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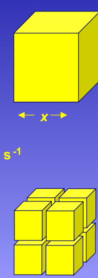
The Imperial College, 6-7 April, 2004

Lab-on-a-Chip and Lab-on-a-Pill
Remote and Distributed Sensing

The Advantages of Miniaturisation

$$t = \frac{x^2}{2D}$$

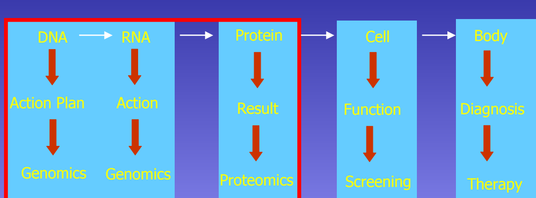


$D = 10^{-5} cm^2 s^{-1}$

cube (x)	volume	time (t)
1 mm	1 µL	500 s
100 µm	1 nL	5 s
10 µm	1 pL	50 ms

- Fast Responses
- Reduced Thermal Mass
- Microfluidic Phenomena
- Surface to Volume Ratio increases
- Surfaces and Interfaces become Critical
- Low Cost, Systems Integration & Manufacturing

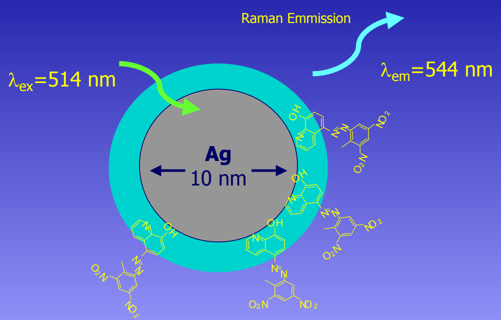
Genes, Proteins, Cells and Bodies



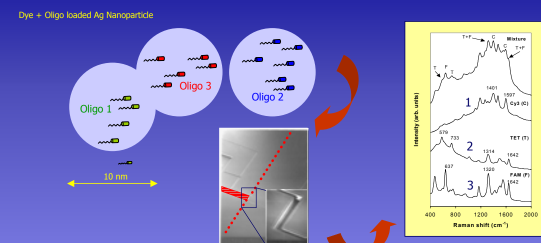
DNA Nanoparticle Sensors

Miniaturisation results in new fluidic phenomena, including large forces due to surface tension, and laminar flow, resulting from interfacial influences. These techniques can be used to improve synthesis in manufacturing (e.g. of nanoparticles).

In Situ Surface Enhanced Resonance Raman Scattering on a Chip



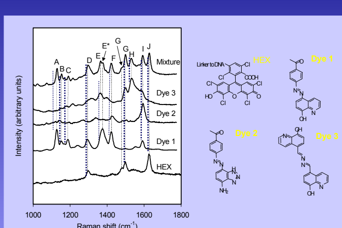
Multiplexed DNA Detection of E.Coli sub-species



The sequences are for E-Coli variants and show the simultaneous detection oligonucleotides:
Oligo 1 (CCC CAC TGC TGC CTC CCG TAG) labelled with carboxyfluorescein (FAM).
Oligo 2 (GAA GGT CCC CCT CTT TGG TCT TG) labelled with 4,7,2',7'-tetrachloro-6-carboxyfluorescein (TET).
Oligo 1 (ATA AAT CGC CAT TTC GTT GAC TAC) labelled with Cy3.

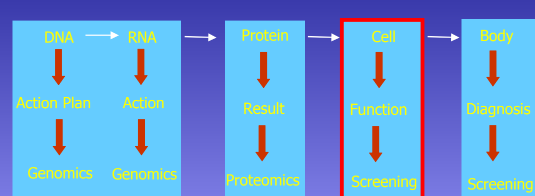
The First SERRS Multiplexing from Labelled Oligonucleotides in a Microfluidic Lab-on-a-Chip,
Cooper, J.M. et al. *J. Chem. Soc. Chem. Commun.* 116, (2004).

Advantages of using SERRS

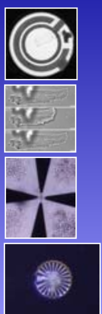


- Fast: 10 sec acquisition time
- In Situ Synthesis of Nanoparticles
- Control of Dispersity of Colloid
- Selectivity (Multiple Fingerprints)
- Suspended Arrays in Lab-on-a-Chip
- Sensitivity (> fluorescence)
- Better Quantification

Genes, Proteins, Cells and Bodies



On-Chip Single Cell Microtechnologies



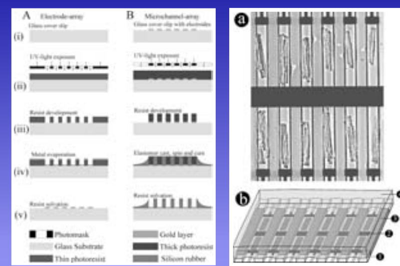
Electrochemical: Adenosine; Inosine; Lactate
Analytical Chemistry, 70, 1164-1170, (1998).
Electroanalysis 12, 631-639 (2000)
Analytical Chemistry 74, 908-914 (2002)

Electrophysiological: Ca^{++}, K^{+}, Action Potential
Biophysical Journal, 2004

Dielectric: Membrane Properties; Ion Flux
Analytical Chemistry 70, 2607-2612 (1998).

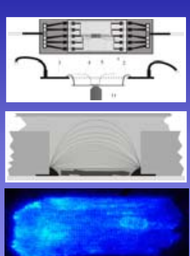
Thermal Nanocalorimetry (ca. 100 μK Resolution)
Analytical Chemistry, 74, 2190-2197, 2002).
Applied Physics Letters, 80, (11) 2029-2031, 2002

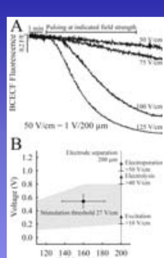
pL Volume Cell Array Technologies: Hard & Soft Lithography



Fabrication of Electrode Array (Hard Lithography) and Microfluidic Channels (Soft Lithography), providing Array-Technologies for Cell Screening.

Field-Stimulation Technologies

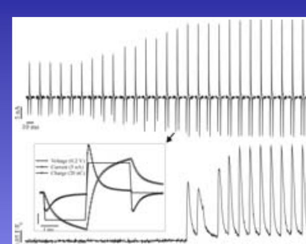




Cell array field stimulation: Miniaturisation serves to keep absolute voltages below threshold levels (e.g. electrolysis), whilst maintaining high fields.

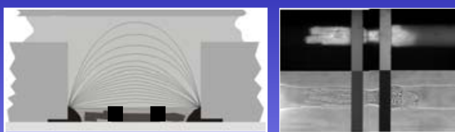
Biophysical Journal, 85, 2003 1766-1774

Full Electrophysiological Characterisation



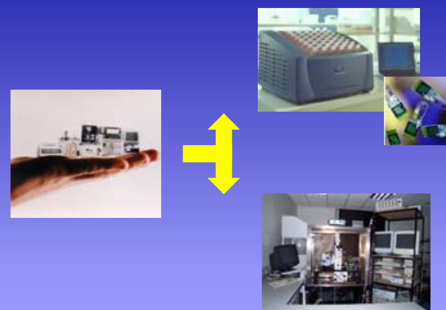
Top: showing current in 100 pL-volume electrochemical cell, over first 250 msec;
Bottom: Cell membrane potential, shown as Fluo-3 trace
Detail: Electrochemical currents and potentials within a single microcell.

Cell Chips for Heart Cell Electrophysiology



Left: Multiplexed electrophysiological measurments using field stimulation. Right: Methods for introducing nanoparticles into cells for functional screening, and for cell electropermeablisation enabling control of intracellular environment

Future Trends:- Lab-on-a-Chip or Chip-in-a-Lab?



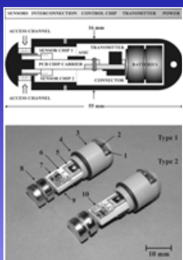
Genes, Proteins, Cells and Bodies

DNA → RNA → Protein → Cell → Body

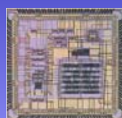
- DNA ↓ Action Plan ↓ Genomics
- RNA ↓ Action ↓ Genomics
- Protein ↓ Result ↓ Proteomics
- Cell ↓ Function ↓ Screening
- Body ↓ Diagnosis ↓ Screening

Future Trends: Distributed Sensors in our Bodies

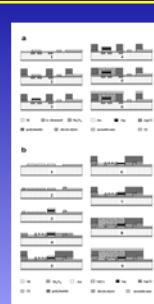
Lab-on-a-Pill: Remote Chemical Imaging

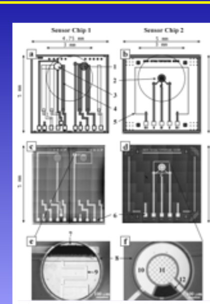


pH, O_2, Temperature, Conductivity
Transmitter: 39.1 MHz, Range 1 m
ASIC: controlling sensors and transmission
Power consumption: 12.1 mW - 40 hrs
Weight: 13.5g
Data Resolution and Rate: 8 bit & 1 kb s^{-1}



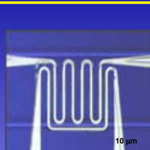
Fabrication

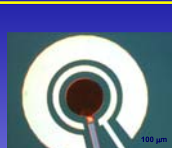


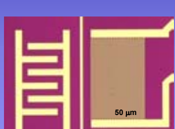


Routes for Fabrication (Left and top) Temperature, pH and Conductivity; (Left Bottom) Oxygen; Right (a, c, e) Temperature, pH and Conductivity; (b,d,f) Oxygen. The two chips are mounted back-to-back with a polymer interface.

Microtechnology: Distributed Sensors

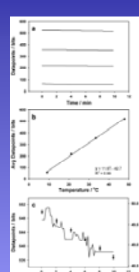






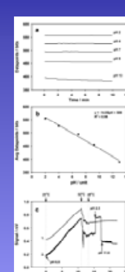
Examples of Devices: CMOS pH and temperature sensor chip; Platinum Resistance Thermometer; Three electrode Oxygen Sensor, Capacitive & Conductivity sensor and Pressure sensor

Results: in Vitro

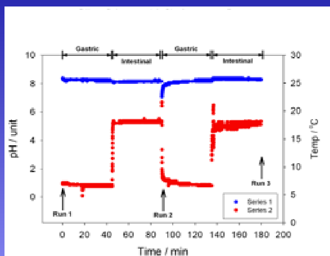


Left: (top) Temperature stability (middle) calibration and (bottom) dynamic temeprature change

Right: (top) pH stability (middle) calibration and (bottom) dynamic temperature and pH change (independent of each other)

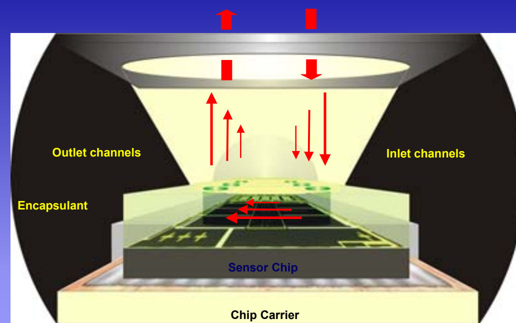


Lab-on-a-Pill: Remote Chemical Imaging



Measurement of Temperature and pH in (dead) whole body of a pig

Future Aims: Microfluidics and Sensors



The Incredible Voyage

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