Electronics Design Centre

University of Glasgow

Wireless Biosensing

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JWNC The James Watt Nanofabrication Centre

Outline

- Capsule-based devices
  - Lei Wang, Lawrence Chirwa, Erik Johannessen
- Sensing-system-on-chip
  - Paul Hammond
- Multi-sensor arrays
  - Mark Milgrew, Mathis Reihle

Our Focus – A Global Problem

- Bowel cancer is the second biggest cancer killer in the world
- Incidence/Mortality
  - Global (2002) 1m new cases annually → 500,000 deaths
  - US (2002) 166,000 new cases → 60,000 deaths
  - Europe (1998) 372,000 new cases → 112,000 deaths
  - UK (2002) 35,600 new cases → 16,100 deaths
- In perspective (UK data)
  - Road accidents → 1 death every 3 hrs (3,200pa)
  - Breast cancer → 1 every 40 minutes (12,400pa)
  - Bowel cancer → 1 every 30 minutes (16,100pa)

- BUT, if discovered early, survival rates >90%

Current direction: Bowel Cancer Screening

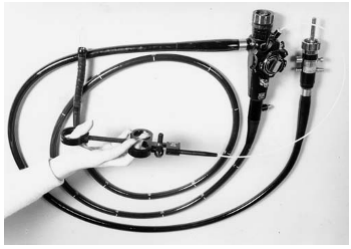
Faecal Occult Blood Test

- Unpleasant to use
- Dietary compliance
- 50% false positives
- Costs £5-10

Wireless BioDevices

Colonoscopy

- Requires sedation and bowel preparation
- 1 in 250 lead to complications (perforation) and 1 in 5000 will die
- Costs £1000
- Takes 3 days of a patient's time



Sensor Pills – early work

- Components
  - 1 pressure sensor
  - 1 transistor
  - 1 battery
  - 10 ft string
- Enabling technology
  - the transistor

R. S. Mackay Berkeley, 1959

The Video Pill

- View of the stomach and the intestine

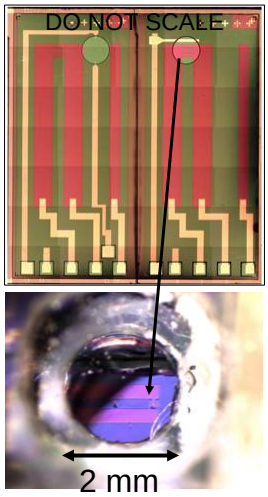
Given Imaging

Other modalities

- Temperature (easy)
- Pressure – gut motility
- Dissolved oxygen - post trauma
- pH – acid reflux
- Tumour markers - cancers
- Glucose/fatty acids – foods and digestion
- Blood/bleeding

Sensor chip – our early work

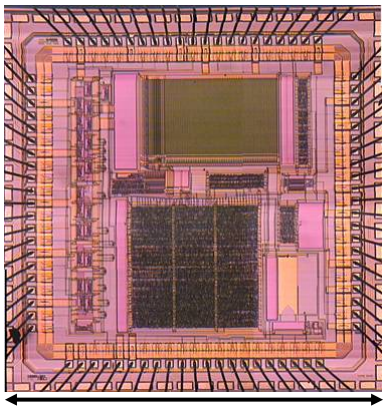
- Lab-on-a-chip concepts
- Miniaturisation of analytical systems
- Fluidics
- High speed
- Multi-sensor
  - Temp
  - pH
  - DO
  - Conductivity (σ)



System-on-Chip

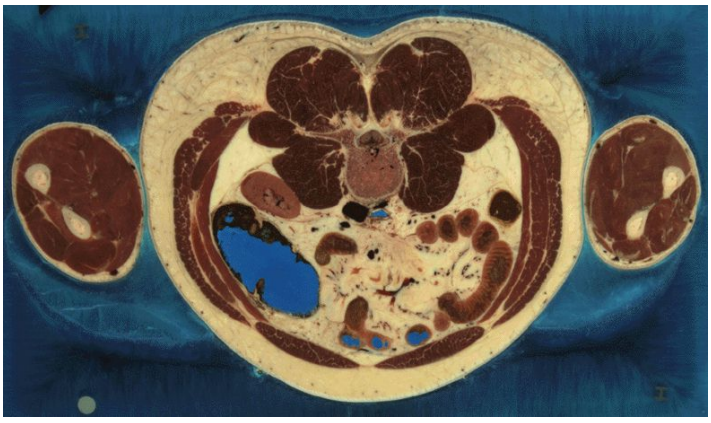
- **Single chip comprising**
  - **Microcontroller**
  - **ROM and RAM**
  - **8 Instrument channels**
    - **pH, T, DO, σ**
  - **Data conversion**
  - **Wireless encoder**

0.6 μm 2 poly 2 metal CMOS from AMS via Europractice



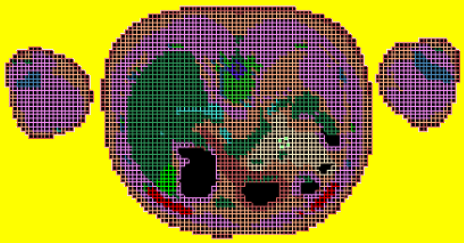
5 mm

Getting data out of a pill



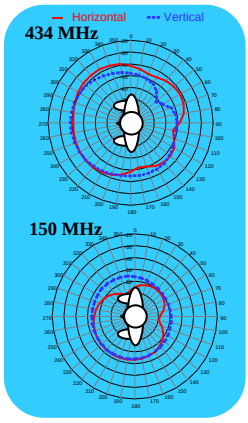
Diagnostic device you eat is a nice idea
BUT we are complicated specimens
Radio environment is complex

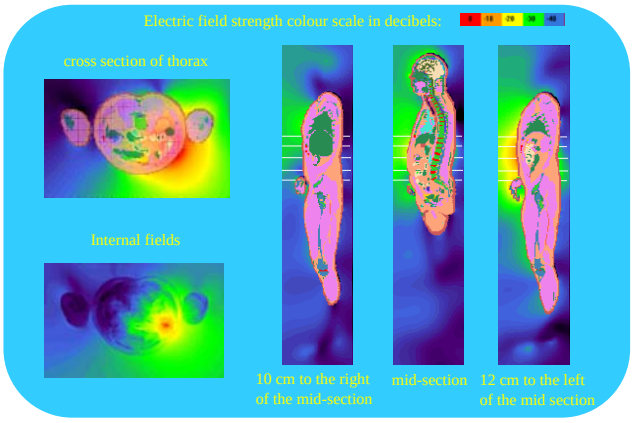
Visible Human Male



3-dimensional computer model of the human body.
(model comprises of over 4.5 million cubes)
Each cube is assigned with the respective tissue electrical and physical parameters.

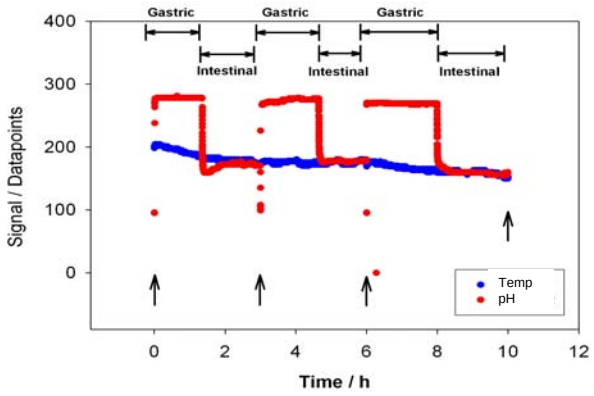
RF simulations





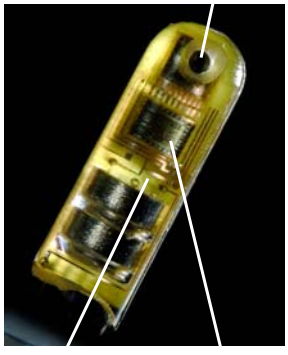
Assembled device

- Typical behaviour (in vitro) – porcine samples

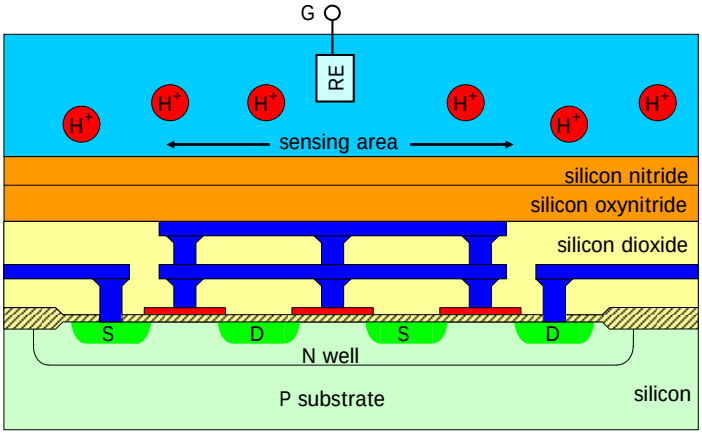


Sensing-System-on-a-Chip

- LIAP
  - Pretty neat, but still want it smaller
- Connections (interconnect) take up lots of space for little functional reward
- What can be done with a single chip?
  - Using CMOS that is widespread
  - Reduce size
  - Reduce power
- Single chip pH meter



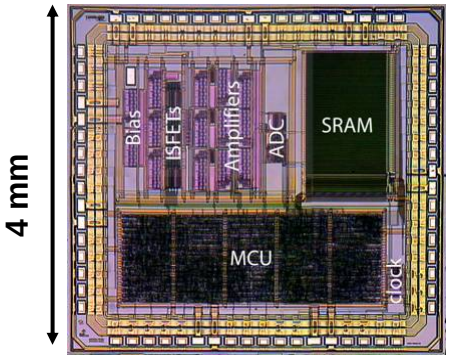
A CMOS Compatible ISFET



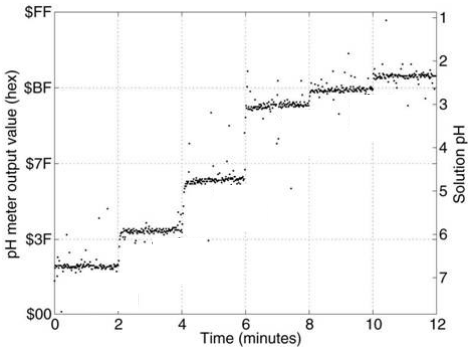
- ISFET threshold voltage proportional to pH

various investigators - Bausells, Wolf, Hammond

pH meter chip



SSOC



Readout

Multi-sensor devices

- Image sensors commonplace
  - Cameras, CMOS or CCD pixel arrays
  - Capture photons
- Biological imaging with photons widespread
- Can we be more direct?
  - Imaging with ions
- Build CMOS imaging arrays for protons
- Cell-based assay

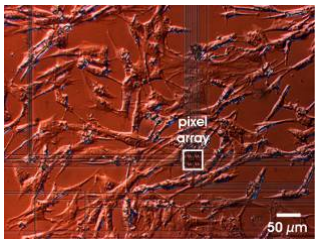
Implementation

- Foundry technology.
  - Standard 0.35 μm CMOS process
  - Access via Europractice IC service

To be presented at ISSCC ‘08

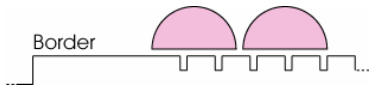
Surface Topography

- 2 x 2 array



- Step height: 600 nm
- Pixel: 3 x 6 μm^2
- Spacing: 10 μm

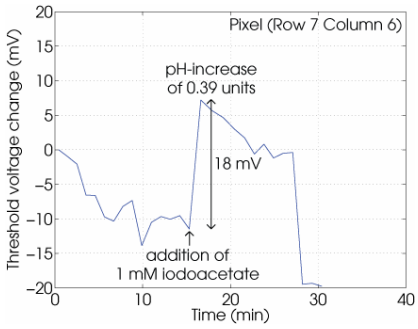
- 16 x 16 array



- Frame border
- Pixel: 11.6 x 11.6 μm^2
- Spacing: 0.6 μm

Glycolysis Bioassay

- Example pixel



- Sensor array

- Decrease in pH due to lactate (before addition of glycolysis inhibitor) and CO_2 diffusing out of cells into medium
- Increase in pH due to vanishing $[H^+]$ in micro-environment between cells and sensor array surface

Summary

- Lab-in-a-pill
- Difficult environment for wireless
- Need to be more proactive about miniaturisation
- Multi-sensor technologies