Devices for Monitoring Physiological Analytes

YINAN TANG
Background

- Biosensor and its electrochemical transducer
  - Simple, inexpensive, accurate and sensitive platform
  - Inherent miniaturization for both the detector and control instrumentation

- Application Fields
  - Medical diagnostics
  - Food industry
  - National security
  - Environmental monitoring
Background

- Biosensor and its electrochemical transducer
Background

- Blood glucose meter
  - The first and the most widespread commercial biosensor
  - Developed by Leland C. Clark in 1962
  - Enzyme-electrochemical device on a slide
  - Dominate the $5 billion/year diabetes monitoring market over the past two decades
Outline

- Electrochemical fundamental
  - Three-electrode electrochemical sensor
    - Potentiostat circuit design
    - Handheld blood glucose meter
    - Continuous glucose monitoring system
  - Implantable electrochemical glucose sensor
    - Challenges and outlook
Some Electrochemical Detection Fundamental

- Faradaic Current $i$
  - $A^+(\text{surface}) + e^- \rightarrow A$
  - $i \uparrow$ with applied potential until reaches a limiting value
- In the whole system
  - $A^+(\text{bulk}) \rightarrow A^+(\text{surface}) \rightarrow A$
    - Diffusion Control Rate Limiting
- Faradaic Current $i \propto [A^+]$
Some Electrochemical Detection Fundamental

- **Amperometry:**
  - Redox reaction is enabled by an applied potential
  - Current is measured to determine [Analyte]
Three-electrode electrochemical sensor

- Control potential across the double layer at the WE.
- But how to measure it?
- Using a well-behaved RE.
- RE can maintain a constant potential when no current flows through it.
- CE is added to balance the current generated at the WE.
Basic Potentiostat Circuit

- A potentiostat is a control and measuring device.
  - Maintain a fixed potential between the WE and RE
  - Measure the current from the WE, delivering a usable signal to an output terminal

- Current Measurement
  - WE is connected to gnd.
  - \( V_{\text{out}} = I \times R_f \)
  - e.g. \( 1 \mu A \times 100k\Omega = 0.1V \)
Basic Potentiostat Circuit

- A potentiostat is a control and measuring device.
  - Maintain a fixed potential between the WE and RE
  - Measure the current from the WE, delivering a usable signal to an output terminal

- Potential Control
  - Negative feedback
  - No current through RE
Electrochemical Glucose Sensors

- A hot and active field

About 6,000 peer reviewed articles have been published on electrochemical glucose assays and sensors, of which 700 were published in the 2005–2006 two-year period.
Electrochemical Glucose Sensors

- A hot and active field

- Detection Mechanism

  \[ \text{Glucose} + \text{O}_2 \rightarrow \text{Gluconic Acid} + \text{H}_2\text{O}_2 \]
Handheld Blood Glucose Meter

- Small battery-operated devices

A blood sample is taken

Blood is put on monitor to check glucose levels

If glucose levels are too high insulin is administered, if glucose levels are too low carbohydrates are ingested

One way to administer insulin is through an insulin pump
Handheld Blood Glucose Meter
Handheld Blood Glucose Meter

- Small battery-operated devices

Performance Matrics
- Sample size
  10μL => 0.3 μL => Capillary action
- Data storage and manipulation
- Power
- Test strip calibration
- Rapid and accurate measurement
Continuous Real-time Glucose Monitoring Systems

- Real-time devices on the market
  - Medtronic Guardian® & Paradigm® Real-Time
  - Abbott FreeStyle Navigator
  - DexCom STS™
Continuous Glucose Monitoring Systems (CGMS)

- Components of a CGMS
Continuous Glucose Monitoring Systems (CGMS)

- Components of a CGMS
- Clinical Significant
- Advantages of CGMS

Meaningful data
Reduce hypoglycaemia
Patient education
Increased motivation

A confirmatory fingerstick is required prior to taking action.
Implantable Electrochemical Glucose Sensors

GOx
Glucose + O₂ ===> Gluconic Acid + H₂O₂

→

GOx + Glucose ==> GOx-H₂ + Gluconic Acid
GOx-H₂ + O₂ ==> GOx + H₂O₂

• Major Issue: O₂-dependent measurement
• Alternative approach

GOx-H₂ + Med_{ox} ==> GOx + Med_{red}

• E.g. Iridium and Iridium Oxide (Ir/IrOx) nanoparticles
Implantable Electrochemical Glucose Sensors

**Features:**

- Wireless telemetry link for powering and data transmission
- Minimized implant size with TSMC 0.1 8um CMOS technology and flip-chip bonding of the sensor
- Pulse-position-modulation (PPM) for data transmission
Challenges

- Biocompatibility of implantable/subcutaneous sensor
- Biochemical interference, patient-to-patient variability

Outlook

- Power generation inside biological system (enzyme fuel cell)
- Energy-based monitor (RF, thermal, optical technology)
- Revolution in near-patient diagnostics and medical decision making
  - Faster decision-making
  - Improve compliance
  - Optimize treatment
- Earlier treatment
- Reduce complications
- Reduce healthcare cost
References

Thank you all!
Any Questions?