Numerical Investigation of the Performance of Coulter Counter with Novel Structure

Jinhong Guo, Tze Sian Pui, Abdur Rub Abdur Rahman, and Yuejun Kang

***Abstract*—Coulter counters are instruments designed to count particles of various shapes and sizes. A significant limitation of the contemporary coulter device is high throughput. In this article, a novel coulter structure is proposed and the change of resistance due to particle translocation is studied numerically. The simulation results show the resistance change affected by the cell size as well as the cell location. The cases when cells stick together and non-stick to translocate in the channel are also analyzed numerically. A coulter device with multiple sensing units is modeled and simulated to investigate the effect of cross-talk between sensing channels. The studies provide useful instructions for the design of solid-state vertical micro Coulter counter for high throughput particles counting and scaling up for a counter array.**

***Index Terms*—micro coulter counter, particle counting, resistance change, size effect.**

I. Introduction

Coulter counters play an indispensible role in bioinstrumentation used for sizing and counting the particles or biological cells suspending in the electrolyte [1]. The conventional Coulter counter has one channel that connects two reservoirs containing the electrolytes. A pair of electrodes separated by the channel measure the resistance across the channel. When particles or biological cells pass through the channel, the electric field in the channel is perturbed, causing a change in resistance. The size and number of particles or biological cells can be correlated by characterizing the electrical impedance changes, such as pulse number and pulse amplitude. As a fundamental bio-detection device, Coulter counter have been used in analysis of pollen [2], human cell [3], bacteria [4], viruses [5], single molecules [6] and DNAs [7].

The measured pulse amplitude in Coulter counter can provide important information about properties of cell. This includes the distribution of cell size and shape in a sample measurement. In general, one pulse corresponds to a cell and the pulse amplitude is proportional to cell size. Researchers have extensively studied the relationship of the resistance change caused by a spherical particle at the axis of cylindrical pore [8] . The mathematical equations to predict resistance changes have been derived. The ratio of diameter particle to channel diameter determines what appropriate equation to use. It is also found that the resistance change is affected by the cell's off-axis position. The off-axis translocation of cell in channel leads to a higher resistance change than the cell translocation along the axis [9]. As there is no numerical solution to provide the accurate prediction for off-axis effect in particle counting, we take the consideration of particle flow along the axis in our modeling and simulation.

Recently, a planar four channel counters haven been demonstrated to improve throughput of counting [10]. The design in a 1D parallel channel configuration, however, is limited to scalability owing to complexity in fluidics, electronics, channel layout and electrode routing. In our approach, we aim to exploit 2 dimensional (2D) scaling of device throughput. The counter sensor with multiple sensing channels will be built on a monolithic silicon chip using standard CMOS manufacturing processes. The geometry of the sensing unit is optimized in the simulation and the effect of electrical cross-talk from neighboring channel is investigated. The rest of this paper is structured as follows. Firstly, we discuss the theoretical modeling. Next, we present our results and discussion. Then we end with our conclusions.

II. Novel Structure and Theoretical Modelling

The structure of Coulter counter consists of two reservoirs connected by a cone and cylindrical channel with radius D and length L as illustrated in Fig. 1(a). The computational domain contains the whole part. The electrical potential excitation electrode is placed on the top reservoir and the ground electrode is located on the bottom reservoir. The cell translocation along the z-axis leads to a resistance change. As Fig. 1(a) shows, the cell diameter is d, which is half of the channel diameter D by default; The counting channel length L is set up to 2/3D initially and in the cone part, the oblique angle $\theta = 54.7^{\circ}$ and the height is 400 μm.

In the numerical investigation of crosstalk, the coulter counter array with two sensing channels is showed in Fig. 1(b). The distance between the channels is 600 μm. A 3D representation of this structure is modeled in COMSOL [11]. We have simplified the computational model without considering the surface charge density of the cell. Under that condition, fluid will always keep neutral with translocation of cell along the z-axis. Consequently, the resistance change is only due to the translocation of cell rather than the ion and fluid transport, of which the change can be obtained by solving the Electrical Current governing equation. The analysis is showed as follows in details.

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and hence provides a good linearity by maintaining a constant Ron of the MOSFET for the entire input range. The switch is sized based on the settling time required for the ADC.

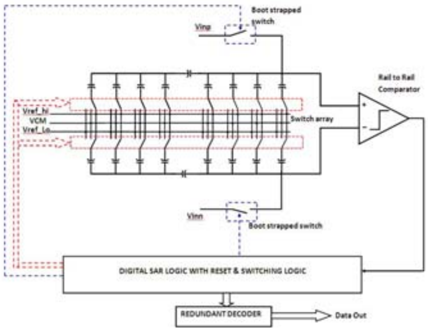


Fig. 1. Architecture of the proposed SAR ADC.

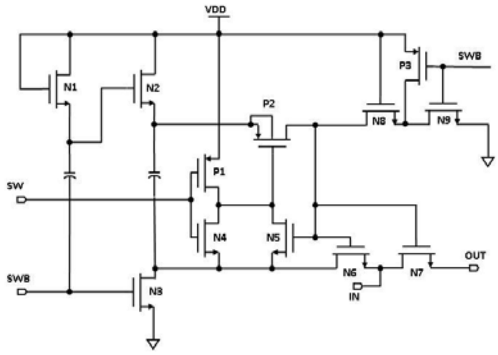


Fig. 2. Bootstrapped switch.

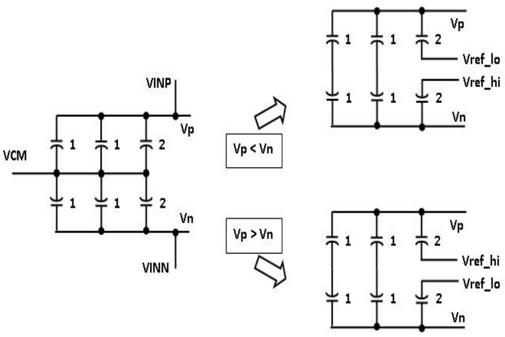


Fig. 3. Common mode resetting triple level switching scheme.

B. Common Mode Resetting Triple Level Switching

The ADC uses the common mode resetting triple level switching as shown in Fig. 3[4]. During the sampling period the ADC capacitor array bottom plates are connected to VCM and the differential input is sampled on to the top plates of the capacitors. Based on the decision from the comparator, the bottom plate of the capacitor array will be switched to either Vref_hi or Vref_lo. Since the charging and discharging voltage swing is halved because of the use of third voltage level (VCM), the energy consumption will be 4 times lesser than the conventional method. The resetting is done by connecting the bottom plates of the two capacitor arrays together to VCM during the reset period.

C. Capacitor Array and Redundant Code

The capacitor array was sized such that the kT/C noise is lesser than quantization noise of an 11 bit ADC. As per [8] the unit capacitor for an 11 bit ADC with a swing of 1Vp-p differential needs to be at least about 416fF.The process variation information for the capacitor matching set the minimum capacitor limit to 416fF to obtain an ENOB of at least 10.4. Hence a 416fF capacitor was used along with the non-binary redundant algorithm [1] to obtain a higher ENOB. This redundant algorithm introduces an additional bit in the conversion and hence an 11 bit ADC will take 12 cycles to perform a conversion. This additional bit helps in overcoming the errors that can happen due to incorrect DAC settling and comparator errors. The step size is non-binary and the redundant algorithm gives us a way to correct the errors of previous steps at the later steps. The algorithm relaxes the settling time of DAC and the capacitor. The settling time of the redundant SAR ADC can be expressed as [2].

$$Settling\ time = \tau \times \ln(p/q) \tag{1}$$

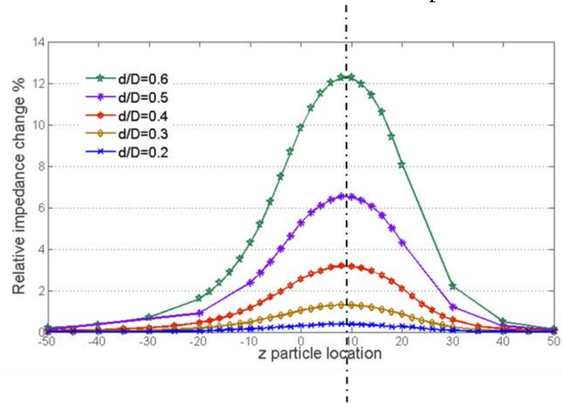
where p is the step size voltage change and q is the redundancy in that corresponding step and τ is the settling time of the capacitor array. This design used an 11 bit ADC with one redundant bit. The optimum sizing can be found by iterative simulation of the algorithm and the best sizing that gave a settling time of 2.4τ was found to be p(k)={1024,512,233,129,69,37,20,11,6,3,2,1}. To reduce the size of the capacitor array, a segmented capacitor array was utilized as shown in Fig. 1. An attenuation capacitor is inserted in between the MSB and LSB side of the array. Hence the size of the MSB capacitors can be reduced without changing the effective capacitor value. The sizing of the attenuation capacitor is based on [4].

D. Comparator

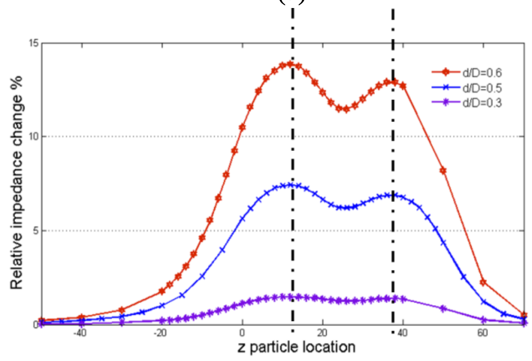
A rail-to-rail latched comparator shown in Fig. 4 is used in the design. This comparator based on the design [3]. A 104MHz clock signal is used for the SAR ADC. The comparator has to be able to resolve faster than half of the clock cycle period (i.e 4.8ns). Hence low threshold transistors were used for the latch, digital gates and input transistor of the comparator whereas as normal threshold devices with longer lengths were used in the current mirrors. The comparator is sized such that it can operate with a resolution of 12 bits with a speed of less than 4.8ns.

E. Digital SAR Logic and Switching Array

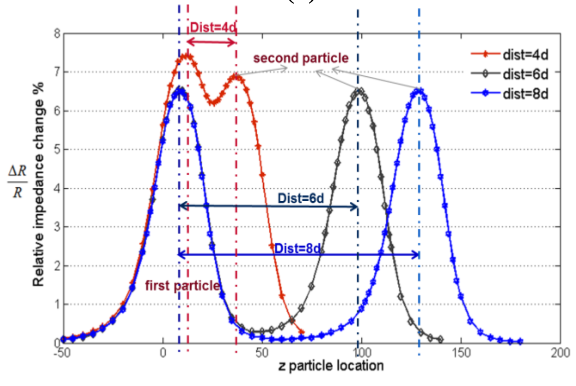
The switching arrays connected to the bottom plates of the capacitor arrays were implemented using MOSFET switches. These switches connect the bottom plates to the reference voltages. The SAR logic controls the switching activities of the switching arrays. Based on the decision of the previous bit, it switches the capacitor to either Vref_hi or Vref_lo. The digital SAR logic works at 104MHz and the logic generates the necessary timing signals and sampling signals internally. The SAR ADC takes 16 cycles to perform a conversion. The logic generates the sample signal that is used to sample the input on to the capacitor array in the first 3 cycles. The conversion starts from 4th cycle and takes 12 cycles to determine the 12-bit output. The last cycle is the used to latch the output and reset the capacitor array and then a new conversion cycle begins the centre of the aperture. The electric field is highly distributed around the aperture, which non-linear distribution can induce a dielectric force on particle.



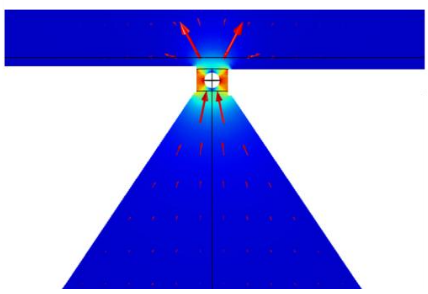
(a)



(b)



(c)



(d)

Fig. 2. Effect of particle size and translocation style on resistance change (a) The relative resistance change with respect to various particle size (b) The relative resistance change of two particles with different size stick together to flow through the sensing channel (c) The relative resistance change of two particles at different distance along the sensing channel (d) the electrical field distribution and arrow flows of E when particle locating at the center of the aperture.

B. Investigation of Crosstalk between Two Sensing Channels

The potential problem of sensor using multiple sensing channels is false positive detection. A change in resistance of one channel may affect the response of a neighbouring channel, thereby resulting increasing particle counts in the sample measurement. To understand the effect of crosstalk due to neighbouring channel in an array, we vary the distance between two channels in our simulation. The relative resistance change in channel with and without particle is compared. Fig. 3 shows the crosstalk between two sensing channels are negligible. When the distance between two channels is 600 µm, the relative resistance change for channel with particle is 6.3% whereas the relative resistance change for neighboring channel without a particle is only 0.3%. The results offer us an insight to optimize the sensor structure for accommodating more Coulter units. Assuming that the gap between sensing channels is 600µm and the channels are arranged in a 2D array configuration, it is feasible to fabricate more than 250 channels on a miniaturize chip (1 cm^2). Therefore, a coulter counter sensor with multiple sensing channels can be designed to improve throughput of particles counting.

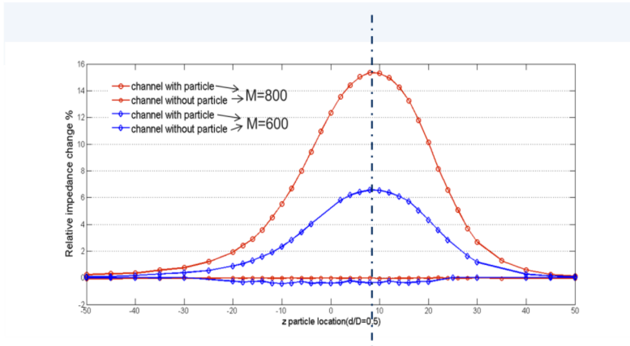


Fig. 3. Comparison of numerical results for two sensing channels separate at 600 µm and 800µm respectively. A change of resistance of one channel does not affect the response of neighbouring channel. The effect of crosstalk between channels is negligible.

IV. Conclusion

A novel micro coulter counter has been proposed and numerically studied to provide some insight into designing Coulter counting devices in a 2D array configuration. The investigation has carried out to the effect of particles size and translocation style on relative resistance change of a sensing channel. The effect of crosstalk between channels is studied to determine the minimum distance between the channels. The concept, demonstrated here on a two sensing channels can be extended for multiple channels in a single chip for high throughput particle counting.

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