (ETU) comprises two coils (one to transmit energy and ASK data and the other to receive BPSK data) and the rest of hardware to implement energy/data functions (see sections 2.5. and 3.2. for the implementation details). A fiber optic coming out of the ETU establishes an optical link to the DAPU (Data Acquisition and Processing Unit) that is an FPGA and a PC (see next Figure).

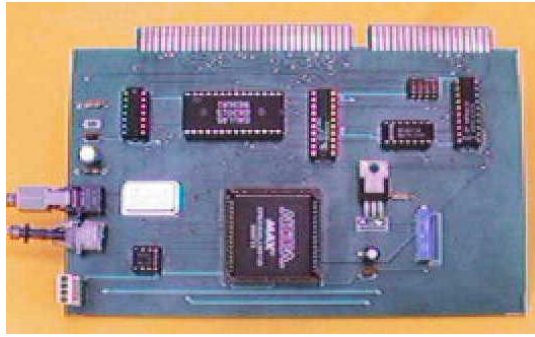


Figure 4-15. DAPU card

Following the communication protocol described in 4.2.1.2 the DAPU processes the AD converted-coded recording information and displays it in the screen of a computer in real time.

4.2.3.2 “In-vitro” results

Before proceeding to “in-vivo” testing of the system, an “in-vitro” experiment was done to verify the overall performance of the device and the complete system. The “in-vitro” set-up is depicted in figure 4-16.

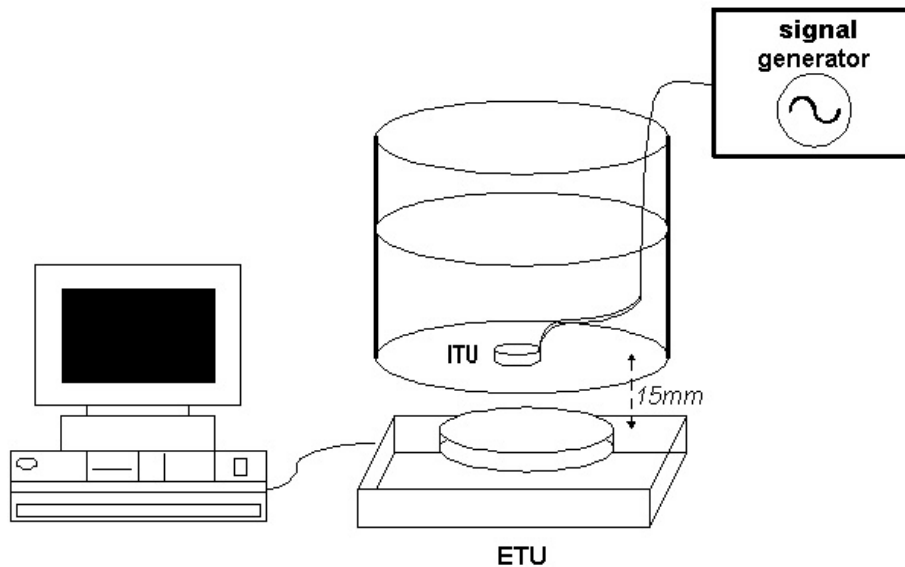


Figure 4-16. “In-vitro” test set-up

The implant was placed in a tank with Normal saline solution 0.9% (154mM NaCl) with the leads coming out to a signal generator. When an active external unit was

placed in the vicinity of the implant, sampled data of the amplified and filtered input signal was received through telemetry following the already described protocol.

Figure 4-17 shows the data received in the external unit located at a distance of 15mm, after being received and D/A converted the signal. The sampling rate was at 22Ksamples/second. In this example a 7mVpeak sinusoidal input signal with a 105Hz frequency was applied. The sampling points were grouped in packets of eight (as described in 4.2.1.1.). In between each group a synchronization frame was sent from the external unit to the implant in order to keep correct track of bit positioning. This was a requirement since both systems are asynchronous.

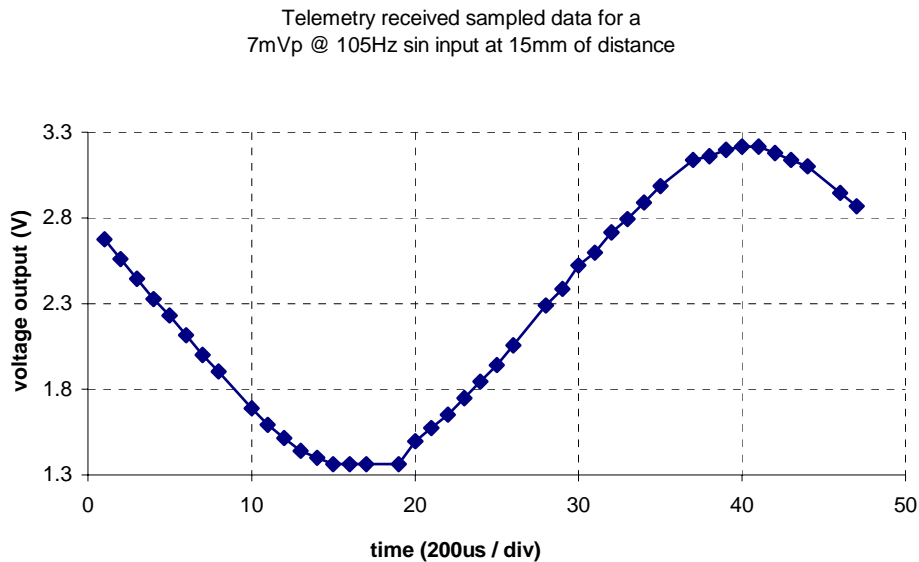


Figure 4-17. “in-vitro” experiment results

4.2.3.3 “In-vivo” results

A final step in the development process was done in order to validate the functionality of the system with a real application that allow the device, once implanted, to process and telemeter out biological data in real time.

4.2.3.3.1 Hemosubstitutes a.k.a. artificial blood

The risk of transmission of infectious diseases through blood transfusions has prompted a significant interest in the development of hemosubstitutes also referred as artificial blood. Accordingly, the research group at the FCIIC⁴ has been working on a project for the development and testing of oxygen-carrying hemosubstitutes (HSs) ^[1]. A very important part of testing the HSs is to evaluate the safety of these products. To evaluate safety of HSs, the long-term effects of the infusion of HSs are observed on a model of hemorrhagic shock. In this model, sixty per cent of the animal's blood volemia is withdrawn and then the animal is re-infused the same volume with either Ringer's lactate or HSs.

Two variables are particularly important in the cardiovascular monitoring of an individual: cardiac output and mean arterial pressure (MAP) ^[2]. Both variables were considered for this project as explained below.

Cardiac output, the volume of blood leaving the heart per unit of time, can be measured using an ultrasonic or an electromagnetic flow meter. Both of these methods require very high power sources and complex signal conditioning, well beyond the power and size specifications given for the ITU. MAP monitoring requires less power and its signal conditioning is simpler than cardiac output. Therefore, it was selected as the variable to be monitored. In the context of the evaluation of the HSs, peri and post operative monitoring of MAP will provide a reliable indicator of the hemodynamical status of the animals, and of the effects of the infusion of HSs.

⁴ Fundación Cardio-Infantil Instituto de Cardiología – Bogota (Colombia)

4.2.3.3.2 Sensor

In order to measure the arterial pressure a Millar Mikro-tip pressure transducer catheter (model SPC-330, main catheter diameter with 3 Fr., main catheter length of 65 cm) was chosen. Its electrical specifications are:

Table 4-1. Intra-vascular pressure sensor

Pressure Range	-50 to + 300 mm Hg
Overpressure	+4000 mm Hg -760 mm Hg
Rated Excitation	2,5-7,5 Vdc
Sensitivity	5 μ V/V/mmHg, nominal
Temperature Error	\pm 1 mm Hg, BSL,
Band at Zero Pressure	23°C to 38°C
Linearity	\pm 0,5%, BSL of full scale
Hysteresis (Combined) drift	Less than 6 mm Hg in 12 hours
Natural Frequency	> 35 KHz
Bridge Resistance	1000 ohms, nominal
Reference Pressure	Atmosphere
Electrical Leakage	Less than 10 μ A at 500 V DC
Zero Offset	Less than \pm 50 mm Hg