Amperometric Sensors: Problem formulation

- amperometric techniques have some selectivity as every RedOx reaction has its own characteristic potential

<table>
<thead>
<tr>
<th>Reaction</th>
<th>$E^0$, V</th>
</tr>
</thead>
<tbody>
<tr>
<td>$Cu^{2+} + e \rightarrow Cu^+$</td>
<td>+0.16</td>
</tr>
<tr>
<td>$Pb^{2+} + 2e \rightarrow Pb$</td>
<td>-0.13</td>
</tr>
<tr>
<td>$Tl^{2+} + 2e \rightarrow Tl$</td>
<td>-0.34</td>
</tr>
<tr>
<td>$In^{3+} + 3e \rightarrow In$</td>
<td>-0.34</td>
</tr>
<tr>
<td>$Cd^{2+} + 2e \rightarrow Cd$</td>
<td>-0.40</td>
</tr>
<tr>
<td>$Zn^{2+} + 2e \rightarrow Zn^+$</td>
<td>-0.76</td>
</tr>
</tbody>
</table>
Electrode Reactions

• Current:
  – Faradaic current: current associated with Oxidation/Reduction of species of interest
    \[ A + e \rightarrow B \]
  – Capacitive current: charging of double layer
    \[ \frac{I_c}{A} = C' \frac{dE}{dt} \]
  – Other background currents due to presence of other species e.g. oxygen
Electrode Reactions

- Faradaic current:

\[ A + ne \rightarrow B \]

- Possible limiting steps:
  - electron transfer
  - mass transport

rate of arrival of A = 1/n rate of e-transfer = rate of departure

\[-J_A = \frac{1}{n} \frac{I}{AF} = J_B\]
The rate of charge transfer

\[ \text{Ox} + \nu e^- \rightarrow \text{Red} \]

- First order reaction
  
  the rate of reduction: \( \nu_{\text{Ox}} = k_c [\text{Ox}] \)
  
  the rate of oxidation: \( \nu_{\text{Red}} = k_a [\text{Red}] \)

\[
\begin{align*}
    j_c &= \nu F k_c [\text{Ox}] \\
    j_a &= \nu F k_a [\text{Red}] \\
    j &= j_a - j_c = \nu F k_a [\text{Red}] - \nu F k_c [\text{Ox}] \end{align*}
\]

- The activation Gibbs energy

both processes involve activation \( k = Be^{-\Delta^*G/RT} \)

\[
\begin{align*}
    j &= \nu F k_a B_a [\text{Red}] e^{-\Delta^*G_a /RT} - \nu F k_c B_a [\text{Ox}] e^{-\Delta^*G_c /RT} \end{align*}
\]
The Butler-Volmer equation

- **Reduction reaction**  \( \text{Ox} + ve^- \rightarrow \text{Red} \)
  
  transition state is product like:  \( \Delta^*G_c = \Delta^*G_c(0) + F\Delta\phi \)
  
  transition state is reagent like:  \( \Delta^*G_c \approx \Delta^*G_c(0) \)

  \[ \Delta^*G_c = \Delta^*G_c(0) + \alpha F\Delta\phi \]

- **Oxidation reaction**  \( \text{Red} - ve^- \rightarrow \text{Ox} \)
  
  transition state is product like:  \( \Delta^*G_c = \Delta^*G_c(0) - F\Delta\phi \)
  
  transition state is reagent like:  \( \Delta^*G_c \approx \Delta^*G_c(0) \)

  \[ \Delta^*G_c = \Delta^*G_c(0) - (1 - \alpha)F\Delta\phi \]
The Butler-Volmer equation

\[ j = \nu F k_a B_a [\text{Red}] e^{-\Delta^* G_a(0)/RT} e^{(1-\alpha)F\Delta\phi/RT} - \nu F k_c B_a [\text{Ox}] e^{-\Delta^* G_c/RT} e^{-\alpha F\Delta\phi/RT} \]

if the cell is balanced (j=0) by an external source, E:

\[ j_a = j_c = j_0, \quad f = \frac{F}{RT} \]

now, if a voltage is supplied:

\[ \eta = E' - E \]

\[ j = j_0 (e^{(1-\alpha)f\eta} - e^{-\alpha f\eta}) \]
The Butler-Volmer equation

\[ j = j_0 (e^{(1-\alpha) f \eta} - e^{-\alpha f \eta}) \]

- **The low overpotential limit** \( f \eta \ll 1 \), in practice \( \eta < 0.01 \text{V} \)

\[ j = j_0 (1 + (1 - \alpha) f \eta + ... - 1 - \alpha f \eta - ...) \approx j_0 f \eta \]

\[ \eta \approx \frac{j}{j_0 f} \]  Ohm’s law

- **The high overpotential limit** in practice \( \eta \geq 0.12 \text{V} \)

positive overpotential: \[ j = j_0 e^{(1-\alpha) f \eta} \]

negative overpotential: \[ j = j_0 e^{-\alpha f \eta} \]
Tafel plot

- A plot of $\ln(j)$ vs. overpotential is called Tafel plot.
Electrode Reactions

• Mass transport modes:
  – Diffusion: spontaneous movement due to concentration gradient
  – Convection: transport by gross physical movement, e.g. stirring or flowing the solution, or rotating/vibrating the electrode
  – Migration: movement of charged particles

\[ J(x,t) = -D \frac{\partial C(x,t)}{\partial x} - \frac{zFDC}{RT} \frac{\partial \phi(x,t)}{\partial x} + C(x,t)V(x,t) \]
Mass transport mechanisms

- Migration (for ions) in response to a gradient of potential

\[ J_m = \sum_i \frac{-z_i F}{RT} D_i [i] \frac{\partial E}{\partial x} \]

- Diffusion in response to a concentration gradient

\[ J_d = -D_A \frac{\partial [A]}{\partial x} \]

- Convection in response to pressure gradient

\[ J_c = [A] v \]
**Voltammetry**

**non-polarizable** electrodes: potential changes only slightly with current,  
**polarizable** electrodes: potential changes significantly with current  
reference electrodes are highly non-polarizable

**concentration polarization**

phenomena related to consumption of the reactive species on the electrode

at zero current:  
\[
E = E^0 + \frac{RT}{zF} \ln a = E^0 + \frac{RT}{zF} \ln \gamma + \frac{RT}{zF} \ln c
\]

\[
E = E^0 + \frac{RT}{zF} \ln c
\]

with current:  
\[
E' = E^0 + \frac{RT}{zF} \ln c'
\]

\[
\eta^c = E' - E = \frac{RT}{zF} \ln \left( \frac{c'}{c} \right)
\]
Voltammetry

- concentration polarization

\[ \eta^c = E' - E = \frac{RT}{zF} \ln\left( \frac{c'}{c} \right) \]

First Fick's law:  
\[ J = -D \left( \frac{\partial c}{\partial x} \right) = D \frac{c - c'}{\delta} \]

\[ j = zFJ = zFD \frac{c - c'}{\delta} \]

limiting current density  
\[ j_{\text{lim}} = zFD \frac{c}{\delta} = \frac{cRT\lambda}{zF\delta} \]

using Nernst-Einstein equation,  
\( \lambda \) – ionic conductivity

conc. overpotential vs current:

\[ \eta^c = \frac{RT}{zF} \ln\left( 1 - \frac{j\delta}{zcFD} \right) \]
Potential step experiment

\[ O + ne \rightarrow R \]

- Experiment: potential is increased stepwise to some value, only O is initially present.

- in a planar geometry:
  \[
  C_o(x,t) = C_o(b) \left[ 1 - \text{erf} \left( \frac{x}{\sqrt{4D_o t}} \right) \right]
  \]

\[
\frac{\partial C}{\partial x} = \frac{C_o(b)}{\sqrt{4D_o t}}
\]

\[
J(t) = -D \frac{\partial C}{\partial x} \Rightarrow i(t) = nFAD_o \frac{C_o(b)}{\sqrt{4D_o t}}
\]

Cottrell equation
Potential step experiment

- At a spherical electrode the situation is different as the diffusion equation will have another term:

\[
\frac{\partial C(x,t)}{\partial t} = D \left[ \frac{\partial^2 C}{\partial r^2} + \frac{2}{r} \frac{\partial C}{\partial r} \right]
\]

\[
i(t) = nFAD_o \frac{C_o(b)}{\sqrt{4D_o t}} + nFAD_o \frac{C_o(b)}{r}
\]

- This leads to unique transport properties of microelectrodes (due to their small radius)
Chronoamperometry

- The potential is stepped to $E_2 > E_p$, current is monitored as a function of time

\[ i_d = \frac{nFAD C_{Ox}}{\pi^{1/2} t^{1/2}} \]

Current decay due to mass transfer limitation

Limiting value:

\[ i = \frac{nFAD^{1/2} C_{ox}}{\delta} \]
Potential sweep experiments

Current raise, dominated by the drop in $C_0(0,t)$

Current drop, dominated by the increase in $\delta$.

On microelectrodes we expect sigmoidal shape
Potential sweep experiment

• In the case of stirring, the distance \( \delta \) is maintained;
• The voltammogram will be sigmoidal in the case of stirring
• In aqueous solution distance \( \delta \) is typically 10-50\( \mu \text{m} \) for electrode rotation and 100-150 \( \mu \text{m} \) for solution stirring
Voltammetry

- **linear sweep voltammetry**
  - Linearly varied potential is applied between working electrode and reference electrode while current is monitored
  - Current maximum is proportional to the concentration

- **differential pulse voltammetry**
  - Current difference before and after pulse is measured

- **cyclic voltammetry**
  - Potential is applied in a sawtooth manner
Voltammetry: Example

- electro reduction of p-bromonitrobenzene

\[
\begin{align*}
BrC_6H_4NO_2 + e^- & \rightarrow BrC_6H_4NO_2^- \\
BrC_6H_4NO_2^- & \rightarrow \bullet C_6H_4NO_2 + Br^- \\
\bullet C_6H_4NO_2 + e^- & \rightarrow C_6H_4NO_2^- \\
C_6H_4NO_2^- + H^+ & \rightarrow C_6H_5NO_2
\end{align*}
\]
Electrical double layer

- IHP – Inner Helmholz plane: specifically adsorbed ions
- OHP – Outer Helmholz plane closest approach of solvated ions

Exponential decay
Electrical double layer

- Capacitance of the double layer
  
  \[
  \frac{1}{C_{dl}} = \frac{1}{C_H} + \frac{1}{C_G}
  \]
  
  \[q = C_{dl} A \left( E - E_{pzc} \right)\]

- For concentrate solutions, \(1/C_H >> 1/C_G\) and the capacitance is dominated by the Helmholtz layer

- For diluted solutions \(C_G\) is very small and \(C \sim C_G\).
Electrical double layer

- Current due to charging of double layer limits detectability of the potential controlled techniques

\[ i = \frac{dq}{dt} = C_{dl} a \frac{dE}{dt} + C_{dl} \left( E - E_{pzc} \right) \frac{dA}{dt} + A \left( E - E_{pzc} \right) \frac{dC_{dl}}{dt} \]
Electrical double layer

- Electrocapillary effect

Lippman equation

\[
\left( \frac{\partial \gamma}{\partial E} \right)_{P=\text{const}} = q \\
\left( \frac{\partial^2 \gamma}{\partial E^2} \right)_{P=\text{const}} = -C_{dl}
\]

No electrostatic repulsion, max of surface tension
Linear Sweep Voltammetry (LSW)

- Linearly varied potential is applied between working electrode and reference electrode while current is monitored.
Kinetic and Catalytic Effects

- usually, there is another chemical reaction coupled to the electron transfer
  - consumption of reduced product

\[ \text{Ox} + n e^- = R \]
\[ R + A \xrightarrow{k} B \]

Voltammogram of ferrocene

- regeneration of the oxidized reagent

\[ \text{Ox} + n e^- = R \]
\[ R + A \xrightarrow{k} \text{Ox} + B \]
Amperometric Sensors

- amperometric techniques have some selectivity as every RedOx reaction has its own characteristic potential
- however the selectivity is limited unless modified electrodes are used

Differential pulse polarogram for a mixture of six cations
Amperometric Biosensors

• First Generation – oxygen electrode based sensors
• Second Generation – mediator based sensors
• Third Generation – directly coupled enzyme electrodes
Possible glucose detection schemes

1st generation schemes

2nd generation schemes

3rd generation schemes
oxygen electrode based sensors

\[
glucose + O_2 \xrightarrow{\text{GOD}} \text{gluconic acid} + H_2O_2
\]

Clark’s electrode

- O-rings
- Pt catode
- Ag anode
- Electrolyte gel
- Teflon membrane
- Glucose oxidase on nylon net
- Cellophane membrane
<table>
<thead>
<tr>
<th>Analyte</th>
<th>Enzyme</th>
<th>Response time (min)</th>
<th>Stability (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>Glucose oxidase</td>
<td>2</td>
<td>&gt;30</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>Cholesterol oxidase</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Monoamines</td>
<td>Monoamine oxidase</td>
<td>4</td>
<td>14</td>
</tr>
<tr>
<td>Oxalate</td>
<td>Oxalate oxidase</td>
<td>4</td>
<td>60</td>
</tr>
<tr>
<td>Lactate</td>
<td>Lactate oxidase</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Formaldehyde</td>
<td>Aldehyde oxidase</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Ethanol</td>
<td>Alcohol oxidase</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Glycinate</td>
<td>Glycollate oxidase</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>NADH</td>
<td>NADH oxidase</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>
Measuring oxygen:

\[ \text{O}_2 + e^- \longrightarrow \text{O}_2^- \quad E=\text{-0.7V} \]

Problems: fairly high potential (interference is probable), oxygen needs to be controlled and replenished (e.g. By oxygen generating reaction or by pumping oxygen containing buffer)

Measuring hydrogen peroxide:

\[ \text{H}_2\text{O}_2 \longrightarrow 2\text{H}^+ + 2e^- + \text{O}_2 \quad E=\text{+0.65V} \]

Problem: still fairly high potential (interference from e.g. ascorbic acid)
Mediator Based Sensors

- Oxygen is substituted with another oxidizing agent (electron transfer agent)
- Iron ions or complexes are most common mediators

\[
\text{Fe(III)} + e^- \rightarrow \text{Fe(II)}
\]
Free Fe$^{3+}$ are subject to hydrolysis and precipitation.
glucose + GOD\textsubscript{Ox} \rightarrow \text{gluconolactone} + GOD\textsubscript{R} + 2H^+

GOD\textsubscript{R} + 2Fc^+ \rightarrow GOD\textsubscript{Ox} + 2Fc

2Fc - 2e^- \rightarrow 2Fc^+
Good Mediator

• Rapid reaction with enzyme
• Fast electron transfer kinetics
• Low overpotential
• Independent of pH
• Stable in Ox and R forms
• Doesn’t react with oxygen
• Non toxic
### Fc derivatives

<table>
<thead>
<tr>
<th>Derivative</th>
<th>$E$ (V)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>$k$ ($10^5$ dm$^3$ mol$^{-1}$ s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,1'-Dimethyl</td>
<td>0.100</td>
<td>0.8</td>
</tr>
<tr>
<td>Acetic acid</td>
<td>0.142</td>
<td>—</td>
</tr>
<tr>
<td>Ferrocene&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.165</td>
<td>0.3</td>
</tr>
<tr>
<td>Amidopentylamidopyrrole</td>
<td>0.200</td>
<td>2.07</td>
</tr>
<tr>
<td>Aminopropylpyrrole</td>
<td>0.215</td>
<td>0.75</td>
</tr>
<tr>
<td>Vinyl</td>
<td>0.253</td>
<td>0.3</td>
</tr>
<tr>
<td>Monocarboxylic acid</td>
<td>0.275</td>
<td>2.0</td>
</tr>
<tr>
<td>1,1'-Dicarboxylic acid</td>
<td>0.290</td>
<td>0.3</td>
</tr>
<tr>
<td>Methyltrimethylamino</td>
<td>0.387</td>
<td>5.3</td>
</tr>
<tr>
<td>Polyvinyl</td>
<td>0.435</td>
<td>—</td>
</tr>
</tbody>
</table>

<sup>a</sup> Versus the saturated-calomel electrode (SCE).

<sup>b</sup> Data from [Reference](#).
Various mediators (natural and artificial)

<table>
<thead>
<tr>
<th>Natural</th>
<th>$E (V)$</th>
<th>Artificial</th>
<th>$E (V)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytochrome $a_3$</td>
<td>+0.29</td>
<td>Hexacyanoferrate(III)</td>
<td>+0.45</td>
</tr>
<tr>
<td>Cytochrome $c_3$</td>
<td>+0.24</td>
<td>2,6-Dichlorophenol</td>
<td>+0.24</td>
</tr>
<tr>
<td>Ubiquinone</td>
<td>+0.10</td>
<td>Indophenol</td>
<td>+0.24</td>
</tr>
<tr>
<td>Cytochrome $b$</td>
<td>+0.08</td>
<td>Ferrocene</td>
<td>+0.17</td>
</tr>
<tr>
<td>Vitamin K$_2$</td>
<td>−0.03</td>
<td>Phenazine methosulfate</td>
<td>+0.07</td>
</tr>
<tr>
<td>Rubredoxin</td>
<td>−0.05</td>
<td>Methylene Blue</td>
<td>+0.04</td>
</tr>
<tr>
<td>Flavoproteins</td>
<td>−0.4 to +0.2</td>
<td>Phthalocyanine</td>
<td>−0.02</td>
</tr>
<tr>
<td>FAD/FADH$_2$</td>
<td>−0.23</td>
<td>phenosafranine</td>
<td>−0.23</td>
</tr>
<tr>
<td>FMN/FMNH$_3$</td>
<td>−0.23</td>
<td>Benzylviologen</td>
<td>−0.36</td>
</tr>
<tr>
<td>NAD$^+$/NADH</td>
<td>−0.32</td>
<td>Methylviologen</td>
<td>−0.46</td>
</tr>
<tr>
<td>NADP$^+$/NADPH</td>
<td>−0.32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ferridoxin</td>
<td>−0.43</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Versus the standard hydrogen electrode (SHE).*
How it works...

In real biosensors both GOD and Fc are immobilised.
Directly Coupled Enzyme

- Generally, the enzyme might denature on the electrode surface;
- electron transfer reaction might be slow
- Thus, the surface has to be modified...

- Enzymes can be directly wired to the electrode using organic conducting salts (e.g. TTF/TCNQ) or redox polymers
- Enzymes can be modified to facilitate electron transfer and attachment
Possible glucose detection schemes
Design example: Glucose sensor

- Aim: for use by patient at home (should be simple, reliable and cheap)
- Performance: blood glucose range 1.1-33.3 mM; precision 3-8%; test time 30s; life time 6 month.
- Selective element: Glucose Oxidase – inexpensive, stable over long period
- Transducer: Amperometric (GOD+Fc) – cheap, reliable, easy read-out with LCD.
- Immobilisation: covalent bonding for long life (graphite foil coated with Fc, GOD immobilised)
The transfer coefficient of a certain electrode in contact with $M^{2+}$ and $M^{3+}$ in aqueous solution at $25^\circ$C is 0.55. The current density is found to be 14.0 mA·cm$^{-2}$ when the overvoltage is 130 mV. What is the overvoltage required for a current density of 85 mA·cm$^{-2}$?