

Droplet-Based Bio-Chips Experiment Report

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**«Design for Micro & Nano Manufacture (NoE PATENT-DfMMM)»
Network of Excellence funded by the European Commission (EC FP6: IST, Unit C2, Contract 507255)**

Outlines

- Experiment Infrastructures
- Experiment report on chemical agents from QinetiQ and MultiSyntech companies.

Experiment Infrastructures

- System Overview
- Bio-chip processing
- FPGA digital signal generating and control module
- DMOS high voltage module
- Contact angle measurement equipment (Physics of Complex Fluids Group)

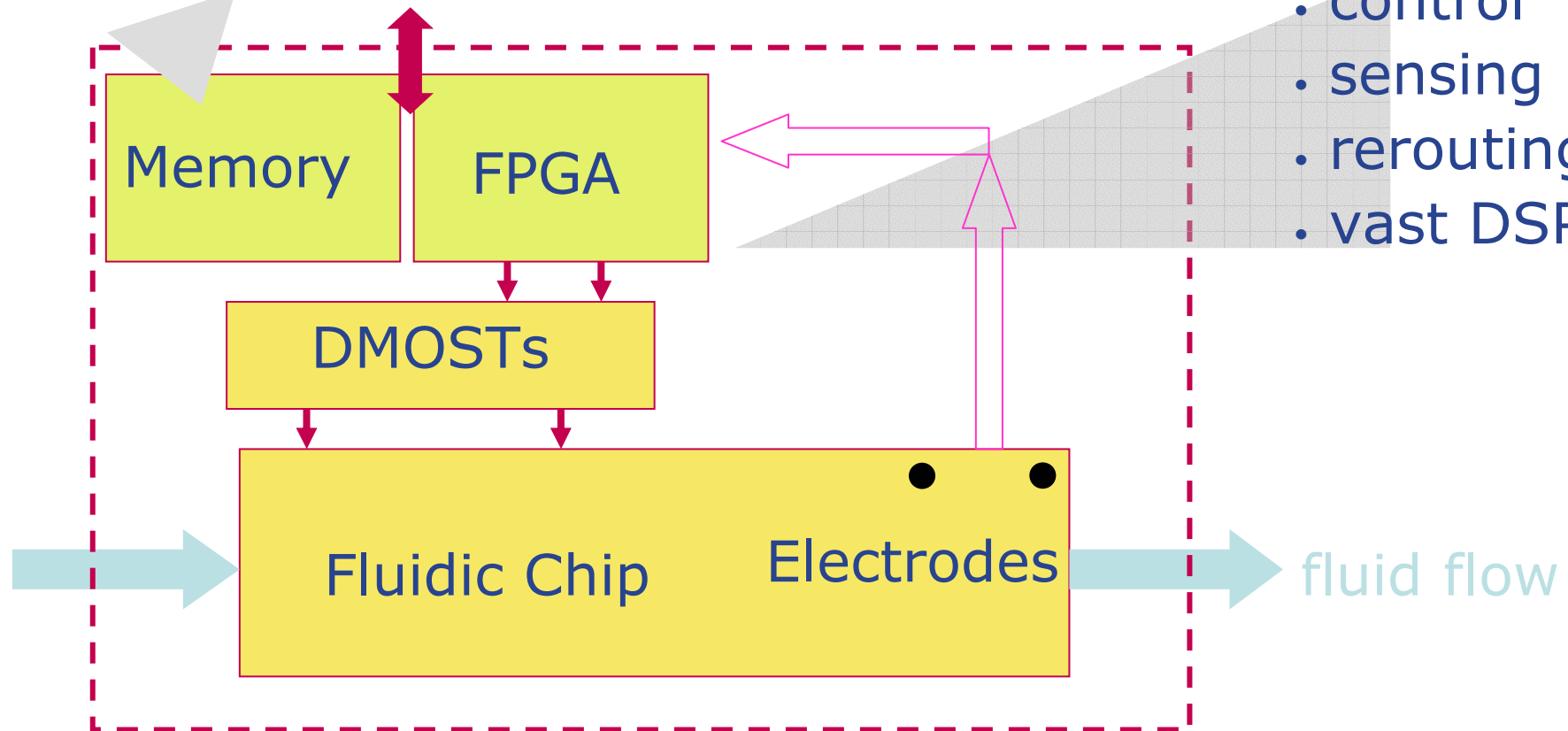
System Overview

• library

(e.g. peptide)

• PDA Com.

- control
- sensing
- rerouting
- vast DSP



• now board -> fluidic SoC later

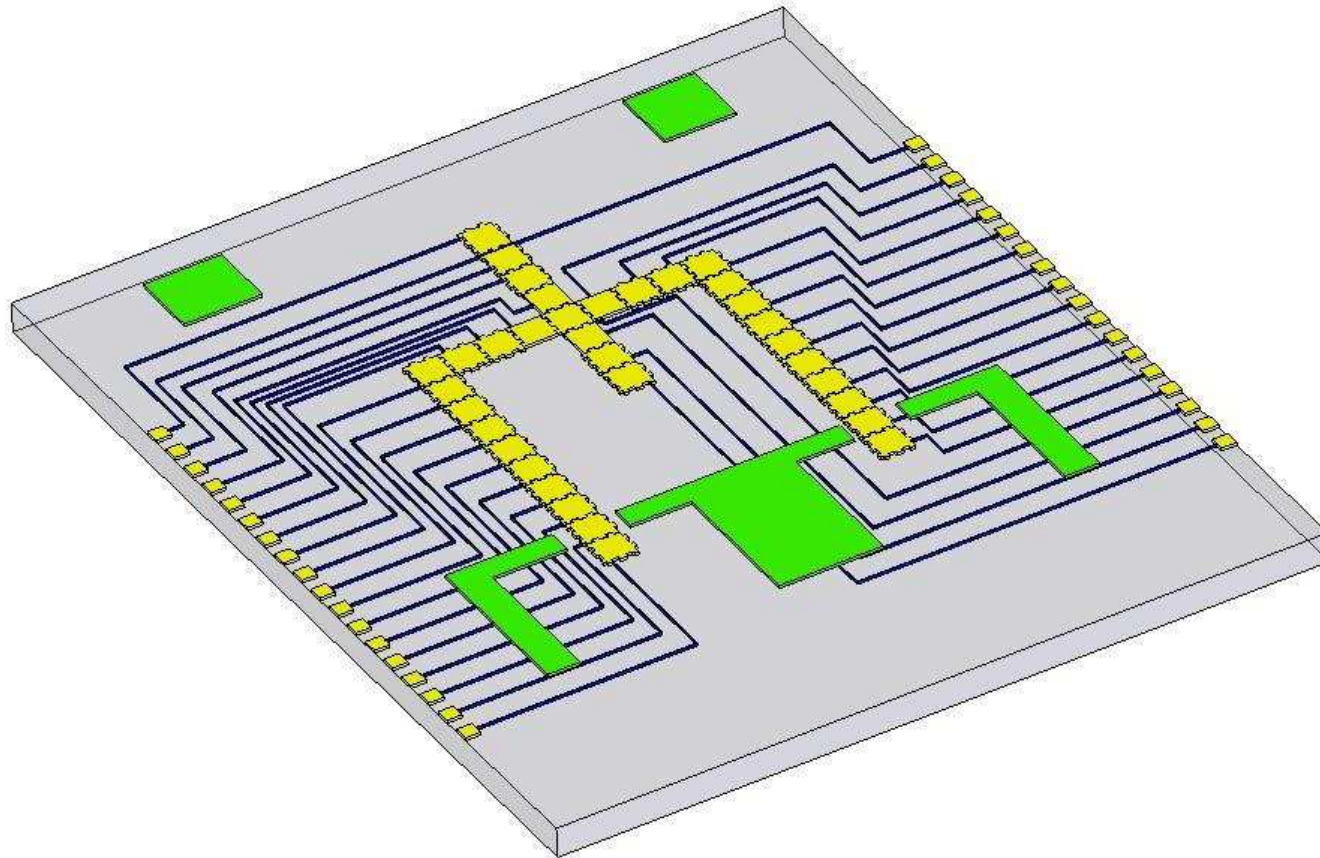
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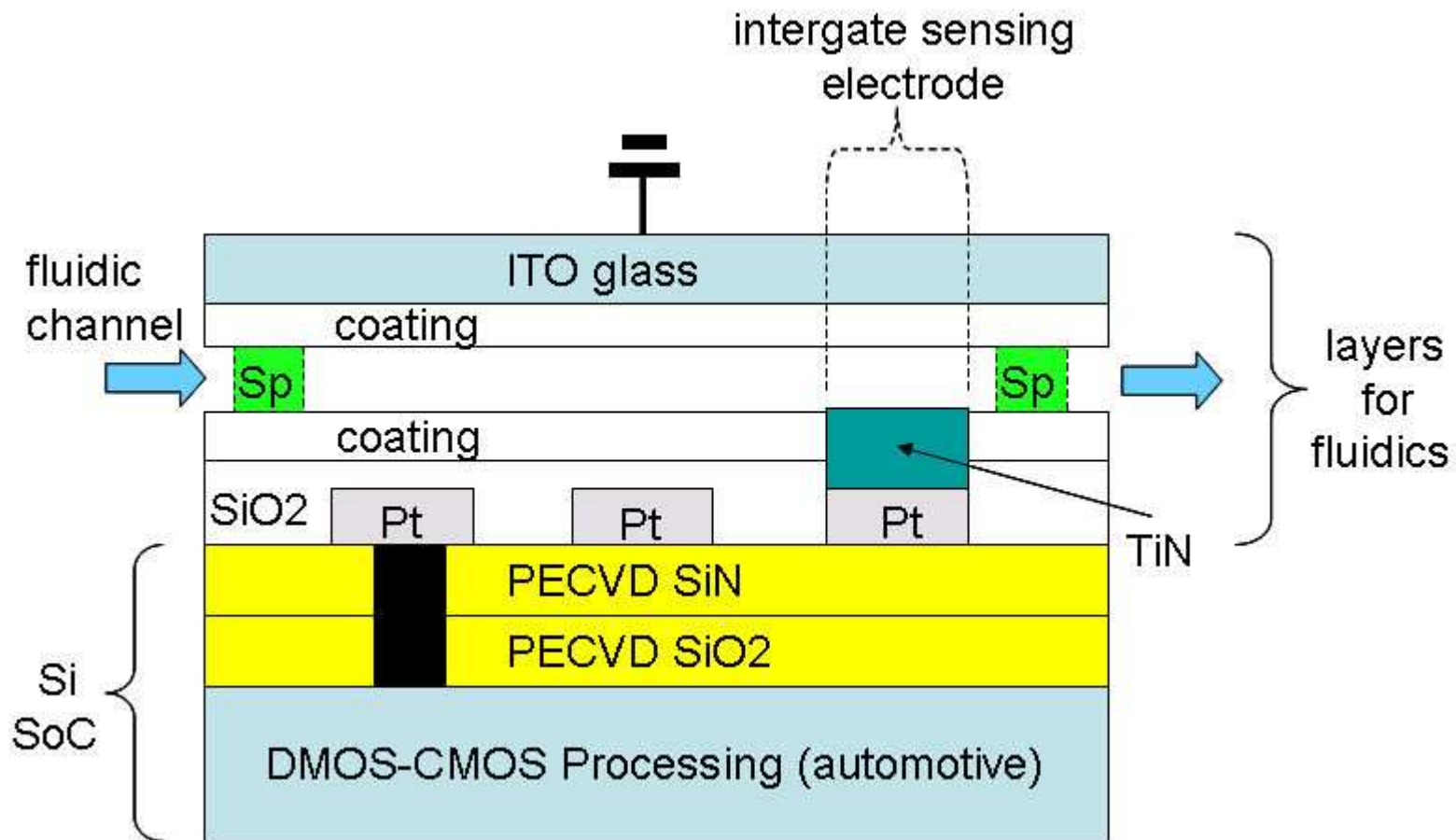
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Bio-chip Layout



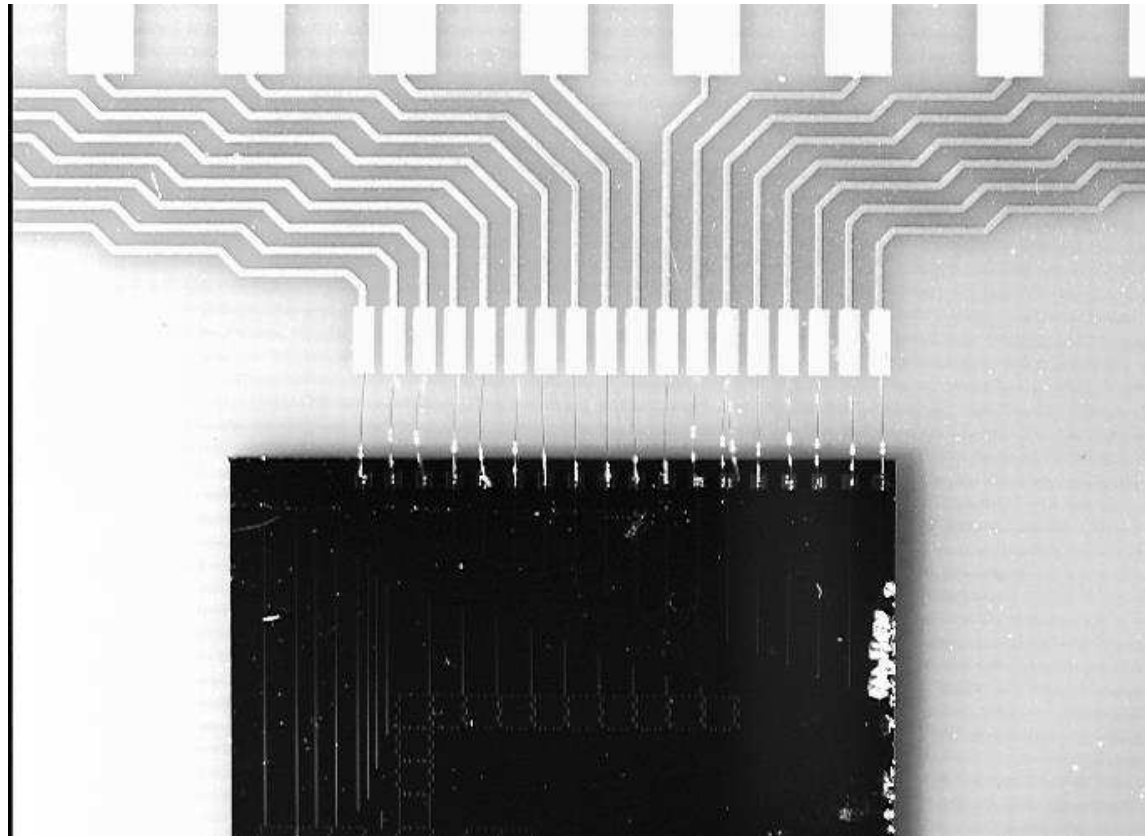
Bio-chip: A Technology Look



Some Dimension Figures

- ❑ Electrode size: 1*1mm.
- ❑ Wire width: 80um.
- ❑ Teflon layer thickness: ~40nm.
- ❑ SiO₂ for insulating: 1um (40~50V estimated as controlling voltage)
- ❑ Improved sandwich insulating structure: SiO₂-SiN(~0.4um)- SiO₂
- ❑ Metal pads on edges: 30*30um.

PCB Connection



First Batch Bio-chips (60V/500Hz, Salt Solution)



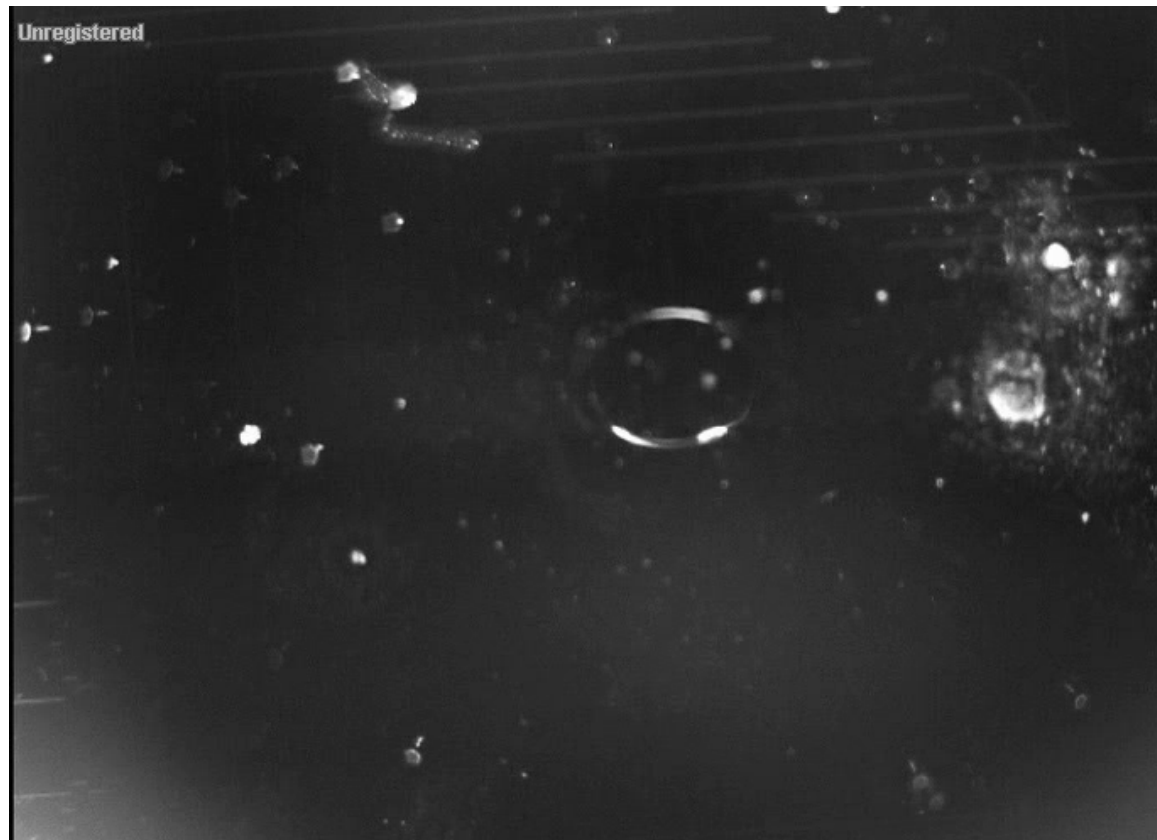
First Batch Bio-chips Spec.

- Using 1 μ m SiO₂ for insulation.
- Control voltage: 60V/500Hz.
- Problem: apt breakdown of the insulating layer under higher voltage or lower frequency (spot defect).
- Controlled by hand.

Second Batch Bio-chips Sandwich insulating layer



Second Batch Bio-chips (110V/200Hz, Salt Solution)



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Second Batch Bio-chips Spec.

- Improvement provided more reliable insulating layer and will not easily breakdown.
- Problem: higher voltage (up to 100V) required to move the droplet.
- Controlled by FPGA + high voltage module.

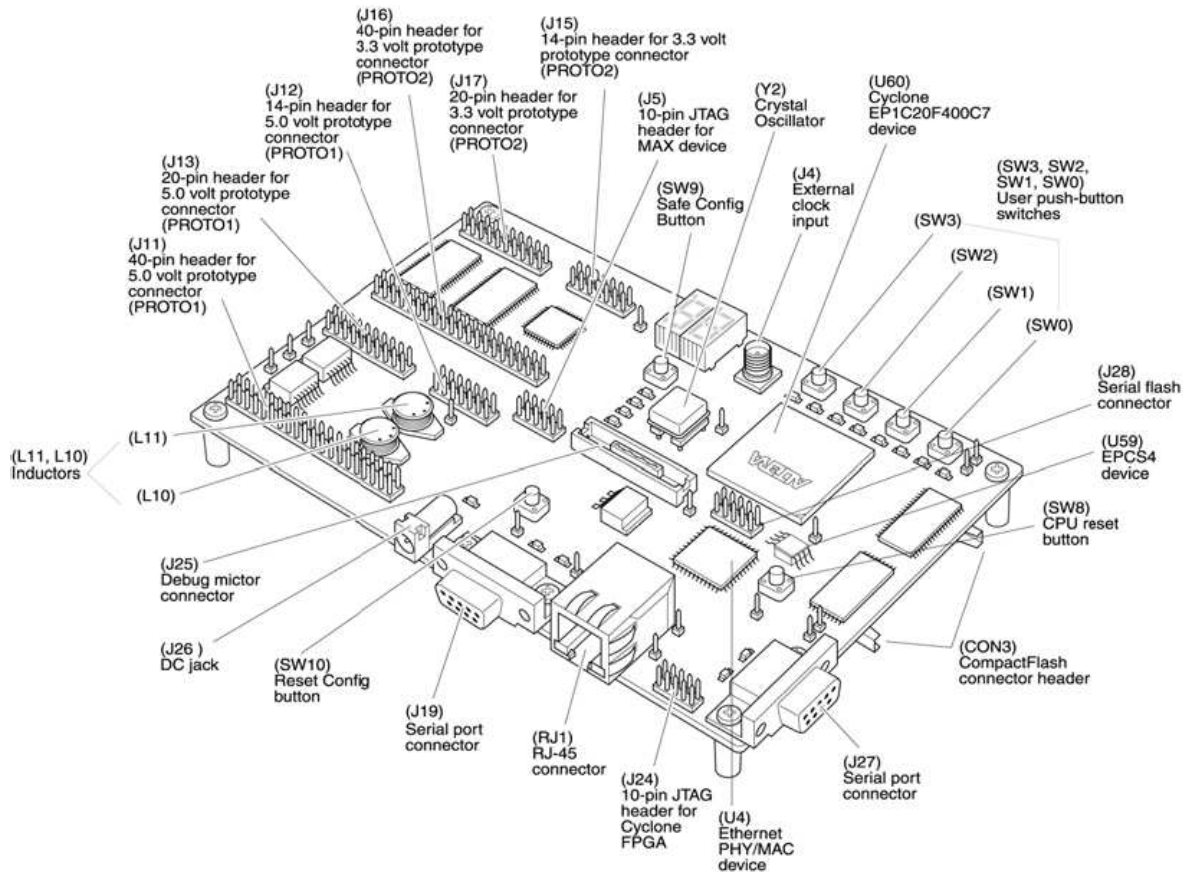
Further Studies

- Play around with the insulating layer technology for a optimized tradeoff between reliability and ease of control.

FPGA digital control module

- ❑ Altera, Nios Development Board Cyclone Edition
- ❑ Prototype control system designed on FPGA
- ❑ Controlling software designed

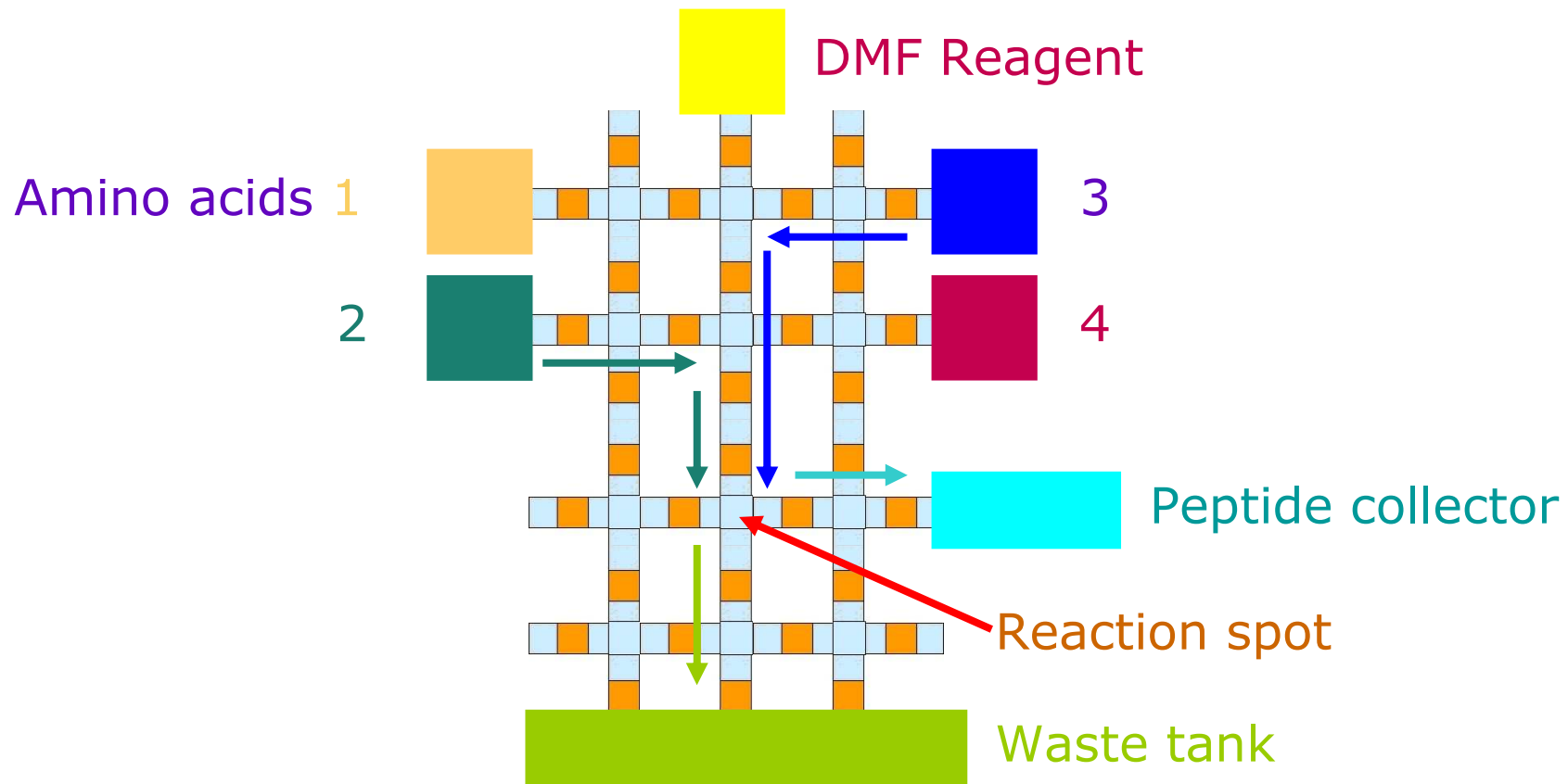
Board Overview



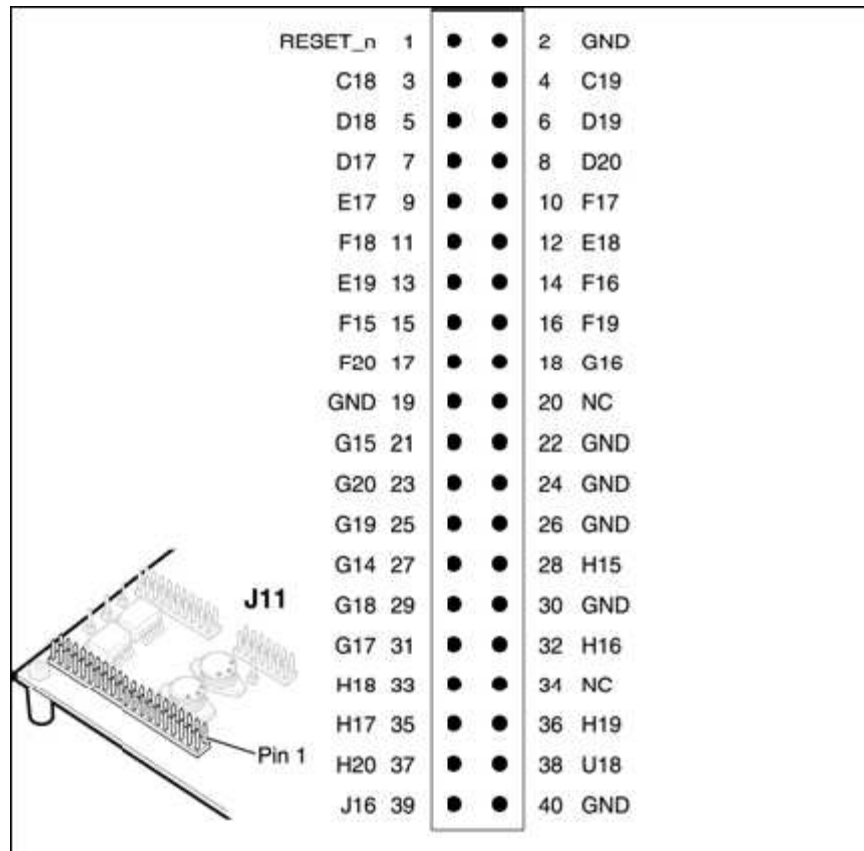
Hardware

- ❑ Nois2 embedded processor core.
- ❑ 512KB RAM
- ❑ Serial communication port
- ❑ 4 level interrupts
- ❑ Timer
- ❑ Up to 100 programmable I/O pins
- ❑ LCD

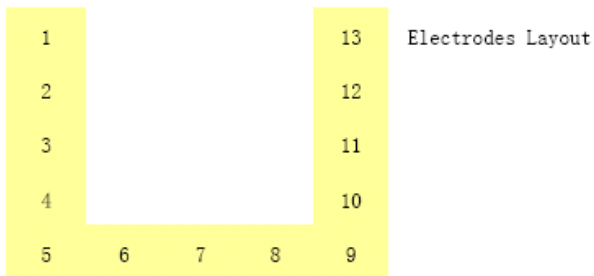
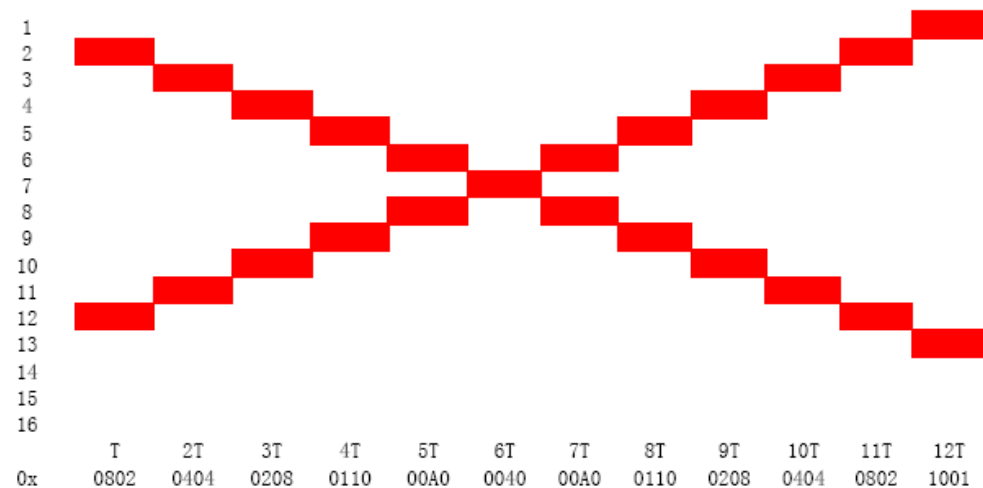
Droplet Transport for Peptide Synthesis



Pin Mapping



Programming for Testing



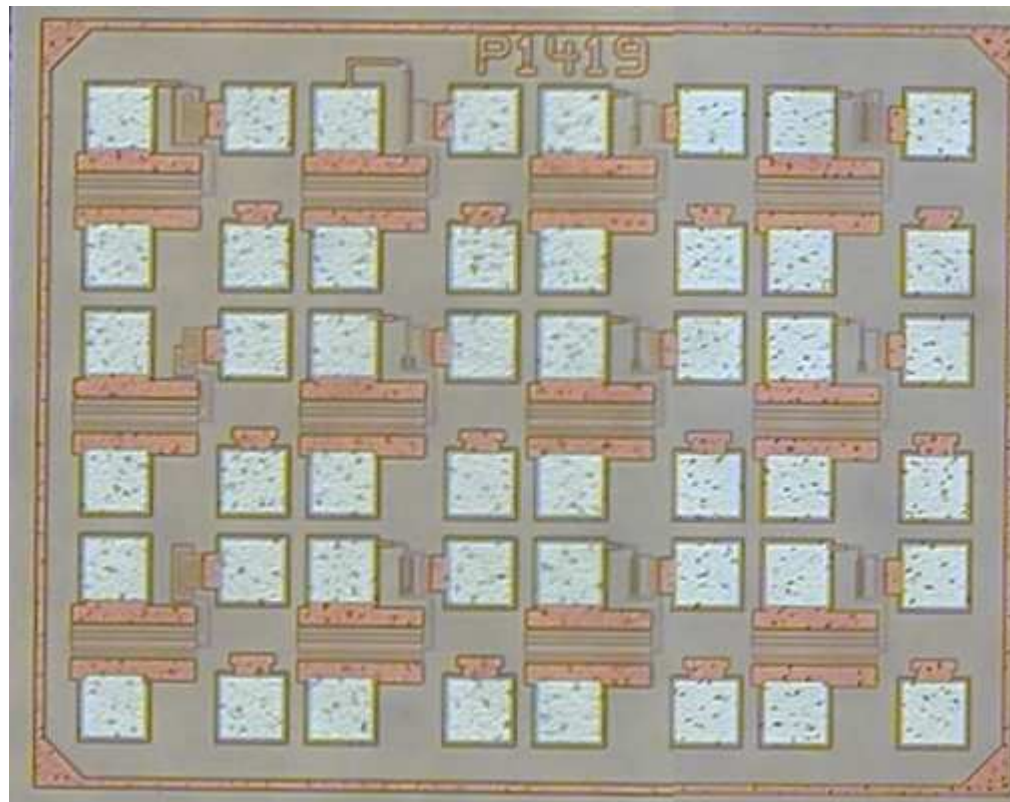
Progress so far...

- Successful integration of the FPGA and high voltage module and the bio-chip for experimental control.

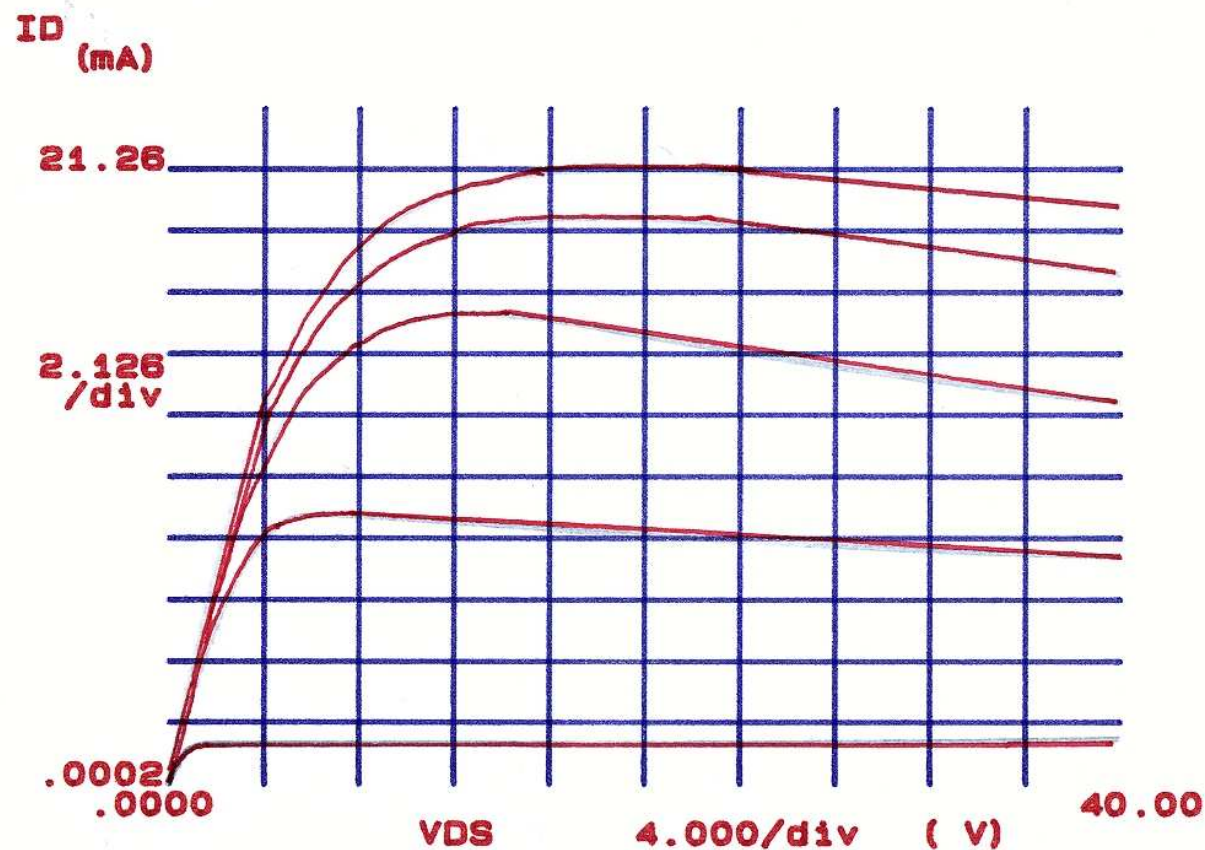
Further Studies

- Easier user interface for giving command to rout droplets.
- uC/OS2 RTOS for real-time controlling/sensing/defect monitoring of the bio-chip.
- Shrink everything on a single chip as the bottom electronics of the MEF system.

DMOS high voltage module (1)



DMOS high voltage module (2)



DMOS high voltage module (3)

- Ability to handle a voltage up to 120V; up to GHz switching.
- 3.3V input logic comparable with stand CMOS.
- Progress: prototype chips processed and packaged. First testing done.
- Normal relays were used for high voltage control in previous experiment.

Further Work

- Combine with the FPGA digital part on a PCB.
- Combine & simulate the complete VHDL code
- Carry out synthesis for 90nm SoC

QinetiQ 1

- some base salt solution and some medium with additional components.
- Using strip electrodes, quite successful.

QinetiQ 2

- ❑ The liquid contains:
- ❑ Balanced salt solution
- ❑ 10% foetal calf serum
- ❑ Penicillin/streptomycin
- ❑ L-glutamine
- ❑ Insulin/transferrin/selenium (all at very low concentrations).

MultiSynTech (Amino Acid)

- ASP, ALA, VAL, LYS.
- DMF and NMP pure solution both very successful in the droplet control experiment

Following Problems Occured

- ❑ 0.5M (0.5mol/L) amino acids in DMF Solution, solid subsides observed, tens of seconds after exposed to air.
- ❑ Consequence: ruin the hydrophobic layer.
- ❑ Possible cause: DMF evaporation led to an unexpected high aa concentration.
- ❑ Solution: use after prepare/lower the concentration/use NMP.

Contact Angel Measurement

- A quantitative way to determine whether one agent is suitable or not for bio-chip manipulation.
- Camera with video processing software.

Methodology

- Measure the contact angle change of one agent on a hydrophobic surface when various voltage is applied.
- The larger the contact angle change, the better this agent's droplet can be controlled.

Measurement Results (1)

Agents	No voltage	40V(5KHz)	50V(5KHz)	Lag	Comments
ASP(DMF)	80.3	71.3	70	no	ok
ASP(NMP)	86.5	72	67.7	yes	good
ALA(NMP)	75.8	59.5	50.5	no	ok
VAL(DMF)	76.8	74	73.7	no	bad
LYS(DMF)	78.1	78	78	/	bad
HBTU(DMF)	77.9	56	46.5	no	good
QinetiQ(2 nd)	109	92	81	no	good

* Most amino acid solution concentration was 0.25M

Measurement Results (2)

Agents	No voltage	40V(5KHz)	40V(2KHz)	40V(1KHz)	Lag	Comments
ALA(DMF)	77.8	71.3	66.1	61.7	no	good
VAL(DMF)	80	80	75.2	68.8	no	good
LYS(DMF)	78.1	78.1	71.3	66	no	good

Conclusion: lowering the control voltage frequency may lead to improved controlling effect.

Contact Angel Measurement Experiment

- Further measurements can be carried out for various agents with a certain concentration. Data can be used to help control a specific agent's droplet and to help simulation work.

Questions?

