State of the Art Biosensor Techniques and their Utility for Molecular Communcation Receivers

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Agenda

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2. Non-invasive: Optical Methods
3. Enzyme-based: Impedance Spectroscopy
4. Enzyme-based: Electrochemistry Method
5. Conclusions
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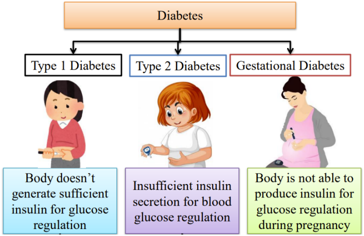
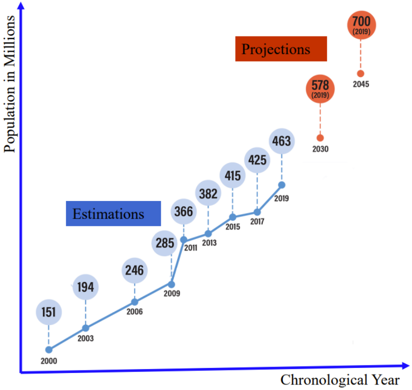
Introduction

Background of Diabetes

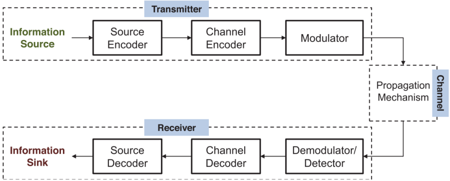


Types of diabetes.

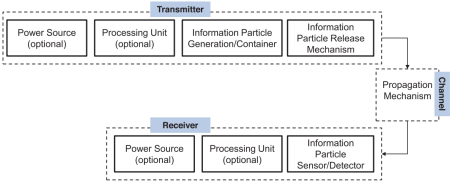


Growing numbers of people with diabetes.

Communication System

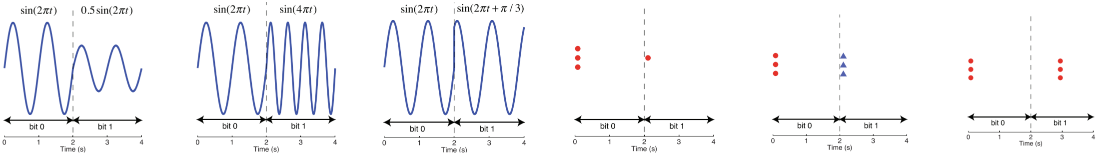


Traditional communication system



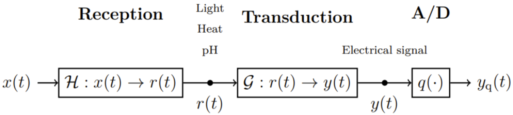
Molecular communication system

Our Research



(a) ASK (b) FSK (c) PSK (d) CSK (e) MTSK (f) RTSK

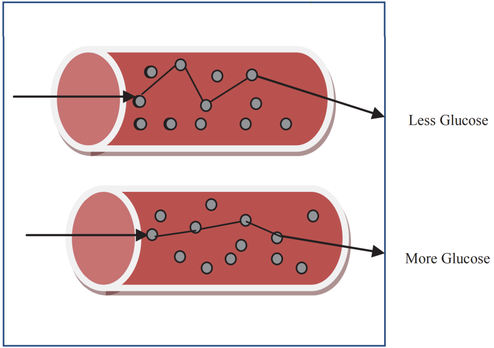
Different modulation methods



Process at the receiver

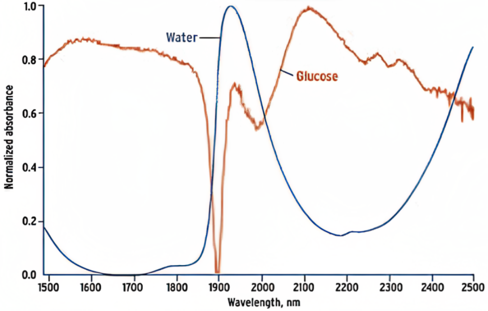
Non-invasive: Optical Methods

Theory



- Optical reflectometry: intensity of reflected light proportional to GC
- Optical transimission: intensity of transmitted light proportional to GC

Example of Near Infrared

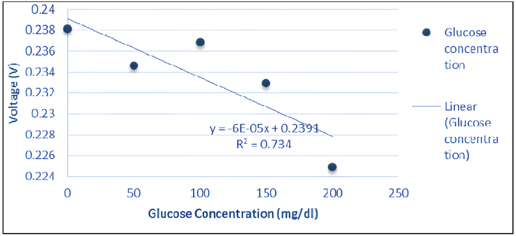


- Glucose absorbance value higher than water at wavelength 1500nm-1800nm
- Transmittance as measurement method
- Transmitted light converted to electric current by photodiode
- Beer Lambert Law:

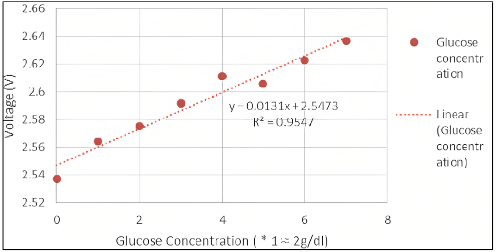
$$I = I_0 e^{-A} \quad (1)$$

$$A = k * l * C \quad (2)$$

Implementation



GC-voltage at λ=1550nm



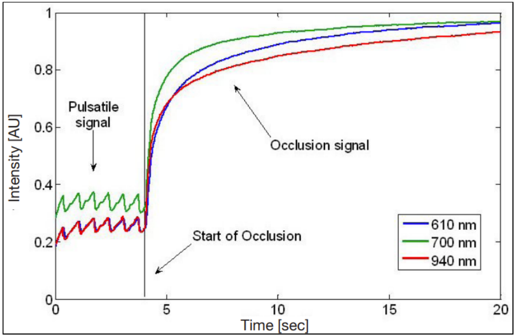
GC-voltage at λ=1300nm

- At λ=1550nm, each 50mg/dl increasing of GC,n3mV raising in photodiode voltage
- Increasing GC results in increasing vlotage, means that main absorbent is water

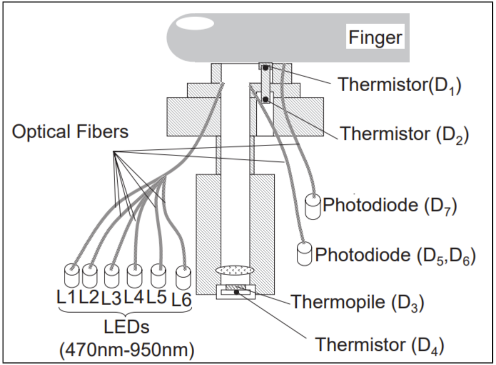
Optical Methods Analysis based on Calrke Erro Grid

method	data	advantage	disadvantage
NIR	A:75% B:25%	intensity is proportional to glucose molecule	high scattering level
MIR		glucose molecule absorption stronger	limited penetration
FIR	A:81% B:19%	frequent calibration is not required	depends on temprature and substance thickness
Occlusion	A:69.7% B:25.7%	enhancement of robustness	
MHC	A:90% B:10%	use well-known various parameters	sensitive to temperature and sweat

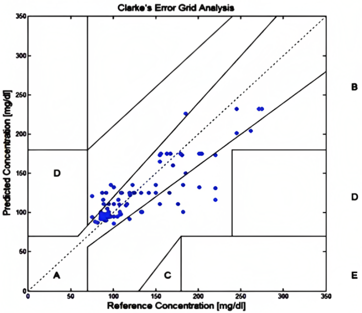
- MIR with 2500nm-10000nm
- FIR with 8000nm-14000nm
- Occlusion: pressure applied by using pneumatic cuff to cease blood flow for few seconds
- Metabolic heat Conformation: $[GLU] = F(heatgenerated, bloodflowrate, Hb, HbO_2)$



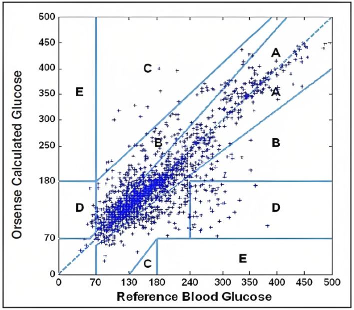
Occlusion signals



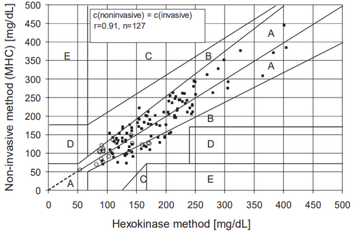
MHC-deveice



NIR-Clarke Erro Grid



Occlusion-Clarke Erro Grid

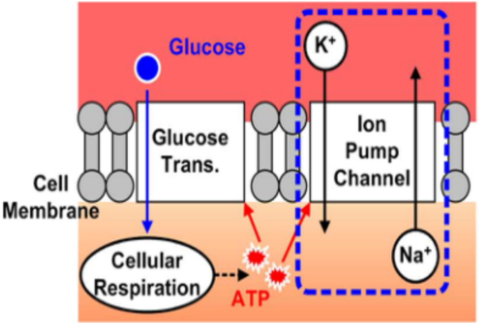


MHC-Clarke Erro Grid

- good performances in real-time, suitable for CCM
- effected by fat, protein, water in body

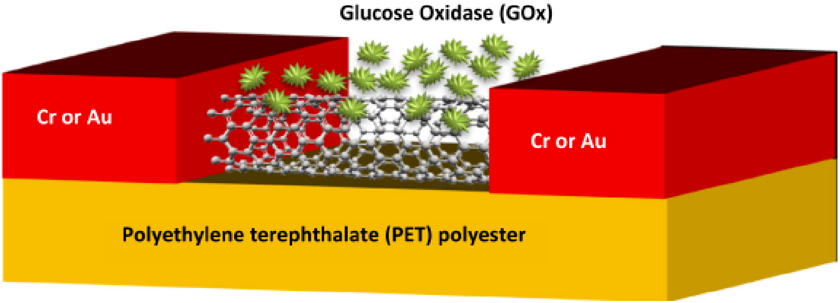
Enzyme-based: Impedance Spectroscopy

Theory

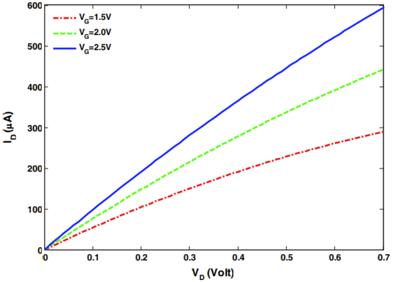


- Glucose converted to ATP
- ATP controls ion pump channel
- Ion permitivity of cell membrane changes
- Detected by field-effect transistor

Model of Impedance Spectroscopy



Proposed combination of metal electrodes, a layer of GO_x biomolecular assembl, and SWCNT Channel in FET



Comprehensive glucose sensing mechanism

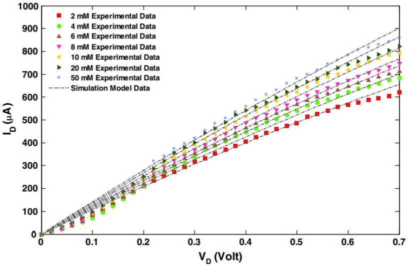
- Bare transistor:

$$I_D = \beta(2V_{GT}V_D - V_D^2)/(1 + V_D/V_c) \tag{3}$$

- Transistor with solution:

$$V_{GT1} = V_{GT} + V_{PBS} - V_T \tag{4}$$

$$I_D = [2(V_{GT1}V_D) - V_D^2]/(1 + V_D/V_c) \tag{5}$$



Comprehensive glucose sensing mechanism

- Transistor with glucose:

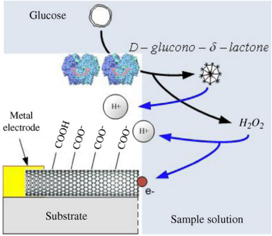
$$I_D = [2(V_{GT1} + V_{glucose})V_D - V_D^2]/(1 + V_D/V_c) \tag{6}$$

- Glucose concentration against gate voltage:

$$V_{glucose}(C) = 1.42V - \exp(-0.1C) \tag{7}$$

- Drain current to glucose concentration:

$$I_D = [2(V_{GT1} + 1.42V - \exp(-0.1C))V_D - V_D^2]/(1 + V_D/V_c) \tag{8}$$



Comprehensive glucose sensing mechanism

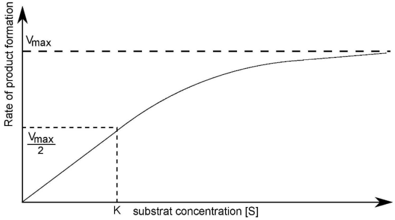
- Involved reactions:

$$O_2 + \beta\text{−D−Glucose} \xrightarrow{\text{GOx}} H_2O_2 + \text{D−glucose−}\beta\text{−lactone} \tag{9}$$

$$H_2O + \text{D−glucose−}\beta\text{−lactone} \longrightarrow H^+ + \text{D−gluconate}^- \tag{10}$$

$$H_2O_2 \xrightarrow{0.7V} O_2 + 2\,H^+ + 2\,e^- \tag{11}$$

Analysis of results



$$E + S \underset{k_3}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} E + P \tag{12}$$

- Michaelis-Menten kinetics:

$$\frac{\mathrm{d}[E]}{dt} = (k_2 + k_3)[ES] - k_1[E][S] \tag{13}$$

$$\frac{\mathrm{d}[S]}{dt} = k_3[ES] - k_1[E][S] \tag{14}$$

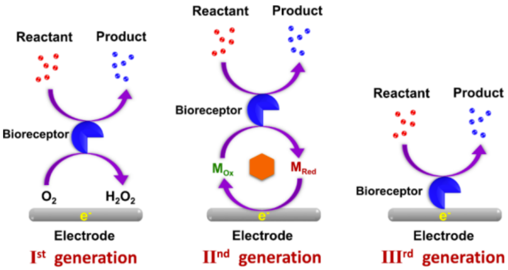
$$\frac{\mathrm{d}[ES]}{dt} = k_1[E][S] - (k_2 + k_3)[ES] \tag{15}$$

$$\frac{\mathrm{d}[P]}{dt} = k_2[ES] \tag{16}$$

Simulation

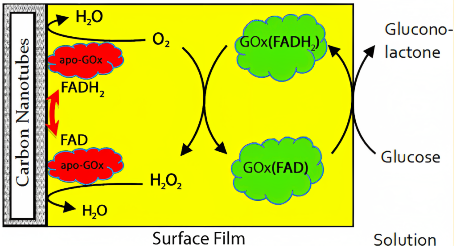
Enzyme-based: Electrochemistry Method

Theory



- 1st-generation: GOx-catalyzed oxidation of glucose, measure generated H_2O_2 by the enzyme or the consume of O_2
- 2nd-generation: O_2 replaced, a sythetic electron recipient
- 3rd-generation: direct electron transfer (DET)

Model of Electrochemistry Biosensor



- Involved reactions:

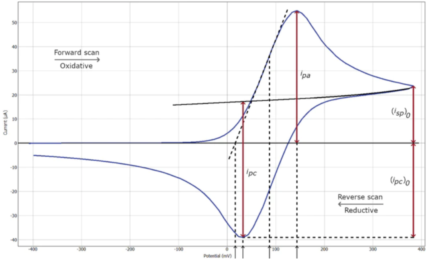
$$O_2 + 4\,H^+ + 4\,e^-(CNT) \longrightarrow H_2O_2 + 2\,H^+ + 2\,e^-(CNT) \longrightarrow 2\,H_2O \quad (17)$$

$$GOx(FAD)^{CNT} + \beta{-}D{-}Glucose \longrightarrow GOx(FADH_2)^{CNT} + D{-}glucose - 1.5\,{-}lactone \quad (18)$$

$$GOx(FADH_2)^{CNT} + O_2 \longrightarrow GOx(FAD)^{CNT} + H_2O_2 \quad (19)$$

$$FAD + 2\,H^+ + 2\,e^- \longleftrightarrow FADH_2 \quad (20)$$

Analysis of Model

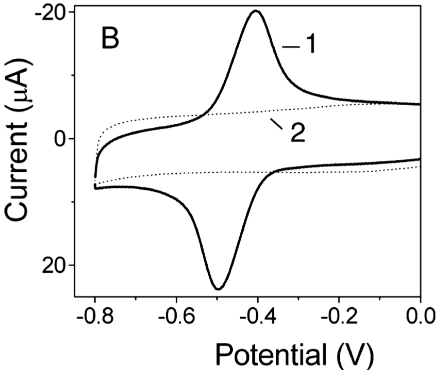


Cyclic voltammetry

- Investigate the reduction and oxidation processes of molecular species
- Peak potential and peak current:

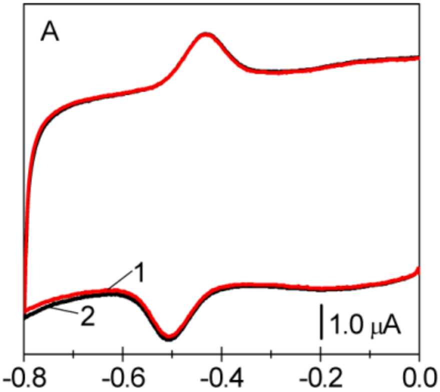
$$\delta E_p = E_{pa} - E_{pc} = 0.059/n \tag{21}$$

$$i_p = (2.69 \times 10^5) n^{3/2} S D^{1/2} C v^{1/2} \tag{22}$$



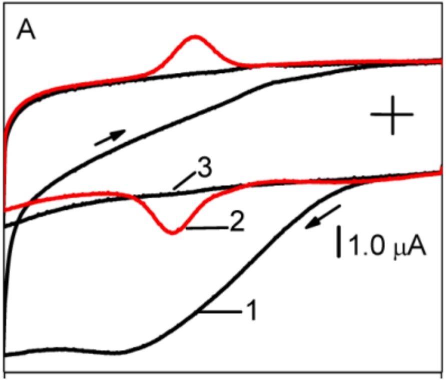
CV of FAD

- O_2-free solutions: exist a pair of peaks



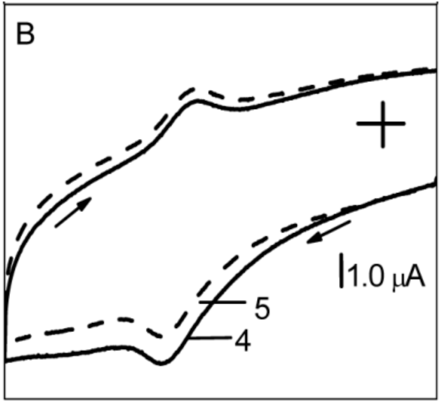
CV of FAD

- Glucose added into O_2-free solution: not effect the result of the electroactivity



CV of FAD

- O_2-containing solutions with only FAD



CV of FAD

- O_2-containing solutions also with glucose: electrochemical peak current of Oxygen decrease

- assumption:

$$i_{ptotal} = (2.69 \times 10^5) n^{3/2} S D^{1/2} C_{O_2} v^{1/2} + i_{FAD} \tag{23}$$

$$C_{O_2 electro} = C_{O_2} - v_{O_2 consumed} = C_{O_2} - k \times log C_{glucose} \tag{24}$$

$$i_{pnew} = (2.69 \times 10^5) n^{3/2} S D^{1/2} C_{O_2 electro} v^{1/2} + i_{FAD} \tag{25}$$

$$\delta i_p = (2.69 \times 10^5) n^{3/2} S D^{1/2} (C_{O_2} - k \times log C_{glucose}) v^{1/2} \tag{26}$$

Conclusions

Conclusions

- Optical methods: change in the refractive index, light absorption, or fluorescence of glucose
  - Detecting glucose changes in real-time
  - Sensitive to other components in the body
- Enzyme-based methods:
  - Impedance spectroscopy: change of impedance proportional to GC
  - Electrochemistry: electrical signal generated by the oxidation of glucose directly measured
  - High-precision
  - Instability due to enzyme, susceptible to denaturation and inactivation over time
- Further work: evaluation of the reconstruction accuracy for molecule concentration signals (pulse position modulated signals, concentration shift keying modulated signals, etc., for receivers with fixed operators

Thank You for Your Attention!

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Questions?