Ultra High Frequency AC stimulation of a Lab-On-Chip through SMA connectors for Cell Manipulation

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Introduction:

Electroporation (EP):

Electroporation is an effect of a E-field on a cell.
The basic set up to generate this effect is a cell suspended between a charged plate and ground, with an electric field generated between, as seen in figure 1.

when voltage greater than or equal to the threshold voltage is applied, pores will form as the e-field disrupts the dipolar components of the membrane, as shown in figure 2. [1]

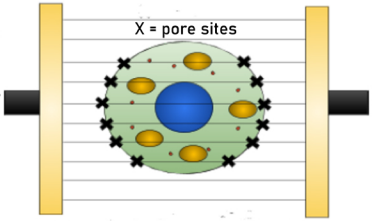

Figure 1: Electroporation of a Cell

The process can be reversable (the cells reseal, unharmed); this has applications such as introducing drugs or DNA containing plasmids into the cell that would usually be too large for the membrane. [2]

The process can also be irreversible, where the cell is destroyed, and have applications such destroying cancer cells.

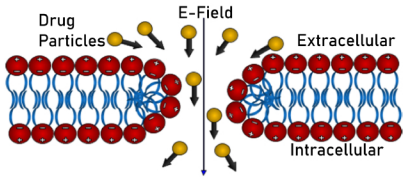

Figure 2: Effects of an electric field on the biphospholipid bilayer (cell membrane)

Dielectrophoresis (DEP):

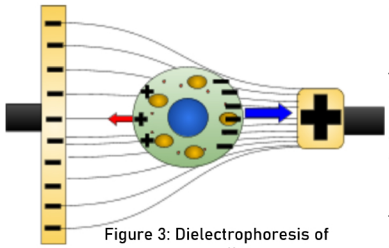

Figure 3: Dielectrophoresis of a cell

Dielectrophoresis is the effect of an non-uniform electric field on a a neural but polarisable particle, such as a cell. [3]

The charged components will be attracted to their relative terminal, however, with the field being stronger for one terminal, the net force will be in favour of that terminal, pulling the entire cell towards it. [3]

This has applications such as cell seperation and sorting. [4]

Project Goals

To design and construct a low-cost , compact and portible setup capable of achieving Dielectrophoresis and Electroporation of cells.
The Setup is comprised of two major components; the exposure site and Ultra High Frequency signal generator.

COPLANAR WAVEGUIDE EXPOSURE SITE - Specifcation :

* 50 ohm impedance matched
* S-Parameters: S22 less than -20db, S1,2 equal to 0
* Mechanically Stable
* Must be low cost to produce
* Design must be microscope compatible

Ultra High Frequency (UHF) Signal Generator - Specification :

* Frequency Range of 0-500MHz
* High Power output

COPLANAR WAVEGUIDE (CPW) EXPOSURE SITE: Design

SMA Connection :

SMA connections will be used to connect the CPW to the signal generator.
SMA connectors have a 50 Ohm impedance.

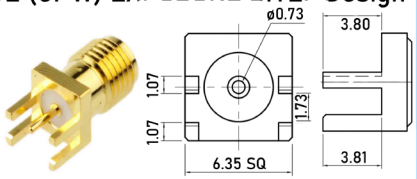

Figure 4: SMA connector & dimensions (mm) [5]

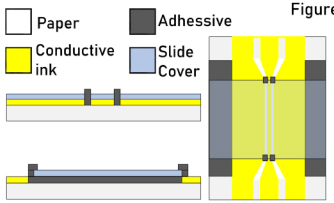

Figure 5: CPW structure & Materials

Structure :

The structure is comprised of a signal line and two ground plates with a gap between them. The gap will be sealed and hold a cell suspension.

In this design, the end sections are thicker than the middle; this is to allow SMA connection.
The structure is made of low cost materials.

CST Design :

Using 'CST Studio Suite' software; a scaled 3D model of the structure (lab-on-chip) could be constructed and simulated across the frequency range 0-500MHz.

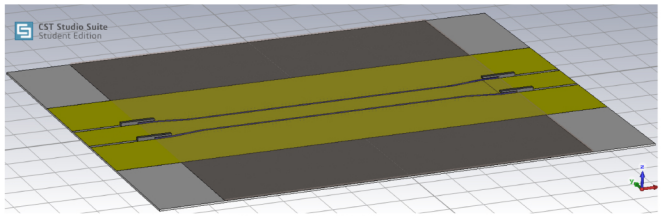

Figure 6: CST CPW Model

Reference Impedance:

The Reference impedance of this design is 50ohm matched, as shown by the graph, figure 7.

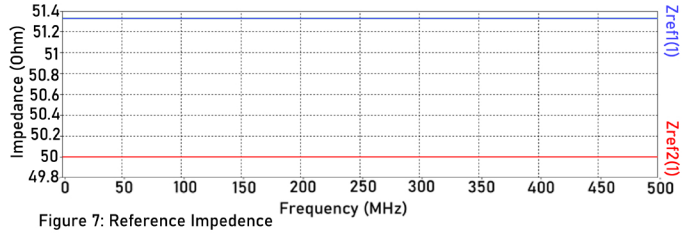

Figure 7: Reference Impedence

S-Parameters:

The S-Parameters for this design is within the range outlined by the specification, this is shown by the graph, figure 8.

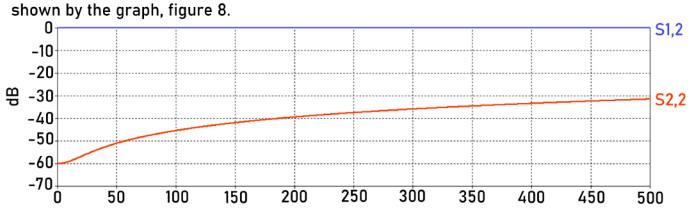

Figure 8: S-parameters

UHF Signal Generator - Design

UHF Signal Generator :

The signal generator is required to supply a signal of specified frequency range.
The design consists of two major components; a Phase Lock Loop (PLL) and a Power Amplifer.

Phase Lock Loop (PLL) :

For this project, a HMC832A evaluation board is being used, similar to that of Figure 9.
The HMC832A Phase Lock Loop (PLL) with intergrated Voltage Controlled Oscillator (VCO) and capable of supplying a frequency range of 25-3000MHz, which is fits within the specified frequency range.

Figure 9: HMC832A Evaluation Board (Analog Devices) [6]

Power Amplifier (PA):

Using a HMC8500PM5E PA, the power of the signal produced by the PLL can be amplified.
This will help generate a larger electric field across the CPW gap, which is being used to maniplulate cells.

The Amplifier will require a homemade PCB to be created in order to connect it to the PLL, this will be first designed using the software 'Eagle'.

Figure 10: Acquired HMC8500PM5E Sample

UHF Signal Generator :

These two components can be connected via SMA. Together, they should produce a signal generator capable of producing a signal 25-500MHz, with a gain range of 19-18db, with a maximum gain of 18db at 500MHz.

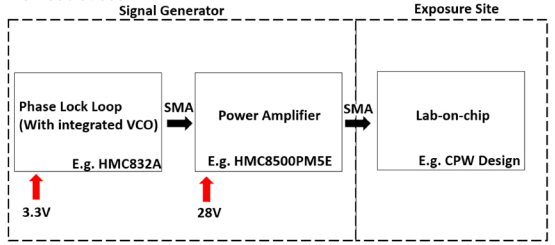

Figure 11: Simple UHF signal generator / exposure site diagram

Conclusion and Future Work

This project is currently in a research and design phase, with designs potentially altering for fabrication or testing reasons.

The design specification for the setup has been shown by simulations and designs to be achievable, the next stage of the project will be practically implementing these designs and/or variations of those designs.

Future work on this project will include:
* A homemade PCB evaluation board for the Power Amplifier
* The UHF signal generator built and tested
* The CPW chips fabricated
* The effects of electroporation and/or Dielectrophoresis observed using the set up

REFERENCES: [1]: Piotr Marszalek, D.-S Liu, Tian Y. Tsong "Schwan equation and transmembrane potential induced by," Biophysical Journal , vol. 58, pp. 1053 - 1058 , 1990.
[2]: Xiaofan Du, Jing Wang, Quan Zhou, Luwei Zhang "Advanced physical techniques for gene delivery based on membrane perforation," 2018.
[3]: Pohl, H. and Crane, J., 1971. Dielectrophoresis of Cells. Biophysical Journal, 11(9).
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