Chapter 2

Processor Based Integrated Circuits

You may start as circuit designer using gates, adders, multiplexers and so, but soon you will find that it is better to include a processor and a memory in your design, so additions in functionality are easy to integrate. Here is where you notice the hardware versus software implementation advantages. Let's explain how hardware and software are involved in your design decisions: Any project idea can be implemented completely using hardware, it means that every single decision is made by a transistor or set of transistors, connected in a way that will result in a voltage indicating what will happen with an output signal. If your project has many decisions to make, data to store, operations to make, you can use the simulator, estimate how many transistors the circuit need. On the other hand, if all the decisions your project is making are translated into a programming language, you can estimate how much memory the program will need to be stored. And the memory size can be easily translated into transistor count. This way you can compare if your hardware based version is smaller –using less transistors- than your software based version. We will get into this subject with more detail ahead.

2.1 Relevance and Potential Uses

Stimulation systems provide signals and test patterns to be used in a variety of applications. Potential uses and applications for stimulation systems constantly increase as existing tests and lab procedures are desired to be miniaturized or new tests are conceived, whether they are for Lab analysis, prosthetic testing, pollution analysis, or point-of-care.

Current experiments need a stimulation system so tests can be repeatedly performed in order to store results, perform analysis, and obtain statistics and finally report state of the art conclusions and results. On-going experiments whose focus is to obtain novel results on a specific research area should be supported by a stimulation system that eases the experiment and allows researchers to define and change the stimulation patterns and tests.

Once stimulation systems are found useful in a specific application, the next natural step is to add intelligence to the system, so it can precisely reproduce test procedures, improve performance by learning from previous results, and evolve according to upcoming needs. Potential uses for this stimulation system include a wide range of experiments, from detecting pathogenic cells in fluid samples, bacteria or viruses in blood and urine droplets, microbes or fungi in food items and water, and also target agents in the environment, the human body, or industrial processes.

Specifically, particle manipulation experiments are expected to become part of the everyday life, so usual lab tests can be performed by a miniature device, in site, and by non-specialized personnel. In characterization efforts, all kind of particles and cells are separately stimulated in order to determine their characteristics so manipulation and test procedures become known and can be used in future tests.

Current research is also going to automated tests using stimulation systems, where prosthetic devices are analyzed to check if they react as their human counterpart does; a set or sequence of signals, similar to those generated by the brain in order to control or to sense that body part, is applied to the prosthetic part to determine if proper behavior has been achieved and the body part is ready to use.

Besides, when a stimulation system is configurable as the one presented here, its use may extend to related applications, such as cell disruption, embryo viability tests, DNA manipulation, and serial/automated medical lab tests.

2.2 Design Variables

As circuit designers learn along their experience, there are trade-offs between design variables. The most important of these variables are: circuit speed, circuit area, and power consumption. Secondary variables are pin-out and time to market. Circuit speed involves how fast the used processor and peripherals will run; area is the space the circuit will take in the silicon wafer; power consumption refers to how much battery power will take to fully and continuously execute the application program. All these variables are discussed in detail ahead.

2.3 Chips and Intelligent Systems

Early designs and implementations for portable labs are initially prototyped on development boards, printed circuits, or FPGAs, and there are some design efforts to produce a miniature device which may eventually lead to low-power Lab-on-chips and portable labs. Along with miniaturization efforts, intelligent testing goes its own way on current research work; it will become part of the future fully automated lab processes and tests, so it has to be defined in general terms and be able to be programmed for complex future tests.

About miniaturization and intelligence current developments, several works are referenced here: reviews of stimulation experiments using proposed or designed integrated systems, automation of effective and programmable particle manipulation using MEMS and a bio-cell processor, DEP filters which could continuously eliminate cells suspended in water, and so on.

An early chip proposal was the engine for a micro-fluidic Lab-on-Chip system; it was presented by Gascoigne as a high voltage integrated circuit which transports droplets on programmable paths; it creates forces over multiple droplets while varying electrode excitation voltage and frequency. Electrodes are driven with a $100V_{pp}$ periodic waveform; the maximum waveform frequency is about 200Hz. This prototype chip has a 32x32 array of 100V electrode drivers. Fabricated in a 130V SOI CMOS technology dissipates 1.87W max, in a 10.4x 8.2 mm^2. The chip is programmable: the routes of multiple droplets may be set arbitrarily within the bounds of the electrode array and the stimulation waveform amplitude, phase, and frequency may be adjusted.

Newer proposals present designs for Lab-on-a-chip integrating one or several sub-systems: Delizia proposes a large array of capacitor sensors for detecting dielectric permittivity variation. It uses an 11-bit resolution ADC at a sampling rate of 100 Kilo-samples/sec; it is implemented in 0.35 μm CMOS technology. The noise coupled to the signal at the chip pad is reduced by using an on-chip analog-to-digital converter. Simulation results show a SNR=65.7 dB and an ENOB value of 10.6b. Its power consumption is about 150 mW. Readout chain is implemented in 0.35 μm CMOS technology with a 3.3 V supply voltage.

Keilman presents a proposal of a bio-analysis system that may be part of future low-power bio-analysis platforms. The analysis technique uses the electro kinetic phenomenon for noninvasive biological cell manipulation. This work generalizes the concept of test micro-structures using standard CMOS process by providing a generic electrode structure, which, when integrated with a processor, is capable of generating an arbitrary electric field shape, thus facilitating a programmable sequence of different cell manipulations.

Shih et al proposes an adaptive biochip integrating DEP traps and a programmable array for the multi-sorting applications of bio-molecules. The magnitude and direction of the DEP force are controlled via the distribution of time-variant non-uniform electric fields. The voltage on each individual electrode of the multi-sorting array is programmable.

When a programmable or configurable system is desired, a user interface comes in hand for operation, since it allows repeatable and reliable setting of test parameters. There is on-going work on programmable and configurable testing, although it does not come together with miniaturization efforts. A device presented by Manaresi is a 64 mm^2 chip implemented in a two-poly three-metal 0.35 μm CMOS technology, featuring an array of 320x320 actuation electrodes, 20μm x20μm micro sites, including addressing logic, an embedded memory for electrode programming, and an optical sensor. The chip enables software-controlled displacement of living cells, and the manipulation does not damage the viability of the cells.

Similarly, Jungyul Park presents an integrated MEMS-based bio-cell processor; the purpose is the automation of transporting, isolating and immobilizing individual embryo cells for effective manipulation.

An interesting topic on SoC is that modular designs should be able to integrate between them by using standard existing interfaces so a complex system is built by connecting several simple functional blocks. New developments of digital blocks or cores should take integrated systems for particle manipulation to the next level: future designs should include in one design the stimulation system, the fluidic device, the actuating elements, the sensing circuitry, the data collecting system, the analysis system and the storage device.

As an early example, there is a software configurable architecture able to implement a variety of AC electro-kinetic techniques. The architecture is developed as a flexible IP block and in conjunction with integrated micro fluidic devices and other third-party IP blocks, form the analysis function. This design is basically a two dimensional randomly addressable electrode array being driven by one of four sinusoidal analog signals. The so called Lexel™ array and supporting circuitry are designed on a single chip using a standard 0.18µm CMOS process.

Table 2.1 *Referenced works on Intelligent Labs-on-Chip and Bio-Chips.*

Year	Category	Application	Focus	Integration	Intelligence	Implementation Specifications
2003	Proof of concept/ DEP processor	Droplet manipulation	Droplet based chemistry	No, all external elements	Application dependent	Proposal, fluidic processor versatile platform
2004	Proposal/ Particle manipulation	Diagnostic instrument		Stimulation, circuit, electrodes array	No	No
2004	Design / Bio-cell processor	MEMS, embryo cell	Manipulation automation, MEMS based bio-cell processor	Processor, DEP valves	Automated tests	MEMS based bio cell processor
2005	Implementation/ Low power bio-analysis platform	Bio Analysis		Stimulation system, fluidic device, 2D electrode array.	SW configurable, IP modularity, four output channels	IC
2007	Design/ Stimulation chip	Lab-on-chip	Stimulation systems for electrode arrays	Electrode array, excitation circuit, drivers,	Programmable droplet routes and waveform parameters. Expandable architecture	Fout=200 Hz; demo chip in a 130-V 1.0 µm SOI CMOS. 1.87 W, 10.4 x 8.2 mm^2
2007	Design/ Programmable Bio chip	Bio-molecules multi-sorting		DEP traps, programmable array.	Programmable stimulation	IC

Year	Category	Application	Focus	Integration	Intelligence	Implementation Specifications
2008	Design/ Stimulation and read-out Chip	Lab-on-Chip	Capacitor sensors and actuators array	Sensors array, ADC, Amplifiers, Readout chain	Programmable gain	Simulation for actuators. Implemented in 0.35 μm CMOS
2009	Design/ Field array micro-system	Bio-medical		Sensors, actuators	No	Integrated circuit (IC)

Table 2.1 summarizes the work done by referenced research works that go on the line of Systems-on-a-chip and Lab-on-a-chip. Scope refers to the level achieved in that work: a novel proposal, a detailed design, or a finished and tested implementation. Category refers to the target element in a Lab-on-chip structure; it can be a fluidic device, a stimulation chip, an actuator/sensor set, etc. Focus summarizes de orientation of the work so it shows that it is specific for a particular experimental environment. Intelligence refers to the capabilities of the system to be considered intelligent: programmable functions, uses a processor, configurable operation, includes user interface. Integration refers to the elements covered by the design and the possibility to integrate it into other existing modular designs: a fluidic device, sensors and actuators, stimulation circuitry, a standard user interface, and modularity or IP blocks usage. Implementation (intended or developed) for that proposal or design: printed circuit, integrated circuit, or simulation only. Application refers to the expected or target application, such as air and water pollution, lab test and analysis, medical treatment, or generic particle manipulation.

2.4 Opportunity Areas

The detailed analysis of the state of the art on this area allows us to determine the need of a system like the one presented in this work. A wide range of applications are using electrical signals to stimulate a fluidic device for experimentation on particle manipulation. The majority of those tests are performed manually controlling the parameters of the applied signals. Also, most of the experiments are specific for a certain type of particle, using certain waveform within a narrow frequency range. This design tackles the need for automated test procedures, configurable operation, miniaturization of the design and a modular design style to ease integration of this system into existing or future designs.

Existing stimulation systems are about using limited logic to synthesize a desired frequency and deliver it to an experimental device; from there, a specific and non-configurable signal or pattern is obtained, and it can be used only for that specific purpose.

The system in this work is a processor based design that can execute a variety of application programs, a memory system that is optimally used to contain program and data while delivering a variety of signals and patterns in a wide frequency range, and the configuration capabilities to allow users to adapt it to specific tests and applications with no modifications to the hardware or software.

The automation of testing and stimulation procedures obtained from this system can speed up current research work by providing a reliable way of repeating, configuring and adapting the system to a specific application, whether it is used as an autonomous system or integrated to an existing Lab-on-a-chip.

2.5 Systems and Labs on a Chip

The integration in one chip of all the components needed for an application, known as System on a Chip (SoC), has been the optimal implementation for many embedded systems. In functionality it can go as far as designers' dream of it, from containing a little logic up to a processor and peripherals that can be programmed to perform multiple functions.

A SoC containing a set of components like processor, memory system, peripherals and configurable application software can lead to a design that is reliable, modular, programmable and easy to integrate into other designs.

A generic diagram for a design can be presented as in Figure 2.1: a user interface configures, programs, and operates a stimulation system; this system delivers selected electrical signals and patterns to a fluidic device containing the sample and particles to be manipulated; a sensing system can collect info from the stimulation effect and, either go directly back to the interface, or pass through a characterization system where it can be useful for identifying a specific type of particles.

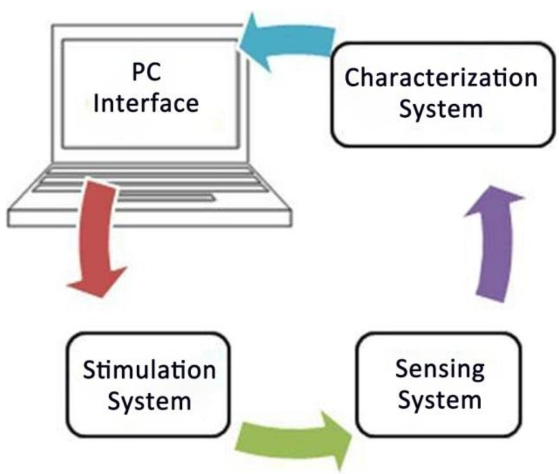

Figure 2.1 *The electric stimulation system in a particle manipulation environment.*