A new platform of an electronic pill with bidirectional communication system for miniaturized and low power biomedical applications

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Abstract

Electronic pills, smart capsules or miniaturized microsystems swallowed by human beings or animals for various biomedical and diagnostic applications are growing rapidly in the last years. This paper searched out the important existing electronic pills in the market and prototypes in research centers. Further objective of this research is to develop a technology platform with enhanced feature to cover the drawback of most capsules. The designed telemetry unit is a synchronous bidirectional communication block using continuous phase DQPSK of 115 kHz low carrier frequency for inductive data transmission suited for human body energy transfer. The communication system can assist the electronic pill to trigger an actuator for drug delivery, to record temperature, or to measure pH of the body. It consists additionally to a 32bit processor, memory, external peripheries, and detection facility. The complete system is designed to fit small-size mass medical application with low power consumption, size of 7x25mm. The system is designed, simulated and emulated on FPGA.

1. Introduction

Evolution of technology in recent years opened the door for advanced microelectronic systems to be used in medical treatments and diagnostic analysis. Such systems known as smart pills, electronic digestible capsules and intelligent microsystems are rising quickly in this field, they enhance the treatment of several diseases (cancer, diabetes,…) and carry out biomedical analysis in GI tract (temperature, pH, motility, …), GI diseases affect 60-70 million people annually while diagnosis and treatment exceed €10 Billion Euro per year.

Back to four decades, Mackay invented the first radio telemetry capsule with one transistor in 1957 and the first successful pH sensor capsule was achieved in 1972, since then research and developments were carried out enhancing and expanding in this field.

2. Electronic Capsules

Recent years, complicated electronic capsules with state-of-the-art technology termed by Lab-on-chip, pharmacy-on-chip, Biochips and BioMEMS are used to describe the recent modern capsules that perform sophisticated biomedical treatment and analysis, they can be categorized according to their function into two groups:

- Actuators as drug delivery systems
- Sensors as pH, temperature, image, …

Table 1 listed the capsules with their specification.

2.1. Capsules as Actuators

Drug delivery system is an issue of optimization for many interests, immediate release drug will be absorbed in the upper part of the small intestine after the stomach, extended release drug is desired to be absorbed in the lower level of the intestine. Achievement of the second by normal coating tablets is difficult due to the complexity of the GI tract of human being, intubation is an alternative solution, but it is uncomfortable for patients.

Alternative solution will be of more interest, and the idea of developing swallowed capsules devices was demonstrated, over two decades engineers are trying to develop different capsules with the capability to control the time and the location of the drug release.

The earlier capsules in this domain were HF, InteliSite, and Telemetric Capsules. They are triggered by a radio frequency (RF) pulse from a generator outside the body, the heat generated in the circuit will melt a thread releasing a needle that pierces the container and spells out the drug. State-of-the-art in this domain are the Enterion™ capsule and ChipRx™.

Table 1: List of Capsules with their Specifications

Capsules			Freq. in MHz	Size mm	Localization	Power Supply	Company/Institute	Remarks
Actuators	Drug delivery	InteliSite	6.78	35x10	Scintigraphy	External	Glaxo, US	Pulsed release
		Telemetric	108	39x11	Cogwheel	Battery	Strasbourg, Fr	Radioactive free
		Enterion	1.8	32x12	Scintigraphy	External	Phaeton, UK	Pulsed release
		HF Capsule	4	28x12	X-Ray	External	Battelle, DE	Pulsed release
		Gastrotarget	N.A	N.A.	Yes	Battery	Uni. NY, US	Dummy Unit Localizer
		ChipRx	N.A.	N.A.	No	Battery	Uni. Irvine, US	Continues release
Sensors	pH, temp, pressure	Temperature Pill	1	35x9	No	Battery	NASA, US	known as NASA pill
		SmartPill	N.A.	N.A.	In Progress	Battery	Diagnostics, US	Multi-sensors
		BRAVO	433	25x6	No	Battery	Medtronic, US	Attached to Esophagus
		Radio Pill	0.35	22x9	No	Battery	Mackay, US	1st radio pill in 1957
		Heidelberg pH	1.9	18x8	Polarization	Battery	Heidelberg, DE	
		Microcapsule	433	23x10	Ultrasonic	Battery	Uni. Shanghai	MEMS Tech.
		Tohoku pH	N.A.	2x2	N.A.	Battery	Uni Tohoku, JP	In progress
		IDEAS	38	36x12	No	Battery	Uni. Glasglow, UK	Mutli-sensors
	Image	PillCam/M2A	N.A.	27x11	Image	Battery	Given Imaging, IL	Pioneer
		Norika	2400	23x9	Image	External	RF System Lab, JP	State-of-the-art
		Endoscope	433/315	30x11	Image	Battery	Uni.Kyungpook, Kr	
		IVP	900/1	23x11	Image	External	IMS, DE	High power transmis.

The Enterion capsule uses a piston sealed inside it, while a trigger signal is received the piston will be released and the drug container will be ejected out after the filament is burnt.

The above mentioned systems are pulsed type drug release, the drug is released at once in one location.

A continues drug release is described by ChipRx, using MEMS technology several holes are circulated around the container providing continues mode release system, these holes are regulated by biological stimulis where a biosensor will be used to regulate the amount of drug needed by the patient (pharmacy-on-chip).

Previous determination of the location before drug release is an important issue. Scintigraphy, X-Ray and radioactive compounds are used to locate the position of the capsule. Such location schemes aren't practical. The patient must undergo several gamma scans to identify the location.

Telemetric capsule uses a cogwheel means for localization. Enhancement in localization is of more interest and more work can be done in this domain to achieve a practical solution for position determination.

2.2. Capsules as Sensors

Monitoring the variation of temperature, pH, motility and other functions are getting easier and comfortable for patients. The need to collect biomedical information within a specific location is of high interest, most of the existing sensor capsules don't provide location determination. Earlier products in this field are the Radio Pill, BRAVO, Heidelberg and Temperature capsules. Almost all of them use internal battery for power consumption. New capsules in this field are

IDEAS, SmartPill and Tohoku capsules. IDEAS and SmartPill provide multi-sensors microsystem for real time analysis.

Retrieving video images from within the GI tract with wireless endoscopy was a breakthrough in year 2000, M2A from Given Imaging was the 1st to develop such a system, later RF System Lab from Japan produced the Norika capsule which is the-state-of-the-art in this domain. Another new system from IMS Stuttgart is the IVP (Intracorporeal Videoprobe).

M2A/PillCam are powered by battery while Norika and IVP by external magnet field. A trade off must be taken between using battery inside the body with limited power supply and exposing the body with RF signal to power up the camera and LEDs.

3. "ePille" System Design

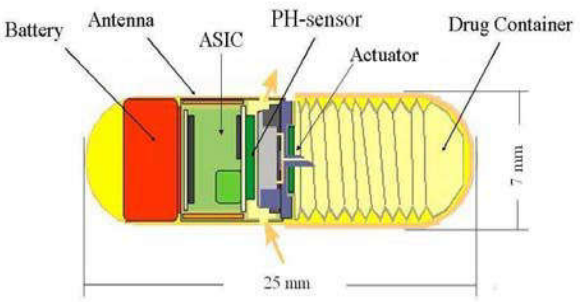

Figure 1 ePille® concept for drug delivery

Figure 1 shows the concept of the electronic pill (ePille®). It is designed to establish bi-directional communication channel from-to the body, trigger an actuator for drug delivery and record temperature or pH value via temp sensor or chemical sensor.

A further feature is an attempt for localization using near field magnetic induction method within 20 cm circular range and having a resolution of ±1 cm.

3.1. SIRIUS Processor

The SIRIUS core (acronym for Small Imprint RISC for Ubiquitous Systems) stands in performance somewhere between the very successful architectures of the ATMEL AVR (ATmega 8bit) , the TI MSP 430, the PicoBlaze - and well below the ARM 7/9– class of 32bit machines, the LEON (SPARC), Motorola 68xxx and other 32bit architectures (NIOS II, MicroBlaze). Figure 2 shows the block diagram of the core.

The processor has the following specification:

- Load-Store architecture with 16bit external data bus.

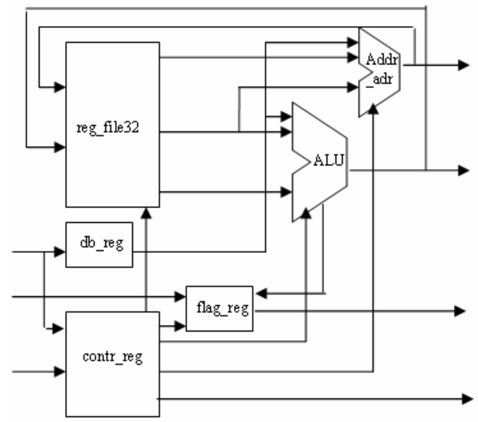

Figure 2 Block diagram of SIRIUS core

- RISC architecture with 3 stage pipeline and 1 Instruction/clock cycle and an average of 0.8 MIPS/MHz performance.
- 16bit/32bit internal bus structure with 32bit ALU and 16x16 MPY,
- Orthogonal register set of 16 registers, 12 x16bit, 4 x 32bit, the 16bit universal registers may be combined to double registers and handled as 6 x32bit registers.
- Instruction pointer 32bit and stack pointer 32bit are part of the register set.
- Stack oriented architecture with unlimited nesting levels.
- Pointers 16 bit as well as 32bit supported.
- Multiplex bus system, separated 8bit IO bus and fast memory bus, all IO is connected via a separate 8bit bus with own address space
- Address space 64k or 4G depending on pointer addressing,
- Vectored hardware interrupt and software interrupt (exception)
- Compact 16 bit instruction format with only three modes
- Instruction set architecture with 56 instructions optimized for compact C-Compilation
- Netlist version made from gate primitives, able to be mapped on every existing technology without using macros.
- Performance about 100 MIPS in 0.35µm CMOS and 50 MIPS in actual FPGA-technologies
- Fully static, extreme low power design, all registers made from flip-flops.
- Comes with Software IDE, C-Compiler and Simulator and basic BIOS.

3.2. Communication Block

The communication block consists of an asynchronous DQPSK with 115 KHz carrier frequency, including a digital PLL at the receiver side. The data rate is 9600 Baud.

The modulation technique is a continuous phase soft shift keying using Gaussian filter for smooth phase transition from one state to the other.

The data frame package carries up to 255 bytes of data information with preamble and 16 bit CRC sum check. The system includes 4B/5B coding for 1 and 2 bit error detection as well burst error for frames less than 16 bits.

The modulator process the serial data by converting into two parallel bit for quadrature form. A differential encoding is set to eliminate the difference of phase reference between the transmitter and receiver side. A soft shift keying is provided by Gaussian filtering for smooth phase transition. This signal is supplied to a numerically controlled oscillator (NCO) to generate a frequency between 107-123kHz depending on the phase shift.

The demodulator process contains the reverse steps of the modulator. It consists of Schmitt-trigger for digitizing the received analog signal, a digital PLL to lock the received signal, a decision circuit to estimate the symbol value, a decoder and parallel-serial converter to recover the original data.

4. Hardware verification and Layout

The SIRIUS processor and the communication block have been emulated on FPGA Cyclone II, an emulation test board was designed to test the system's functionality as shown in figure 3.

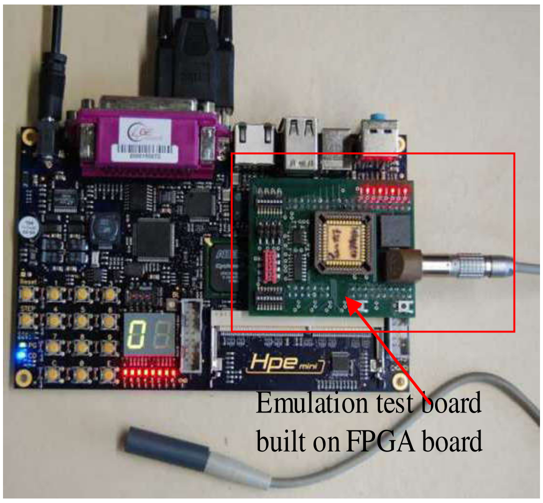

Figure 3 Emulation of the digital part on Cyclone II

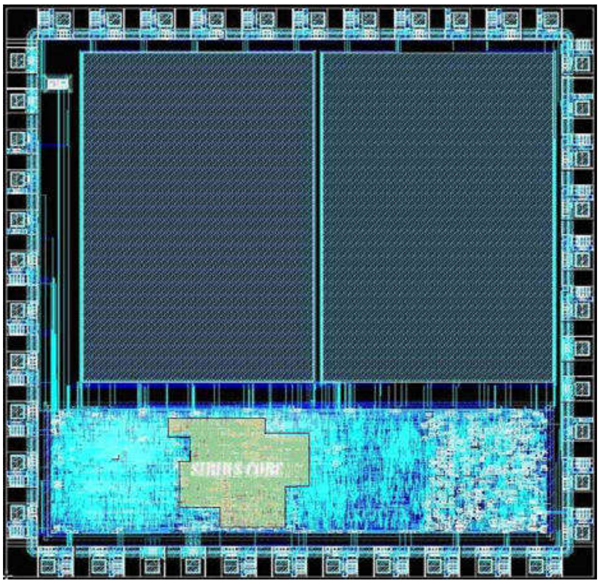

Figure 4 First prototype layout of the digital part in 0.35 µm AMIS technology, size of 11mm²

A single coil was used for transmission and receiving mode. A serial combination of the coil, capacitor, and resistor were used for transmission mode while a parallel combination of the coil, capacitor, and resistor were used for receiving mode. The Q factor is seven and the bandwidth is 16 kHz with center frequency of 115 kHz.

Table 2 Results of Synthesizing for 0.35 ASIC Library and for ALTERA Cyclone II

Block	Number of primitives (ASIC)	Logic Elements (Cyclone II)
SIRIUS core	4197	2870
ROM	392	106
Bus controller	92	335
PIO	52	20
SIO	388	132
SPI	241	123
I2C	343	191
Interrupt controller (12 Intr)	773	346
ISO-14443 Interface	1407	617
QPSK Interface	3186	1252
Timer	214	88

A first routing of the digital circuit was done. A processor, SRAM, external periphery, and communication block was routed using 0.35µm AMIS technology. The first routings showed an area of 11mm² as seen in figure 4.

Table 2 summarizes the achieved results in synthesis for a 0.35µm AMI library as well as for the low entry FPGA Cyclone II device.

5. Conclusion

A complete bidirectional system was designed, simulated, and emulated on FPGA. A first routing prototype for the digital part was done using 0.35µm AMIS technology.

A final layout with complete peripheries and analog components is still under progress.

The system contains wake up manager unit for reduction of power consumption. An external signal will be sent either to wake up the system or shift it to sleep mode.

The system was able to demodulate receiving signal, CRC check sum and save the data in the memory. A transparent mode to resend the data was achieved. The system could trigger an actuator via transmitted command.

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