**BioCMOS**

revolution of analytical instrument and biomedical sensing

*BioCMOS chip*

- **64 x 64 sensor array**
- **1,024 x 1,024 sensor array**

*potentiometric*  
*amperometric*  
*impedimetric*  
*photometric*

4,096 sensors or 1,048,576 sensors on a chip

*internet*  
*

**IoT**  
**Big data**

*BCT-II*

general-purpose equipment to test in laboratory

*BCT-III*

handy equipment specialized for specific application

**BioCMOS**: biomedical CMOS LSI circuit

CMOS is an abbreviation for complementary metal-oxide-semiconductor. CMOS is not only image-sensor where “CMOS” is emphasized in order to distinguish it from CCD image-sensor. Present LSI (Large Scale Integrated) circuits are constructed by CMOS, including processor, memory, transmitter, receiver, controller, and (now) biomedical sensor.
Applications

- Food Security
- Block of Infectious Disease at immigration
- Tailor-made Medicine
- Evidence-based Care
- Portable Diagnostic Inspection System
- Drug discovery
- Police station
- Medical database
- Network
- Traceability
- Customer database

C^4D (Capacitively Coupled Contactless Conductivity Detector)
UV-Vis absorption spectroscopy
Real-time 2-dimensional image of chemical reaction

Stamp-size analytical instrument

Home Healthcare

Parallel detection of different kinds of biomolecules

Network

Network

Parallel detection of different kinds of biomolecules
**Stamp-size analytical instrument**

C⁴D (Capacitively Coupled Contactless Conductivity Detector)

<table>
<thead>
<tr>
<th></th>
<th>electrode</th>
<th>electrode</th>
</tr>
</thead>
<tbody>
<tr>
<td>i</td>
<td>v</td>
<td></td>
</tr>
</tbody>
</table>

**UV-Vis absorption spectroscopy**

**Electrochemical biosensor**

- recognition
- transducer

Molecule to be detected

specific molecular interaction

probe molecule

molecular function

electrochemical measurement

potentiometric, amperometric, impedimetric

Information communication
**enzyme sensor with redox mediator**

![sensor diagram]

**Glucose sensor**

Glucose + ATP $\xrightarrow{\text{hexokinase}}$ G6P + ADP

G6P + NAD $\xrightarrow{\text{G-6-PDH}}$ G6P + NADH

NADH + 2[Fe(CN)₆]³⁻ $\xrightarrow{\text{diaphorase}}$ NAD + 2[Fe(CN)₆]⁴⁺

**Detected glucose [mg/dL]**

- **Diabetic** (5.7%)
- **Potential diabetic** (5.0%)
- **Normal** (4.2%)
- **Hypoglycemia**

**Graphs**

- Detected glucose vs. Glucose in human serum [mg/dL]
- Detected voltage vs. time [sec]

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Detection of single pathogenic microorganism (virus, bacterium, parasite)

measurement of small impedance in pL solution

Detection of dielectric dispersion specific to pathogenic microorganism

\[ f = 1 \text{ Hz} - 3 \text{ MHz} \]
\[ Z = 1 \text{ M}\Omega - 10 \text{ G}\Omega \]

schematic cross-sectional view

pathogenic microorganism insulator Si LSI
electrode

detection of specific pathogenic microorganism

1-2 cycles

sample mixing with antibody-beads

beads captured by magnet

removal of solution

mixing with cleaning solution

introduction to sensor

impedance measurement

~ 10 minutes

~ one minute
The number of specific DNA or RNA is isothermally amplified to a million times in half hour.

**microelectrode cyclic voltammetry**


**On-chip impedance sensor array**

verification using ion solution
BioCMOS chips

- Potentiometric
- Photometric
- Amperometric
- Impedimetric
- Photometric

64x64 sensor array

1,024x 1,024 sensor array
**Smart Electrode**

- gold electrode
- output (0-5V)
- 5V
- 0V
- low noise unity-gain voltage amp.

<table>
<thead>
<tr>
<th>Specification</th>
<th>Value</th>
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<tbody>
<tr>
<td>Sensor type</td>
<td>potentiometric</td>
</tr>
<tr>
<td>Noise (nV/\sqrt{Hz})</td>
<td>40</td>
</tr>
<tr>
<td>Peak-to-peak noise (\muV)</td>
<td>10</td>
</tr>
<tr>
<td>Power</td>
<td>DC 5V, 0.12mA</td>
</tr>
<tr>
<td>Dimensions (mm)</td>
<td>W1.5 x D0.5 x H0.3</td>
</tr>
</tbody>
</table>

**Wafer-scale Chip**

- Microtiter plate type

**On-chip impedance sensor array**

- 64 x 64 impedance sensor array
BCT-II & BCT-III

BCT-II and BCT-III support the various types of biological sensor system as a hand-held and stand-alone analyzer. BioCMOS chip includes potentiometric, amperometric, impedimetric and photometric sensors; more than 4,000 sensors on a chip with a size of less than 1 square cm.

BCT-II is a general-purpose equipment, not specialized for specific application. It is rather development kit to test in laboratory.

BCT-III is a handy and user friendly equipment. It can realize specific applications such as glucose sensor, DNA sequencer, bacteria or viruses counting, ion chromatography, and so on.

By inserting the BioCMOS chip, sensing mode is automatically selected.

**Photo & Potentiometric sensor**

**Impedimetric sensor**

**Photometric sensor**
Language designed specifically for programming measurement

{#$$ "Potential array Vref dependence"}
{#$0 "Vref" "0"}
{#$1 "median" ""}
{#$2 "Vref,min" "0"}
{#$3 "Vref,max" "5"}
{#$4 "Vref,step" "0.1"}
{#$5 "SW" "0"}
{#$6 "array size" "64"}
{#$7 "x" "-1"}
{#$8 "y" "-1"}
{#$9 "step" "1"}

#include ./sub/TR6142.sub

procedure measure;
begin
    call TR6142_putV:r0;
    wait:0.1;
    read:MCU;
    write:MCU;
    r1=data:median;
    plot:r0:r1;
    writeln:r0:(data:min):(data:max):(data:median):(data:mean):(data:stddev);
end;

procedure ref_sweep_forward;
begin
    while r0 < r3 do
        begin
            call measure;
            r0 = r0 + r4;
        end;
end;

#define TR6142 26

procedure TR6142_init;
begin
    send:TR6142:"HV5";
end;

procedure TR6142_putV:v;
begin
    send:TR6142:"D%6.3fE":v;
end;

stand alone

from smartphone

BCT-III

BCT-II

from PC

Export to EXCEL

USB memory

battery

Data visualization
The possibilities are infinite.