Impedance Cytometry for Detection of Particle Counting using Low Phase Noise DDFS – LUT

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Abstract

The elements of DDFS are: Phase accumulator, a phase to amplitude converter also called Look up table (LUT), a Digital to Analog converter and a filter**.** Direct digital frequency synthesis is a method for generating complex high-frequency waveforms for specific applications. This DDFS generates frequency resolution which makes it ideal components in Software defined radios, radar systems, navigational satellites and modern spread spectrum wireless communication systems, but when use for high frequency we get interrupt with spurious noise, larger ROM size, high power consumption. In this paper we are proposing the use of signal generated from DDFS to Impedance Cytometry in which the number of particle get detected by getting the output frequency different from the input frequency. Due to use of small frequency range of signal spurious noise, power consumption and ROM size will be less with effective performance.

Keywords-Direct Digital Frequency Synthesizers (DDFS), Digital to Analog convertor (DAC), Read Only Memory (ROM), Flow Cytometry, Cell analysis and Signal Conditioning.

1. Introduction:

Theoretical research has been done on advanced waveforms with unique characteristics. These advanced waveforms have practical applications in modern communication. In this paper we are trying to relate it to biological field. Major Advantages of a DDFS are that its phase, amplitude and output frequency can be precisely and rapidly manipulated under digital processor control.

- For converting phase information from phase accumulator to amplitude we require larger ROM size but by increasing ROM size power consumption and access time increases so, efforts have been made to reduce the ROM size without degrading the spectral performance by using linear interpolation [1].
- We use conventional architectures which are frequency limited by low speed fabric devices for generation of high frequency, wideband data streams [2].
- A 2 GHz 32 bit ROM based DDFS using 0.13 um CMOS is capable of increasing the operating speed. To improve the efficiency the power hungry phase to amplitude converter is removed and linear D/A converter is replace by nonlinear DAC challenge [3].
- A 2GHz DDFS based on LUT and Rotation is capable of increasing speed and Resolution. In this method, the proposed DDFS is based on the LUT-ROT architecture, which means a combination of LUT and rotation.
- The size of LUT is further reduced by approximation, and multipliers in the conventional PAC are replaced by 7 pipelined rotation units to support high clock frequency [4].
- ROM-less DDFS has been developed to avoid power, area, and speed problems caused by the large ROM table. High-order (more than three) polynomials are utilized to replace the large ROM table and realize the phase to-sin mapper [5].
- Hybrid frequency synthesizers operate over wide frequency range and due to use of copies of fundamental frequency noise performance is reduced. The use of images increases output frequency [6].
- Design of a k band fast hopping synthesizers based on DDS and PLL is designed for a frequency modulation continuous wave radar system. The step frequency is 50 MHz and the lock time is less than 150ns [7].
- DDFS and $\Delta\varepsilon$ Approaches for a fractional frequency synthesizers of Terahertz instruments which will compares the spurious level, power consumption, noise level [8].

The resultant signal generated from DDFS is then applied to sensor for detecting particle. Impedance Cytometry is an emerging research tool for high throughput analysis of dielectric properties of cells and internal cellular components. In bio-related studies, coulter counter and fluorescence-activated cell sorting (FACS) are widely used as high throughput cell counting and classification methods. Coulter counter detects a change in direct current (DC) or low frequency alternating current (AC) impedance signal caused by particle or cell passing through the detection region which can provide information about particle size. This paper is arranged as follows. Section 2 presents the overall system architecture of the proposed DDFS. Section 3 presents Overview of Impedance based micro fluidic Cytometry. Electrode Design, working of Cytometry are explained in section 4 and 5.

2. Basics Study of DDFS:

The phase accumulator is increased by fixed amount known as frequency control word (FCW) at every clock cycle then the phase information is converted to amplitude information by phase to amplitude convertor, then by using D/A convertor digital signal get converted into analog signal. Over all block diagram of the DDFS is shown in figure 1. We gave two input –FCW & clock reference to phase accumulator and phase accumulator integrate the value of FCW at every clock cycle and generated output frequency is given by-

$$f_{out} = {f_{clk} * \mathrm{FCW}}/{2^N}$$

When clocked, the phase accumulator (PA) creates modulo - 2^N saw-tooth waveform which is then converted by the phase-to-amplitude convertor (PAC) to a sampled sinusoid, where N is the number of bits carried in the phase accumulator. The simplest approach for phase-to-sinusoid amplitude is implemented as a ROM LUT. To transfer the whole bit of accumulator to LUT the memory and power consumption will be more so we allow only M number of bits out of N number of bits to the PAC. These effect is known as truncation effect which create phase noise. So, we use a method which requires smaller ROM size for fast responses. The phase increment word FCW is an integer, therefore the frequency resolution is found by setting ΔFCW = 1;

It is equal to –

$$\Delta f = {f_{clk}}/{2^N}$$

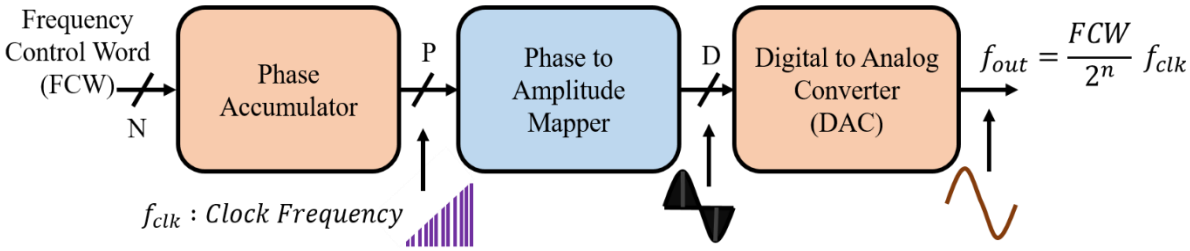

Figure 1. Basic architecture of DDFS.

3. Concept of Impedance Cytometry:

Impedance Cytometry is a technique which uses dielectric or impedance properties of the particles. An externally applied electric field which generated from the DDFS – DAC is used to probe the particles. These can be achieved by applying potential between a pair of electrode and the resulting current flowing through the system is measured. The impedance is the ratio of the voltage to current passing through the system. The development of micro fluidics and lab-on-a-chip type devices has allowed single cell impedance measurements to be performed with high sensitivity and high throughput. Impedance based single cell analysis systems are commonly known as coulter counter which is illustrated in figure 2. They represent a well-established method for counting particles. The main difference from the coulter principle is that we are measuring with AC (alternating current) over a broad frequency range, while coulter works with DC or with AC at very low frequencies.

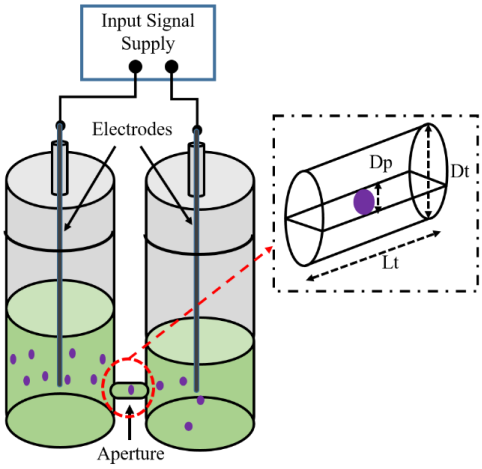

Figure. 2 illustrating the working principles of the Coulter counters

4. Electrode Design:

Three common configurations used in impedance Cytometry is coplanar electrodes, parallel electrodes and constriction electrodes. Each design is based on similar detection method when particle flows between a pair of electrode the electric field between the electrodes get disrupted and the current measure across the electrode will change. In coplanar electrode the fabrication process is easy as single alignment is needed to guide electrodes to the required position inside the channel. Electric field created by coplanar electrode is non- uniform, the impedance measurement relied on the vertical position of the particle in the detection region. To generate homogenous electric field it is placed at the bottom of lateral channel perpendicular to the main channel. The coplanar electrodes have poorer sensitivity and also fringing effect will introduce due to lateral channel. A pair of electrode is used in parallel electrode design. It has better sensitivity as electric field distribution is less divergent. In parallel electrode design fabrication process is complex, as two alignment steps are needed to align the top and bottom electrode configuration. It is also having vertically position dependency, parallel electrode structure is shown in figure 3. Due to lack of direct contact between the electrode and particle the current leakage may occur in which current may pass through high conductivity fluid. The AgCl electrodes placed at inlet and outlet were used instead of thin film electrodes. The drawbacks of these design is that it has lower throughput as compared to other design.

5. Interface of Cytometry:

When electric field is due to the alternating current the polarization of the particles occur due to the charge accumulation at the limits between the aqueous medium and the plasma membrane of the particles. Flow Cytometry is used to found number of particles using coulter counter. Once the sample has been prepared for flow Cytometry analysis from sample, the prepared sample is fed into flow Cytometry. A flow Cytometry contains several key components including the sample, fluidic that move the sample into the flow Cytometry, electrode to which voltage signal is given, detector to sense the change in signal and a computer system to get output data into form that can be analyzed by the researcher. The overall processing of particle counting is depicted in figure 4.

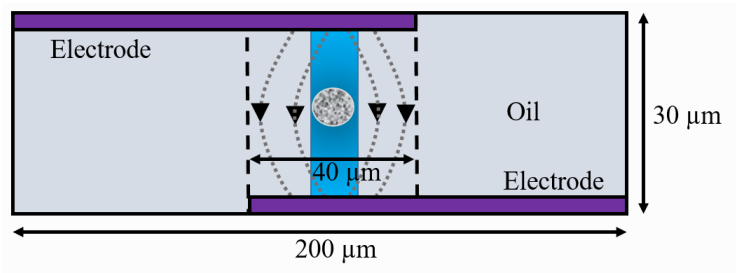

Figure. 3 Electric field effect when particle is in the channel

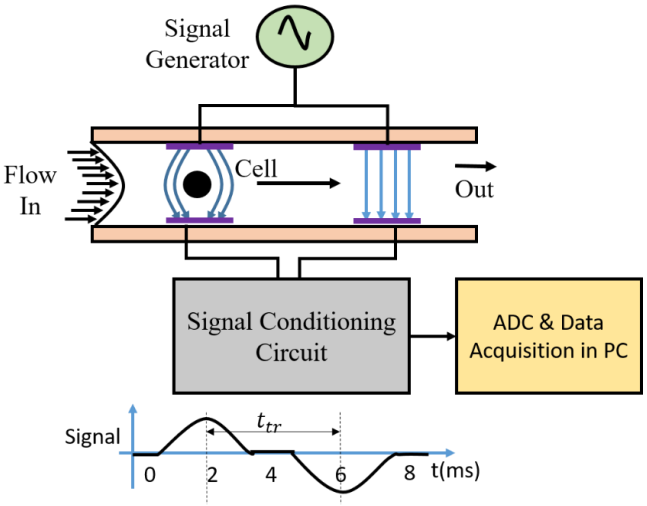

Figure 4. 3D electrode arrangement and electronics interface of an Impedance Flow Cytometry

When there is no particle in the channel then detector or sensor sense the input signal without distortion as there is no change in the electric field and when we apply alternating voltage across the electrode and when there is a particle in the channel then the electric field get distorted and the detector will detect signal different from input signal.

Conclusion

Direct Digital Frequency Synthesizer is found that signal generation at high frequencies will be effectively used for biomedical applications. We get to know how to reduce the phase noise, power consumption and spurious level of signal for the best use and extraction of signal at high quality. High resolution frequency, wide band, high frequency output from the DDFS are easily used and analysed. Generally we see the application of DDFS on radar communication, satellite communication so, we are can relate it to the biological world for better results with good analysis. Based on literature survey we are relating DDFS in Impedance Cytometry to count the number of particle passing through the channel. In the DDFS based impedance cytometry the signal fed to the sensor and resultant signal has to trapped out with the supplied reference signal cancelation so, the particle signal cab be easily analysed.

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