Devices for Monitoring Physiological Analytes

YINAN TANG

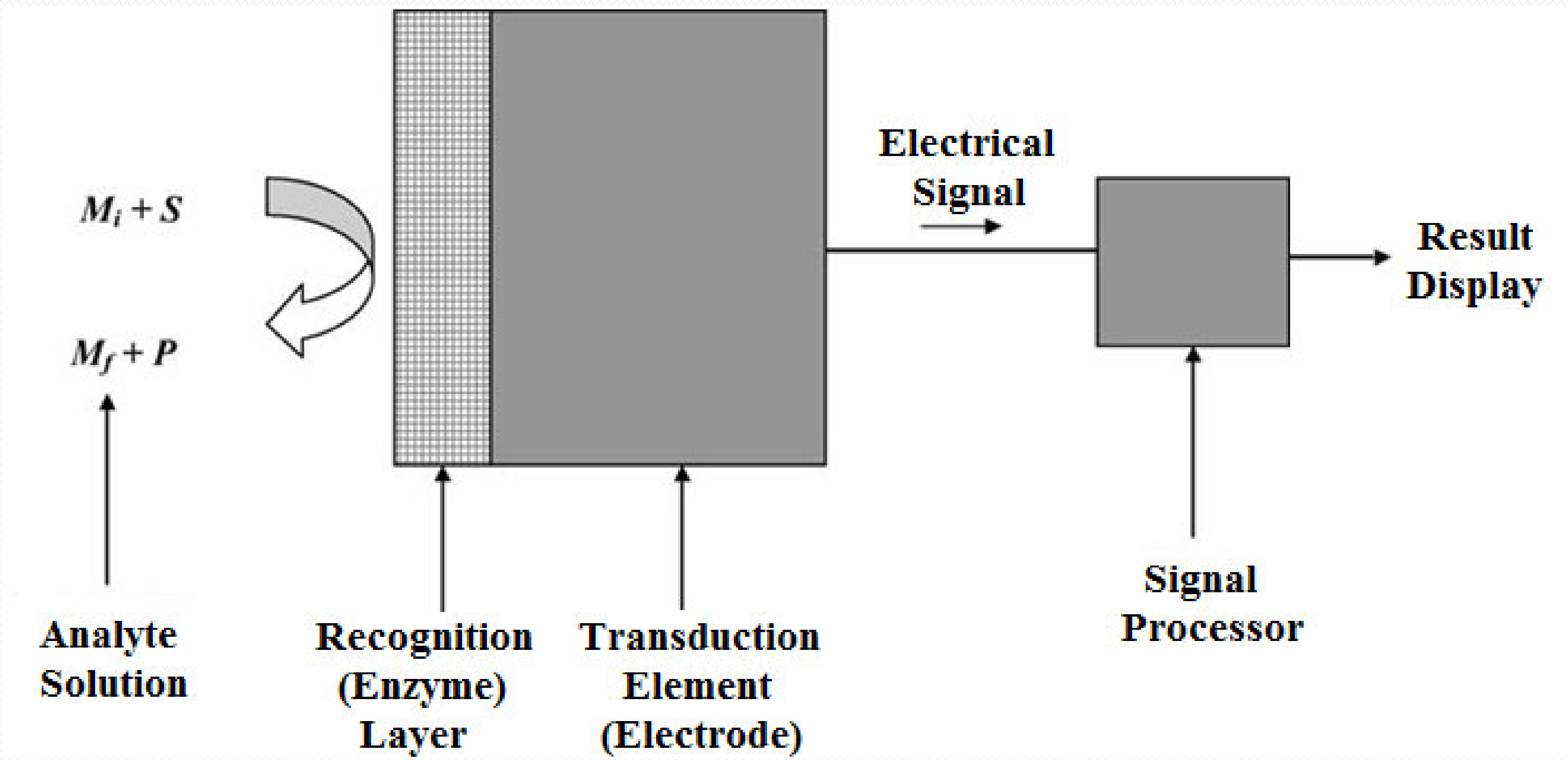
Background

- 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

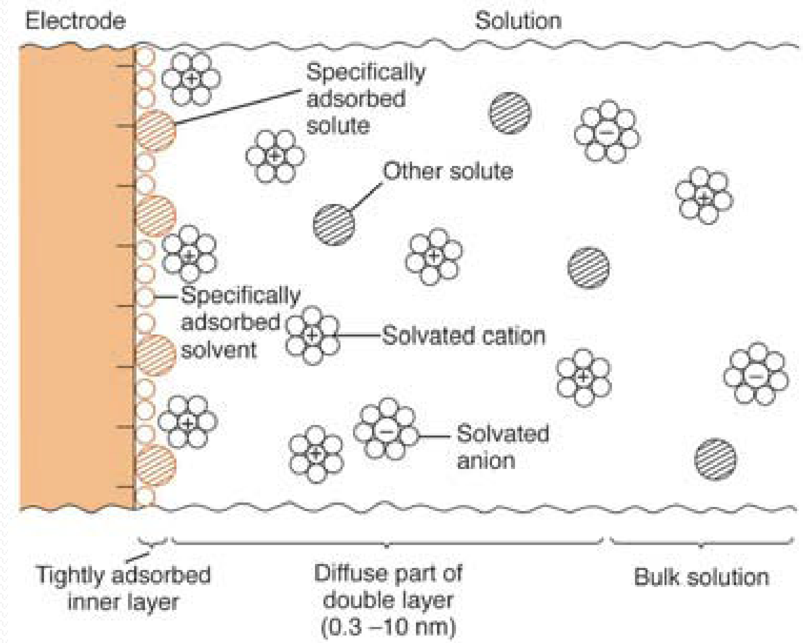
- Electrochemical fundamental
- Three-electrode electrochemical sensor
- Potentiostat circuit design
- Handheld blood glucose meter
- Continuous glucose monitoring system
- Implantable electrochemical glucose sensor
- Challenges and outlook

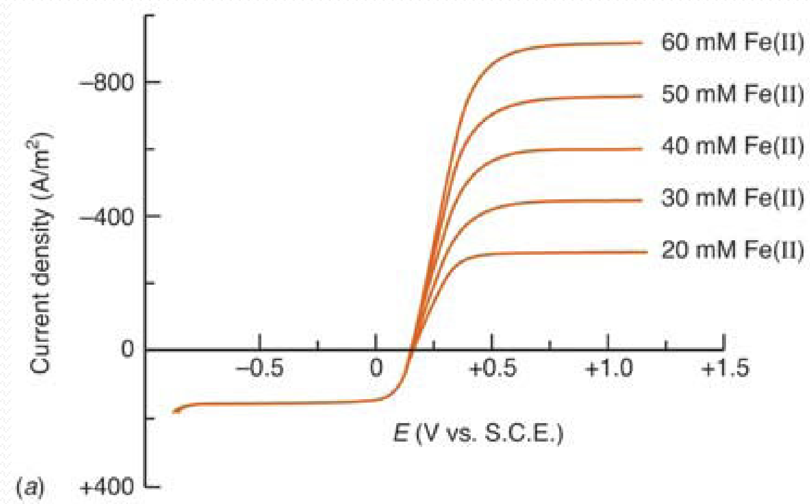
Some Electrochemical Detection Fundamental

- Faradaic Current i
  - A^+(surface) + e^- → A
  - i ↑with applied potential until reaches a limiting value
- In the whole system
  - A^+(bulk) → A^+(surface) → A

Diffusion Control
Rate Limiting

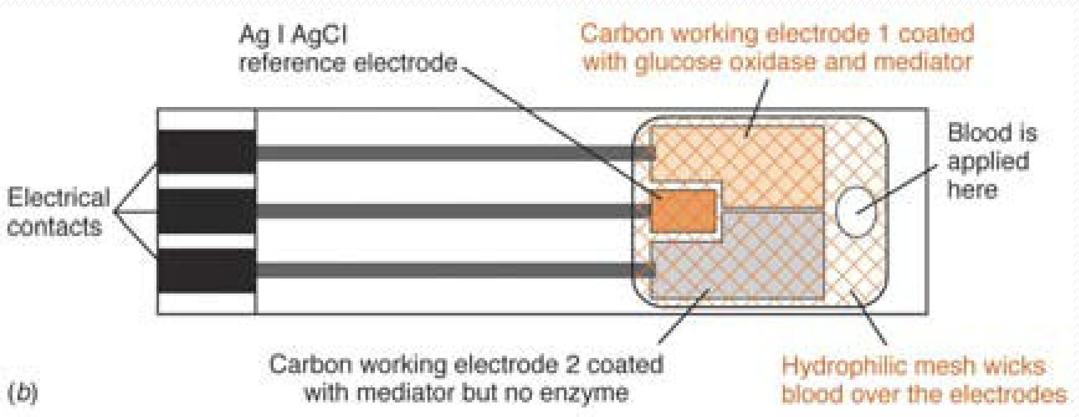
- Faradaic Current i ∞ [A^+]

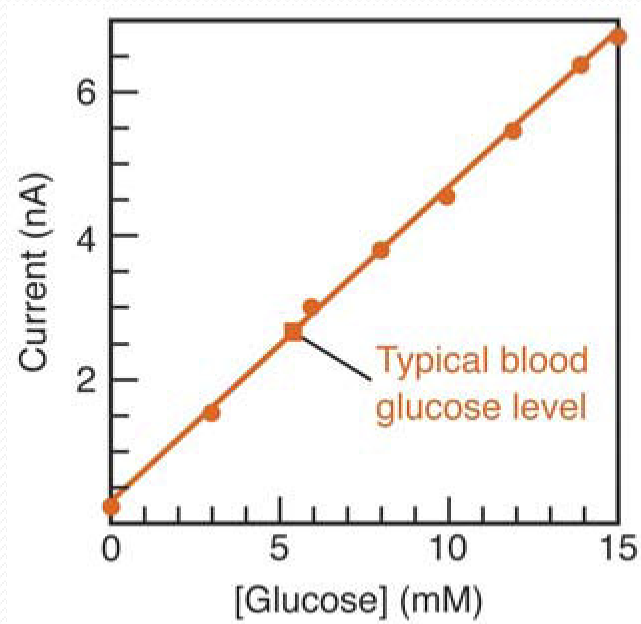




Some Electrochemical Detection Fundamental

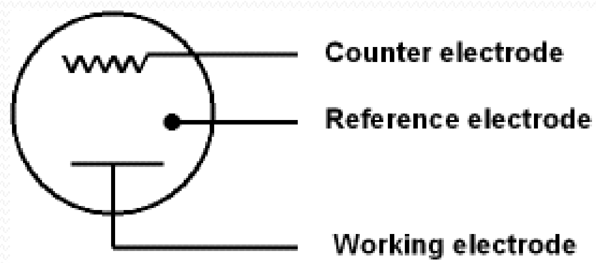
- **Amperometry:**
  - **Redox reaction is enabled by an applied potential**
  - **Current is measured to determine [Analyte]**



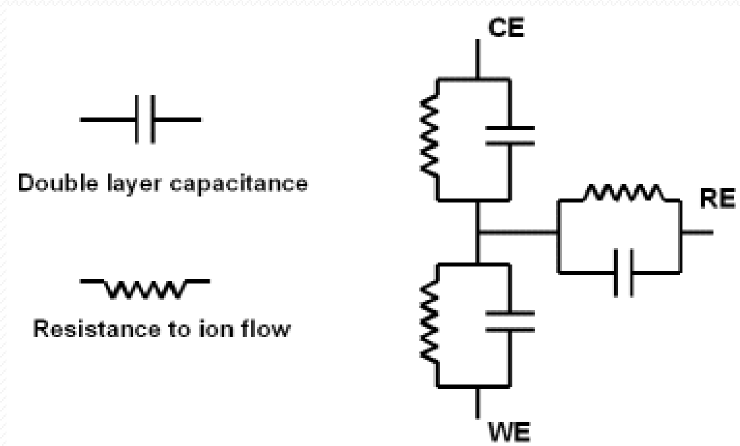


Three-electrode electrochemical sensor

- Control potential across the double layer at the WE.
- But how to measure it?

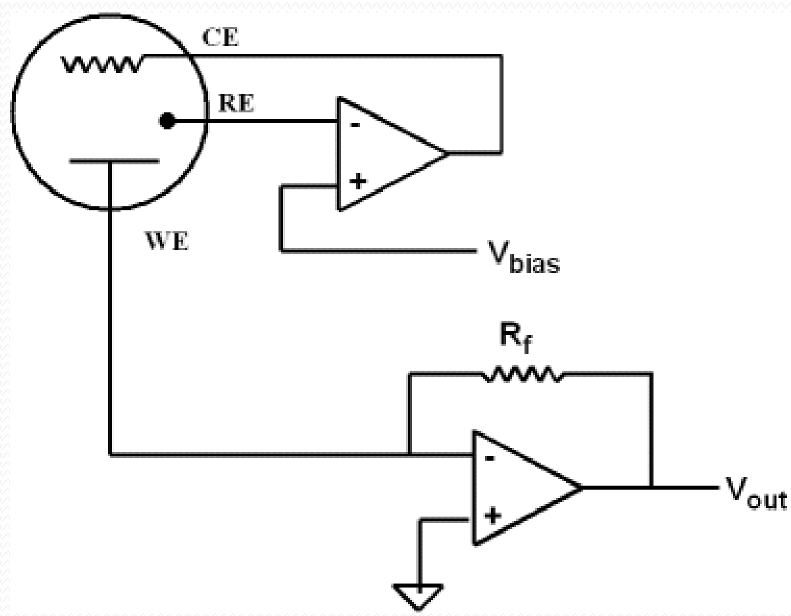


- Using a well-behaved RE.
- RE can maintain a constant potential when no current flows through it.
- CE is added to balance the current generated at the WE.



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

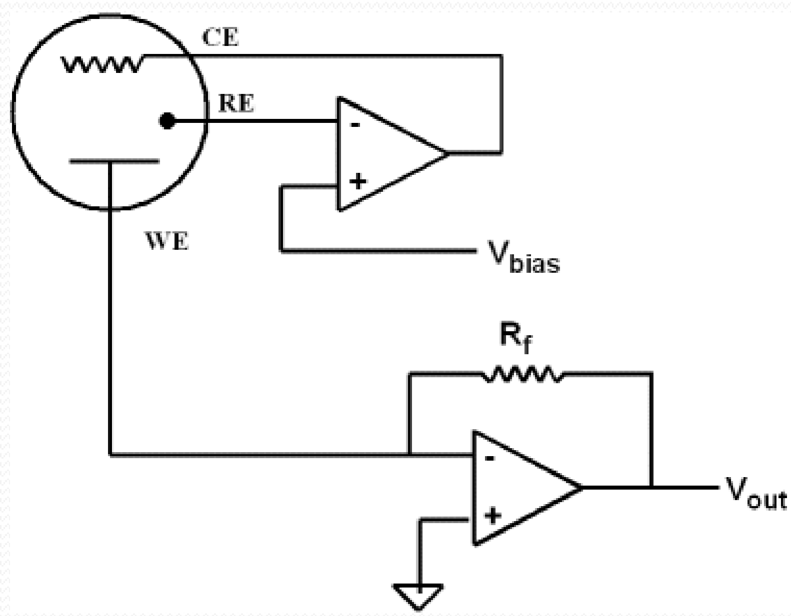


- Current Measurement
  - WE is connected to gnd.
  - $Vout = I \times R_f$

    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

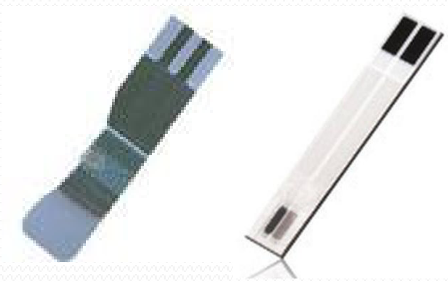
Electrochemical Glucose Sensors

- **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**

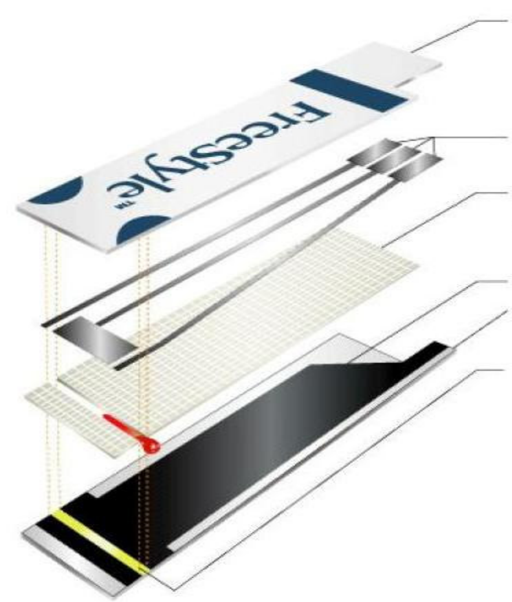


- **Detection Mechanism**

Glucose + O_2

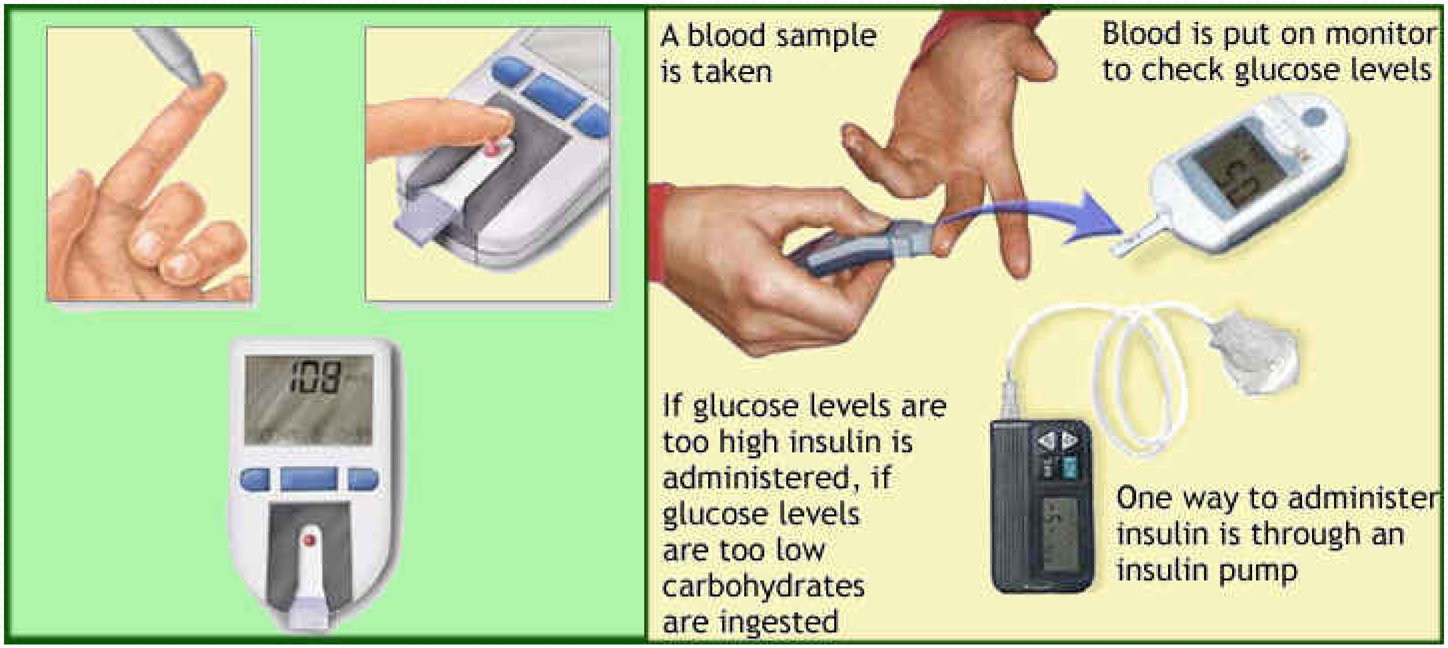
ENZYME ↓

Gluconic Acid + H_2O_2

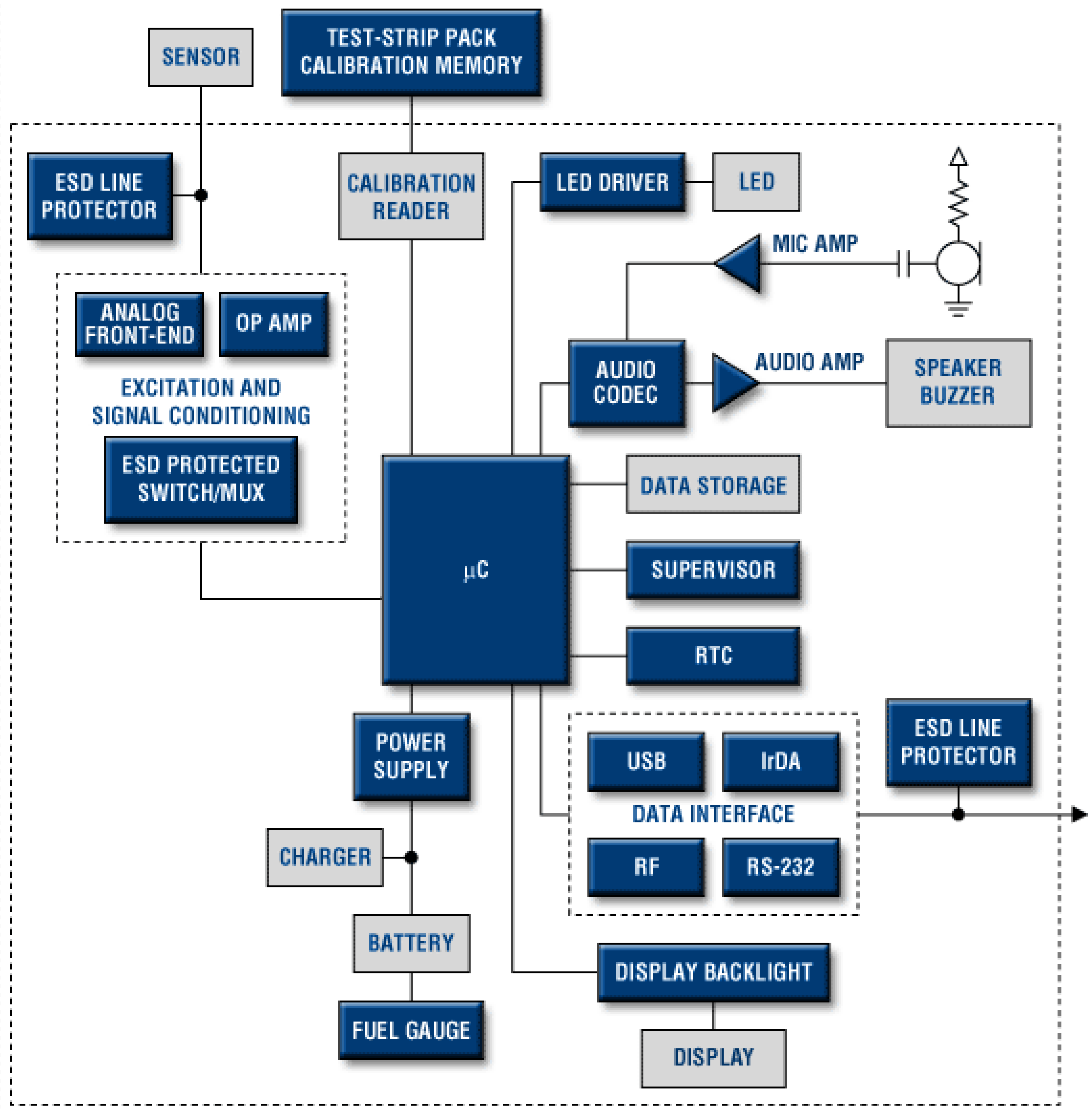


Handheld Blood Glucose Meter

- **Small battery-operated devices**



Handheld Blood Glucose Meter



Handheld Blood Glucose Meter

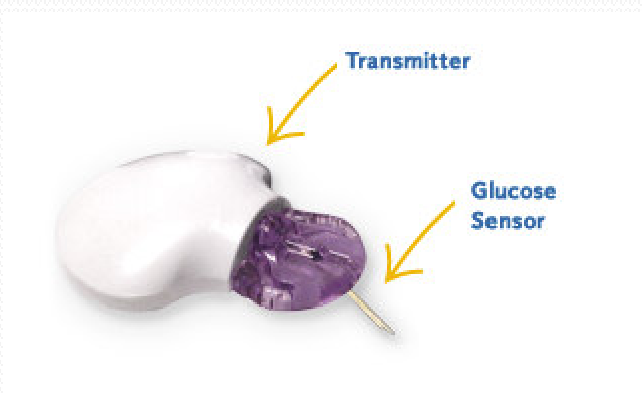
- **Small battery-operated devices**

- **Performance Matrics**
  - **Sample size**

    10µL=> 0.3 µL => Capillary action
  - **Data storage and manipultion**
  - **Power**
  - **Test strip calibration**
  - **Rapid and accurate measurement**

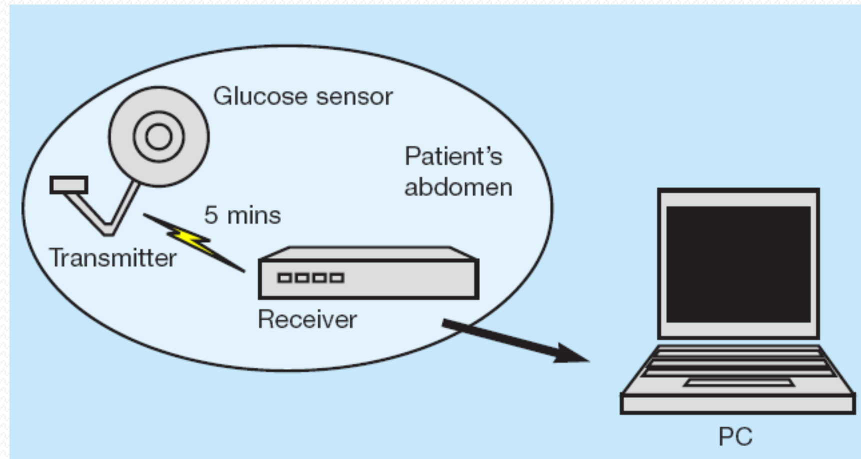
Continuous Real-time Glucose Monitoring Systems

- **Real-time devices on the market**
  - **Medtronic Guardian® & Paradigm® Real-Time**
  - **Abbott FreeStyle Navigator**
  - **DexCom STS™**



Continuous Glucose Monitoring Systems (CGMS)

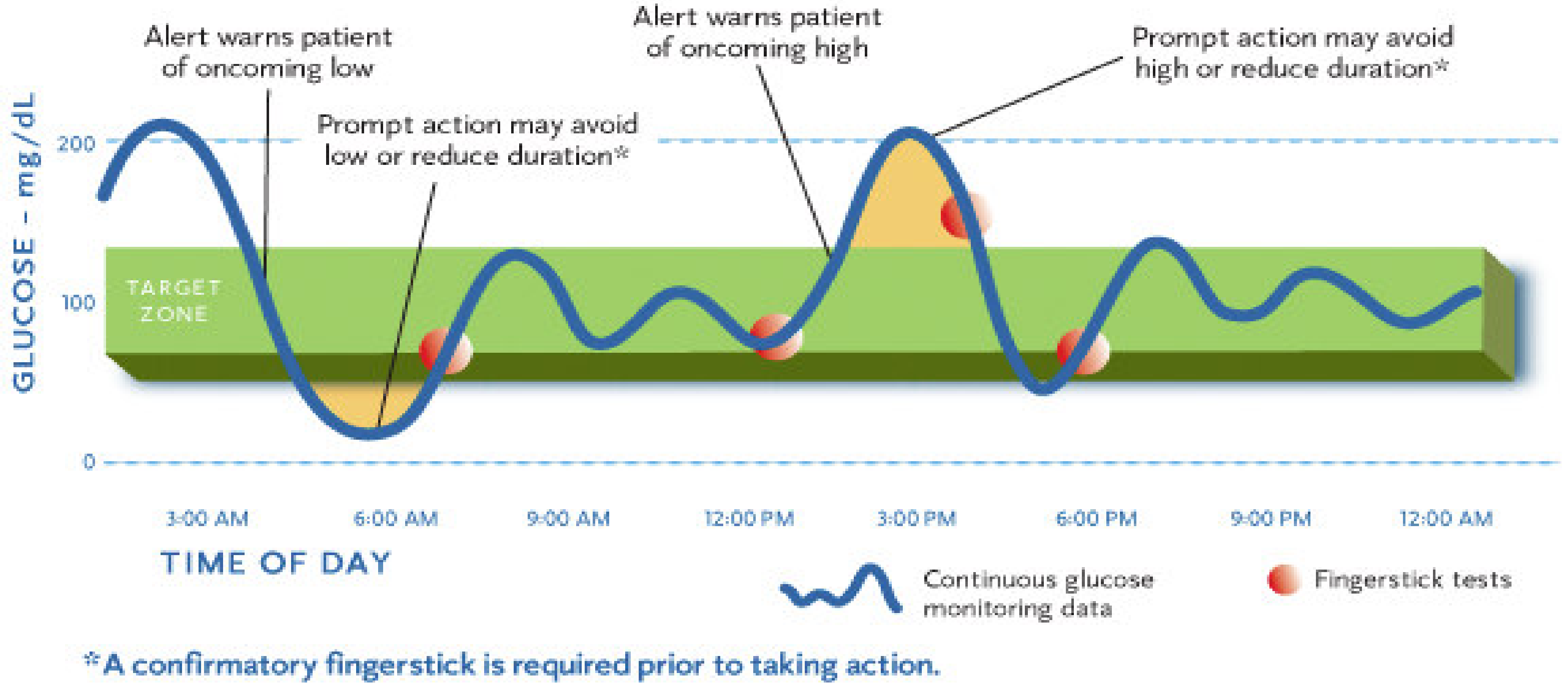
- **Components of a CGMS**



Continuous Glucose Monitoring Systems (CGMS)

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

Meaningful data
Reduce hypoglycaemia
Patient education
Increased motivation



Implantable Electrochemical Glucose Sensors

GOx

Glucose + O_2 ===> Gluconic Acid + H_2O_2

GOx + Glucose => GOx-H_2 + Gluconic Acid

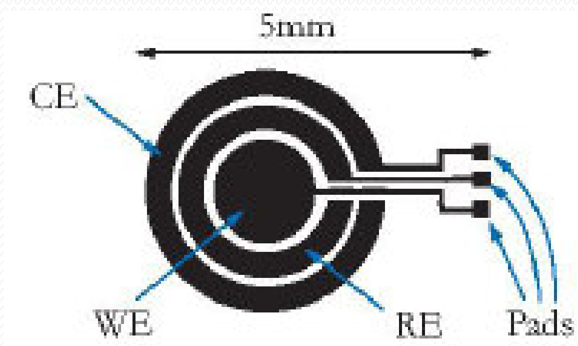
GOx-H_2 + O_2 => GOx + H_2O_2

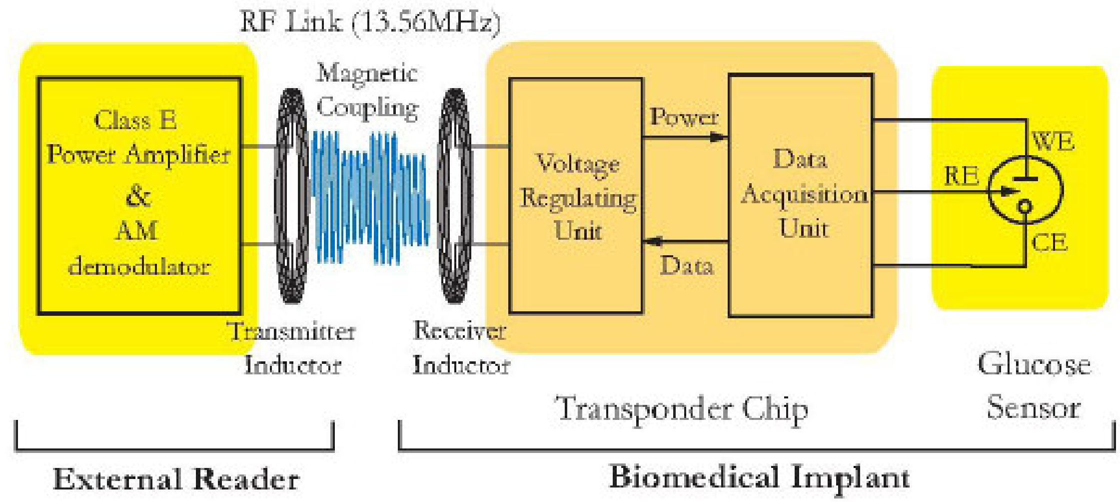
- Major Issue: O_2-dependent measurement
- Alternative approach

GOx-H_2 + 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

- Lojou E, Bianco P. Application of the electrochemical concepts and techniques to amperometric biosensor devices. J Electroceram (2006) 16:79-91
- Ahmadi M. etc. Continuous monitoring of blood glucose concentration using a fully implantable wireless biomedical mocrosystem. Life Science Systems and Applications Workshop, 2006.
- Kerr D, Fayers K. Conitnuous real-time glucose monitoring systems: time for a close look. Practical Diabetes Int (2008)25(1): 37-41
- Wei D, etc. Electrochemical biosensor at the nanoscale. Lab on a chip (2009) 9: 2123-2131.
- Bakker E, Qin Y. Electrochemical Sensor. Anal. Chem. (2006) 78 (12): 3965-3978.
- Irhayem E.A. etc. Glucose detection based on electrochemically formed Ir oxide films. J of Electroanalytical Chemistry (2002) 153-164.
- Beach R.D. Subminiature implantable potentiostat and modified commercial telemetry device for remote glucose monitoring. IEEE Transactions on Instrumentation and Measurement 48(6), 1999.
- Heller A. Implanted electrochemical glucose sensors for the management of diabetes. Annu. Rev. Biomed. Eng. (1999) 01:153-175.
- Li Q and Yuan J. Development of the portable blood glucose meter for self-monitoring of blood glucose. Engineering in Medicine and Biology 27th Annual Conference. 2005.
- Kakehi N. etc. A novel wireless glucose sensor employing direct electron transfer principle based enzyme fuel cell. Biosensor and Bioelectronics (2007) 22: 2250-2255.

Thank you all!

Any Questions?