

Disclaimer

This document is an exam summary and follows the given material of the lecture *Bioelectronics*. Its contribution is a short summary that contains the most important concepts, formulas and algorithms. Due to curriculum content updates, some content may not be relevant to future versions of the course.

I do not guarantee the accuracy or completeness, nor is this document endorsed by the instructors. Any errors that are pointed out to me are welcome. The complete L^AT_EX source code can be found at <https://github.com/tstreule/eth-cheat-sheets>.

Bioelectronics

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General

Formeln

$$\text{Circle: } U_{\text{circle}} = 2\pi r, A_{\text{circle}} = \pi r^2$$

Constants:

$$h = 6.626 \cdot 10^{-34} \text{ Js} = 4.135 \cdot 10^{-15} \text{ eVs}, \quad \hbar = \frac{h}{2\pi}, \quad hc = 1.986 \cdot 10^{-25} \text{ Jm}$$

$$\epsilon_0 = 8.85 \cdot 10^{-12} \text{ As/Vm}$$

$$\mu_0 = 4\pi \cdot 10^{-7} \text{ N/A}^2$$

$$k_B = 1.38 \cdot 10^{-23} \text{ J/K} = 8.617 \cdot 10^{-5} \text{ eV/K}$$

$$q = 1.602 \cdot 10^{-19} \text{ C}, \quad m_e = 9.109 \cdot 10^{-31} \text{ kg}, \quad m_p = 1.672 \cdot 10^{-27} \text{ kg}$$

$$F = 96485 \text{ C/mol (Faraday)}$$

$$R = N_A k_B = 8.314 \text{ J/mol K (Ideal gas constant)}$$

$$N_A = 6.022 \cdot 10^{23} \text{ particles/mol} \quad 0^\circ\text{C} = 273.15 \text{ K}$$

Einheiten

$$\text{Druck} \quad 1 \text{ Pa} = 1 \text{ N/m}^2 = 1 \text{ J/m}^3 = 10 \text{ g/cm} \cdot \text{s}^2$$

$$\text{Induktivität} \quad 1 \text{ H} = 1 \text{ Vs/A} = 1 \Omega \text{ s}$$

$$\text{Power} \quad 1 \text{ W} = 1 \text{ J/s} = 1 \text{ VA}$$

$$\text{electron volt} \quad 1 \text{ eV} = 1.602 \cdot 10^{-19} \text{ J} = 23.06 \text{ kcal/mol}$$

$$\text{Charge} \quad 1 \text{ C} = 1 \text{ As}$$

$$\text{Energy} \quad 1 \text{ J} = 1 \text{ kg m}^2/\text{s}^2 = 1 \text{ Nm} = 1 \text{ VAs} = 1 \text{ CV} = 1 \text{ Ws}$$

Good to know

$$\text{Power in dB} \quad 10 \log_{10} \frac{I}{I_0}$$

$$I = \frac{\text{avg. Power}(P)}{\text{area}(A)} \left[\frac{\text{W}}{\text{m}^2} \right]$$

$$\text{avg. Power} \quad P = \frac{\text{avg. Work in cycle}(\overline{W})}{\text{cycle}(T)} \left[\text{W} = \frac{\text{kg m}^2}{\text{s}^3} \right]$$

$$(\text{avg.}) \text{ Work} \quad \overline{W} = \int_{\text{cycle}} \frac{1}{\text{cycle}(T)} \cdot \vec{F} \cdot \vec{x} \, dt \quad [\text{J} = \text{Ws}]$$

mass m vibrates with an amplitude a along x -axis:

$$\vec{x}(t) = a \sin(\omega t) \cdot \vec{e}_x, \quad \omega = 2\pi f = 2\pi/T, \quad \vec{F}(t) = m \ddot{x}(t)$$

NuS

$$\text{Induktivität} \quad u(t) = L \frac{di_L}{dt} \quad \text{---} \bullet \quad U(s) = sL I_L(s)$$

$$\text{Konduktivität} \quad i(t) = C \frac{du_C}{dt} \quad \text{---} \bullet \quad U(s) = \frac{1}{sC} U_C(s)$$

$$\text{Transformator} \quad u_1 = L_1 \frac{di_1}{dt} - M \frac{di_2}{dt}, \quad M: \text{mutual inductance}$$

$$\text{LCR-Schwingkreis} \quad \omega_0 = 2\pi f_0 = 1/\sqrt{LC}$$

Laplace

$$\lambda u(t) + \mu v(t) \quad \text{---} \bullet \quad \lambda U(s) + \mu V(s)$$

$$u(at), a > 0 \quad \text{---} \bullet \quad \frac{1}{a} U\left(\frac{s}{a}\right)$$

$$u(t-t_0) \quad \text{---} \bullet \quad e^{-st_0} U(s)$$

$$e^{-at} u(t) \quad \text{---} \bullet \quad U(s+a)$$

$$(-t)^n u(t) \quad \text{---} \bullet \quad U^{(n)}(s)$$

$$u^{(n)}(t) \quad \text{---} \bullet \quad s^n U(s) - \dots - u^{(n-1)}(0)$$

$$t^n \quad \text{---} \bullet \quad \frac{n!}{s^{n+1}}$$

$$e^{-at} \quad \text{---} \bullet \quad \frac{1}{s+a}$$

$$te^{-at} \quad \text{---} \bullet \quad \frac{1}{(s+a)^2}$$

$$\sin(at) \quad \text{---} \bullet \quad \frac{a}{s^2+a^2}$$

$$\cos(at) \quad \text{---} \bullet \quad \frac{s}{s^2+a^2}$$

1 Biosensors

1.1 Label assay vs. label-free

Label assay (sandwich):
non-specific binding:
binding:

Label-free assay (OWLS):
other interactions that could happen, except the angle binding.

1.2 Rules of Chemistry and Physics

Bracket notation

indicates concentration $A + B \xrightarrow{k_1} AR$

equilibrium constant

$$K = \frac{k_{-1}}{k_1} = \frac{[A][R]}{[AR]}$$

affinity constant

$$K_a = 1/K$$

cont. flowing cell

$$[AR] \sim q * \text{signal}, q = \text{const}$$

$$[R] \sim R_0 = \text{initial receptor density}$$

1.3 Sensitivity and Specificity

Sensitivity true positive rate (% of correctly identified +)

Specificity true negative rate (% of correctly identified -)

Compensate Sensitivity through LOD.

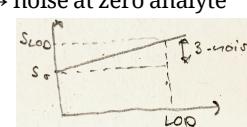
1.3.1 Limit of Detection (LOD)

(Sensitivity) Limitation by non-specific binding (NSB) → noise at zero analyte

LOD

$$LOD = 3 \cdot \text{noise} / \frac{dS}{d[A]}$$

$$S_{LOD} = S_0 + 3 \cdot \text{noise}$$



LOD for intensity/signal

$$LOD_{NSB} = \langle I_{NSB} \rangle + 3 \sigma(I_{NSB})$$

Lowest detectable intensity

$$\frac{\langle I_{POI} \rangle}{LOD_{NSB}} = 1 \quad (\text{POI: proteins of interest})$$

Detectable #proteins

$$N\# = \frac{\Gamma}{m_{\text{protein}}} \quad [\Gamma] = \text{pg/mm}^2 \quad \text{detection limit}$$

2 Optical Microscopy

2.1 Reflection and Refraction

Law of Reflection

$$\theta_{\text{inc}} = \theta_2$$

Law of Refraction

$$\frac{n_{\text{inc}}}{n_2} = \frac{\lambda_0/\lambda_{\text{inc}}}{\lambda_0/\lambda_2} = \frac{\sin \theta_2}{\sin \theta_{\text{inc}}} \quad \text{for } \theta_{\text{inc}} < \theta_c$$

Total reflection

$\sin \theta_c = n_2/n_{\text{inc}}$ always total if $n_{\text{inc}} < n_2$

Paraxial approx.

$\theta \simeq \sin \theta \simeq \tan \theta, \quad \theta \ll 1$

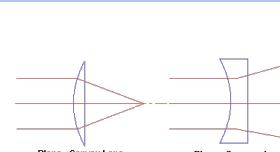
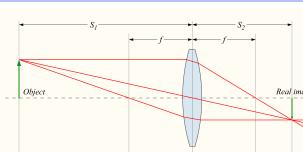
Thin lens approx.

$$R \ll S_o, S_i$$

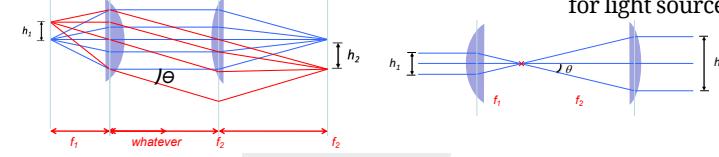
Lens makers formula

$$\frac{1}{S_o} + \frac{1}{S_i} = \frac{1}{f} = \frac{n_{\text{lens}} - n}{n} \left(\frac{1}{R_1} - \frac{1}{R_2} \right)$$

2.2 Ray Tracing



2.2.1 Simple Microscope

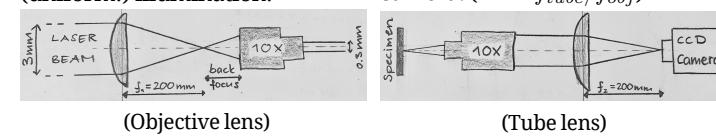


Magnification

$$M = h_2/h_1 \stackrel{*}{=} f_2/f_1 \quad * \text{ since } h_1 = f_1 \sin \theta$$

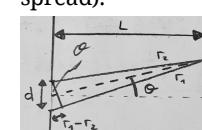
2.2.3 Simple "modern" Microscope

(uniform!) Illumination:



2.3 Fundamental Limits of Lenses & Resolution

Due to a finite aperture will points presented as the PSF (point-spread).



First zero occurs at: $\theta \stackrel{(\theta \ll 1)}{\simeq} \sin \theta \simeq 1.22 \frac{\lambda_0}{d}$

d: radius of the aperture

$$\bullet \sin \theta \simeq \tan \theta = x/L$$

$$\bullet r_1 - r_2 = d \cdot x/L$$

Rayleigh criterion

Resolution

Numerical Aperture

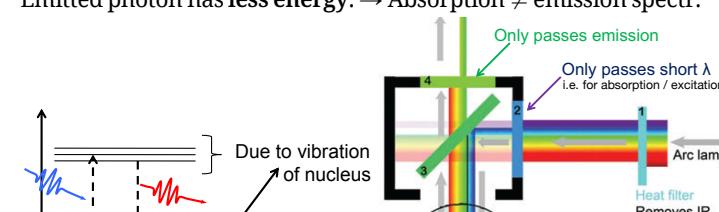
$$\Delta r \simeq f \sin \theta \times M \simeq 1.22 \frac{\lambda_0 f}{D} \times M = 0.61 \frac{\lambda_0 n}{NA} \times M$$

$$NA = n \sin \theta \simeq n \frac{D}{f} \quad n: \text{refractive index},$$

$$D: \text{aperture size of lens, } f: \text{focal length of lens}$$

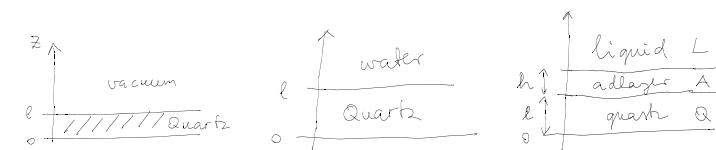
2.4 Fluorescence Microscopy

Emitted photon has less energy. → Absorption ≠ emission spectr.



3 Mechanical Sensors

3.1 Viscoelastic media



Remark: Calculate always at first in rad/s $\xrightarrow{x^{1/2}\pi} \text{Hz}$.

3.1.1 Crystal with thickness l

Resonance frequency $\omega_n = n \cdot \omega_0 = n \cdot \frac{\pi}{l} \sqrt{\frac{\mu_Q}{\rho_Q}}$ [rad/s]

char. wavelength $\lambda = 2l/n$

3.1.2 Elastic plate in water

Resonance frequency $\omega_n = n\omega_0 + \Delta\omega_n$

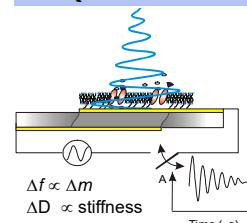
frequency shift $\Delta\omega_n = -\sqrt{n} \sqrt{\frac{\rho_L \eta_L \omega_0}{2}} \frac{1}{l \rho_Q}$, η_L : viscosity

3.1.3 Elastic plate in water with adlayer

In fact is the *resonance frequency* dependent on the adlayer height. But if it is “enough” small, the Sauerbrey approx. is sufficient.

Sauerbrey eq. $\Delta f_n = 2\pi\omega_n = -n \frac{\Delta m}{C}, C = \frac{\sqrt{\rho_Q \mu_Q}}{2f_0^2} = 17.7 \text{ cm}^2 \text{ Hz}$

3.2 QCM-D vs. SPR techniques



$$\Delta m = -\frac{C}{n} \Delta f_n$$

$$\text{LOD}_{\text{QCM}} = C \cdot \delta f \simeq 1 \text{ ng/cm}^2$$

$$\Delta m = d \frac{n_{\text{protein}} - n_{\text{buffer}}}{dn/dc}$$

$$\text{LOD}_{\text{SPR}} = C \cdot \delta\theta \simeq 0.1 \text{ ng/cm}^2$$

3.3 QCM: Quartz Crystal Microbalance

Resonance cond. $f = \frac{n \nu}{\lambda} = \frac{n \nu}{2t}$

Dissipation $D = \frac{1}{\pi f \tau}, \tau: \text{time until } \frac{U_{\max}}{e}$



Modeling of the QCM-D response in air / aqueous solution:

$$\frac{G''}{G} = \frac{G'''}{G'} + j\frac{G''}{G'} \quad \eta: \text{viscosity} (\equiv \frac{G''}{G}), \mu: \text{elasticity} (\equiv G'), \rho: \text{density}, d: \text{thickness}$$

3.4 Strain Gauge

Resistive strain g. $\frac{\Delta R}{R} = k \frac{\Delta l}{l} = k \epsilon, \epsilon: \text{Strain}, k: \text{Gauge factor}$

Capacitive strain g. $C = \epsilon_0 \epsilon_r \frac{A}{d}, (\text{displacement: } d \rightarrow d + \Delta d)$

4 Fluorescent Probes

4.1 Fluorescence Statistics

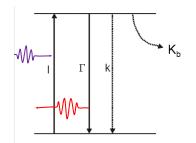
Photobleaching: A fluorescent molecule can emit a limited #photons by excitation before it irreversibly converts to a non-fluorescent molecule.

Quant. Yield $Q = \frac{\Gamma}{\Gamma + k + K_b} \sim 0 - 98\% \text{ (Efficiency)}$

Fluorescence Lifetime $\tau = \frac{1}{\Gamma + k + K_b} \sim 1 \text{ ns}$

Fluorescence emission is a statistical process that is characterized by exponential decays. Molecules in excited state

$$\frac{dN_e}{dt} = -\left(\frac{1}{\tau_1} + \dots + \frac{1}{\tau_n}\right) N_e$$



4.2 FRET – Fluorescence Resonance Energy Transfer

Seeing a different $\lambda_{\text{emission}}$ tells us that two molecules are close.

Efficiency $E = \frac{R_0^2}{R_0^2 + r^6} = 1 - \frac{\tau_{\text{DA}}}{\tau_{\text{D}}} = 1 - \frac{I_{\text{DA}}}{I_{\text{D}}}$

where $\tau_{\text{D(A)}}, I_{\text{D(A)}}$ on Lifetime/Intensity of donor emission in the absence/presence of acceptor.

4.3 Calcium Imaging

→ too slow for t dependency meas.

Calcium ion cannot be visualized/tagged directly: → Design molecules with optical properties that change upon calcium binding.

Single & dual wavelength measurements:

Concentration $[\text{Ca}^{2+}]_i = K_{\text{d,eff}} \frac{R - R_{\min}}{R_{\max} - R}$ where

for single $R \equiv F$ and $K_{\text{d,eff}} = \frac{[\text{Ca}^{2+}]_i \times (F_{\max} - F)}{F \cdot F_{\min}}$

for dual. $R = F_1/F_2 \quad (F: \text{fluorescence})$

The binding of Ca^{2+} leads to...

- change in fluorescence intensity but not wavelength change
- a shift in excitation (and/or emission) peaks (“dual wavelength”)
- changes in fluor. resonance energy transfer (FRET) & life time

4.3.1 Delivery of Calcium Indicators

Loading cells

Once the molecule got cleaved (spalten), it cannot go out and gets fluorescent.

Introduce fluoresc. proteins or (natural) FRET proteins

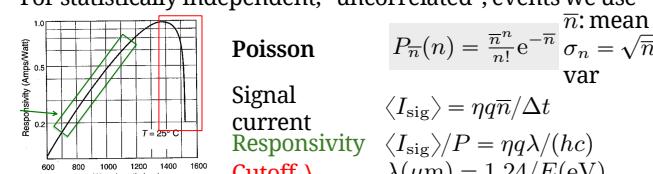
Proteins change emission rate when Ca binds. Relative change ($\Delta F/F$) in fluorescence emission of EGFP can then be meas. directly.

Note: The dye responds *fast*, but it is *slow* to recover. Ca dissociation rate (i.e. recovery) depends on dye's affinity for Ca.

5 Detection and Noise

5.1 Signal

For statistically independent, “uncorrelated”, events we use



Poisson

$$P_{\bar{n}}(n) = \frac{\bar{n}^n}{n!} e^{-\bar{n}} \quad \bar{n}: \text{mean} \quad \sigma_n = \sqrt{\bar{n}}$$

Signal current

$$\langle I_{\text{sig}} \rangle = \eta q \bar{n} / \Delta t$$

Responsivity

$$\langle I_{\text{sig}} \rangle / P = \eta q \lambda / (hc)$$

Cutoff λ

$$\lambda (\mu\text{m}) = 1.24/E (\text{eV})$$

5.1.1 Fundamental Noise Sources

Noise

$$\text{shot } N_s = 2R\eta qB \langle I_{\text{sig}} \rangle = \langle I_{\text{shot}}^2 \rangle R, 2B \simeq 1/\Delta t$$

$$\text{dark } N_d = 2R\eta qB \langle I_{\text{dark}} \rangle$$

$$\text{thermal } N_J = \langle I_{\text{Johnson}}^2 \rangle R = \sqrt{\frac{k_B T_B}{R}}^2 R$$

$$\text{readout } N_r = N_J + N_{\text{amplifier}}$$

$$N_{\text{tot}} = N_s + N_d + N_r \quad \sigma_{\text{tot}}^2 = \sum \sigma_i^2$$

$$\text{SNR}_{\text{curr}} = \frac{\eta \cdot N_{\gamma}}{\sqrt{N_{\gamma} + N_d + N_r}} \quad \eta = \text{QE} \cdot \text{absorb}$$

$$\text{for large numbers } \text{SNR}_{\text{shot}} = \frac{\bar{n}}{\sqrt{\bar{n}}} = \sqrt{\bar{n}} \hat{=} \eta N_{\gamma}$$

5.2 (Optical) Detectors

Photoel. effect

$$E_{\text{ph}} = hf = hc/\lambda = \phi + E_{\text{kin}}$$

incident $E_{\text{ph}} = E_{\text{binding}} + E_{\text{kin}}$ of ejected el.

$$I = \alpha (S \cdot E_{\text{ph}} n / \Delta t), S: \text{sensitivity}, N_d \uparrow$$

Choose binning mode (2x2, 4x4, ...) such that the pixel size of the camera fits the best the maximum pixel size.

max. pixel size

$$\text{max} = 0.3 \frac{\lambda}{NA} \times M$$

5.3 Imaging Deep Tissues

Beer-Lambert's law $I = I_0 e^{-\mu x}$

1st Pinhole by illumination: → focus the illum. to a small spot

2nd Pinhole by detector: → reject out of focus light

→ collect light to PMT

Signal and Noise (Pinhole size):

- more out of focus light → blurry
- less in-focus light → SNR↓

Choose pinhole size $\sim \Delta r = 0.61 \frac{\lambda}{NA} \times M$

5.3.1 2ph-Excitation

1-photon excitation: Excitation rate proportional to excitation light intensity

2-photon excitation: Excitation rate proportional to SQUARE of excitation light intensity

{ } $\{ \}$

- + wavelength↑ → less absorbing/scattering
- + photons need to coincide in space and time to excite
- + No pinhole by detector for 2ph: Collect all the light
- low prob. of occurrence i.e. inefficient
- ultra-short pulse light source needed

6 Optical Biosensors

6.1 EM

Relations:

$$c_0 = \frac{1}{\sqrt{\epsilon_0 \mu_0}} k_0 = \frac{2\pi}{\lambda_0} = \frac{\omega}{c_0} = \omega \sqrt{\epsilon_0 \mu_0} \quad k = \frac{2\pi n}{\lambda} \quad n = \frac{c_0}{c} = \sqrt{\epsilon_r \mu_r} \simeq \sqrt{\epsilon_r}$$

$$\text{Dispersion relation} \quad k^2 = \epsilon \omega^2 = \epsilon k_0^2 c_0^2 = k_0 \frac{\epsilon}{\epsilon_0} = k_0^2 \epsilon_r = (k_0 n)^2$$

$$\text{Plane waves} \quad \vec{E}(\vec{r}, t) = \vec{E}_0 e^{j(\vec{k} \cdot \vec{r} - \omega t)}$$

whereby $\partial_t \hat{=} -j\omega, \partial_x \hat{=} jk_x, \partial_z \hat{=} jk_z, \partial_y \hat{=} 0$ (infinite extent)

$$\text{Depth of penetration} \quad d_p = \frac{\lambda}{4\pi} \frac{1}{\sqrt{n_{\text{inc}}^2 \sin^2 \theta - n_2^2}} \quad (\text{about 500 nm})$$

6.2 Evanescent Field Techniques

Recap

Evanescence

Always total reflection for $n_{\text{inc}} > n_2$
Negligible change of sensitivity compared to the size of the antibodies

6.2.1 SPR – Surface Plasmon Resonance

Plasmon quantum of electron density wave in a metal

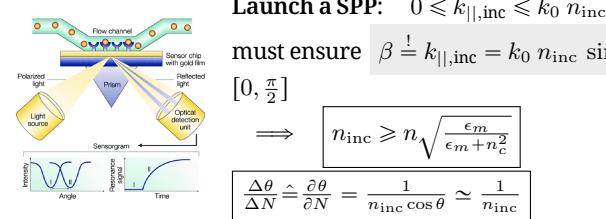
Plasmon Polariton mixt. of photon (diel.) and el. dens. wave (met.) field components point in dir. of propagation

$$\text{SPP} \quad k_{z,i}^2 = k_0^2 \epsilon_i - \beta^2 \quad i = d, m$$

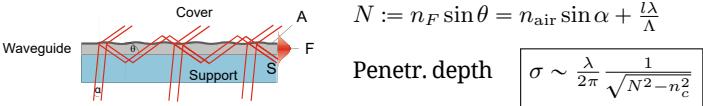
$$\text{Dispersion relation} \quad k_{z,i}^2 = k_0^2 \epsilon_i - \beta^2 \quad i = d, m$$

$$\text{Mom. of inc. wave} \quad \beta := k_x = \frac{\omega}{c} \frac{\epsilon_m \epsilon_d}{\epsilon_m + \epsilon_d} = k_0 \cdot N$$

where N effective refr. index of SP



6.2.2 OWLS – Optical Waveguide Lightmode Spectroscopy



Waves have to be in phase (constr. interf.) → extremely sensitive
constr. interference $0 = 2\pi m = \phi_F + \phi_{FS} + \phi_{FAC}$ ϕ : phase shifts

Ansatz for 3 layer model
 Cover: $C e^{-|k_z z|} (z - d_F/2)$
 Waveguide: $B e^{j k_z z} + A e^{j k_z z}$
 Support: $D e^{|k_z z|} (z + d_F/2)$

Idealized adlayer $n_A = n_C + c_A \frac{dn}{dc}$

Mass calculation $M = d_A \frac{n_A - n_C}{dn/dc}$

6.3 Limitations

Above methods not usable for diagnostic purpose → NSB, LOD

Solution: diffractometric biosensors (Focal Molography)

7 Molecular Adsorption and Electron Transfer

7.1 Quantum Mechanics

Schrödinger eq. $\hat{H}\psi(\vec{r}) = E\psi(\vec{r})$ where $\hat{H} = -\frac{\hbar^2}{2m} \frac{\partial^2}{\partial x^2} + V$

1D potential well $\psi(x) = \sqrt{\frac{2}{L}} \sin(k_n x)$ for $0 \leq x \leq L$

where $k_n = \frac{n\pi}{L}$, $n \in \mathbb{N}$ and $E_n = \frac{\hbar^2 k_n^2}{2m}$

1D potential barrier (tunneling)
 $\psi(x) = \begin{cases} Ae^{jk'x} + Be^{-jk'x} & x \leq 0 \\ Ce^{jk''x} + De^{-jk''x} & 0 \leq x \leq d \\ Fe^{jk'x} & \text{otw.} \end{cases}$

transm./tunneling probability $T = \frac{F^* F}{A^* A} = Be^{-\beta d}$, $\beta = -2\sqrt{2m(V_0 - E)/\hbar}$

7.2 Electronic Transport through Molecules

Quantum conductance (1D) $G = G_0 \cdot T$ $G_0 = \frac{2e^2}{h}$, in parallel: $G = N \cdot G_0$

Tunneling probability $T = Be^{-\beta d} \propto e^{-\beta d} = (e^{-\beta NPD})^N$

1D channel current $j = -(\mu_1 - \mu_2)e v \rho_E$ $\rho_E = DOS = \frac{1}{\hbar\pi} \sqrt{2m/E}$

7.3 Atomic and Molecular Orbitals

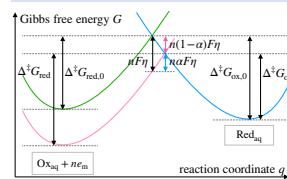
Bond order: defined by difference (#electrons) divided by two
→ If the bond order is different from zero, then the bond is stable

7.4 Transition State Theory $A + B \rightarrow [AB] \rightarrow C + D$

Gibbs free energy $G = H - TS = U + pV - TS$

Ideal gas law $pV = n_{total}RT$

7.4.1 Marcus Theory



See section ?? (Butler-Volmer)

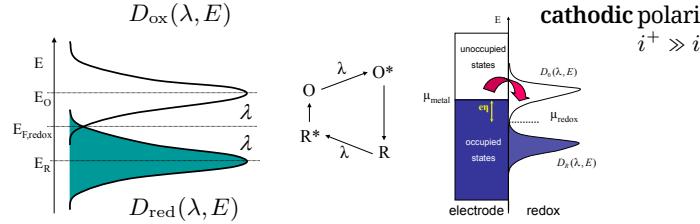
$$k_{red} = v_{red} e^{-\frac{\Delta^\ddagger G_{red}}{RT}}$$

$$k_{ox} = v_{ox} e^{-\frac{\Delta^\ddagger G_{ox}}{RT}}$$

$$\Delta^\ddagger G_{red} = \ddagger G - G_{ox,min}$$

$$\Delta^\ddagger G_{ox} = \ddagger G - G_{red,min}$$

7.4.2 Gerischer's view



8 Potentiometric Biosensors

8.1 Redox Reaction

oxidation: e^- donor (anode) reduction: e^- acceptor (cathode)

Chemical reaction $A \cdot \text{ox} + B \cdot X + z \cdot e^- \xrightleftharpoons{k_{red}} C \cdot \text{red} + D \cdot Y$

reaction quotient $Q = \frac{a_{\text{ox}}^A \cdot a_X^B}{a_{\text{red}}^C \cdot a_Y^D} \cdot a_{\text{ion}} = r_{\text{ion}} [\text{ion}] / 1 \text{ mol/l} \cdot a_{\text{solids}} = a_{\text{gas}} = p_{\text{gas}} / 1.013 \text{ bar} \cdot [\text{H}_2\text{O}]$

Standard conditions $T = 1^\circ\text{C}$, $p = 101.3 \text{ kPa} = 1.013 \text{ bar}$
 "STP" $[\text{ion}] \equiv c_{\text{ion}} = 1 \text{ mol/l}$, $r = 1$ "activity coeff."

8.2 Electrochemistry

Dynamic equi. no net charge over time ($k_1 = k_{-1}$)

Chemical potential $\mu_j = (\frac{\partial G}{\partial n_j})_{p,T,n'}$

Equilibrium $\mu_A = \mu_B$ general: $\sum_{\text{prod}} v_j \mu_j = \sum_{\text{react}} v_j \mu_j$

Chemical potential $\mu_{\text{redox}} \equiv E_F, \text{redox} \equiv E^*$

Equilibrium $\bar{\mu}_A = \bar{\mu}_B$ $\bar{\mu}_j = \mu_j^0 + z_j F \Delta \phi$

Contact potential $\Delta \phi = V_{\text{in}} - V_{\text{out}} = \frac{k_B T}{Q} \ln \left(\frac{[C]_{\text{out}}}{[C]_{\text{in}}} \right)$
 $= -\frac{\Delta_r G}{z F} = \frac{1}{z F} \left(\sum_{\text{ox}} v_j \mu_j - \sum_{\text{red}} v_j \mu_j + z \mu_e \right)$

Nernst eq., $\Delta \phi$

$$E = E^0 - \frac{59 \text{ mV}}{z} \log_{10} Q \xrightarrow{\frac{RT}{zF} \ln Q = \frac{2.303RT}{zF} \log_{10} Q}$$

$$E_{\text{cell}} = E_1 - E_2 \quad \text{or} \quad \text{let } E_1 \stackrel{!}{=} E_2 \rightarrow \text{pH} = \dots$$

8.3 Ion-selective Electrodes (ISE)

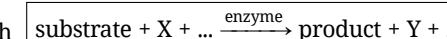
Sensor is separated to solution through a H^+ permeable glass.

pH electrode

$$\text{pH} = -\log_{10} a_{\text{H}^+} = \frac{K' - \Delta \phi}{0.059 \text{ V}}$$

8.4 Bioenzymatic Electrodes

Find out how much of an enzyme was initially present



Detect "a lot" X
 ↔ "very few" substrate was initially present

9 Amperometric Sensors

9.1 Electrochemistry

Overpotential

$$\eta \equiv \Delta \phi_{\text{appl}} - \Delta \phi^0 \equiv \phi_s - \phi_m \equiv E - E^0 \quad E^0: \text{Nernst}$$

$\eta = 0$ (equilibrium i.e. no net current)
 1st: $n \propto Q$, 2nd: (equiv. weight) $W_{\text{eq}} = M/z$

$$m = \frac{Q}{zF} M = \frac{I t}{zF} M = n \cdot M \quad [m] = g, [n] = \text{mol}$$

9.1.1 Butler-Volmer equation Effect of η on barrier height G

Let ϕ_s : potential of ions in solution

ϕ_m : potential of e^- in (metallic) electrode

z : valency of oxidized species

n : #of transferred e^-

$z - n$: valency of reduced species

transfer coeff. α $nF\eta = n(1 - \alpha)F\eta + n\alpha F\eta$ @equi. ($\eta = 0$)

$$f \equiv \frac{F}{RT} = \frac{1}{25.69 \text{ mV}} \quad k_{\text{red}} = k_0 e^{-n\alpha f\eta}, k_{\text{ox}} = k_0 e^{n(1-\alpha)f\eta} \quad k_0 \equiv k_{\text{red}} = k_{\text{ox}}$$

The Butler-Volmer eq. relates what we measure (the current) with what we would like to determine (the concentration of an analyte):

$$\text{Butler-Volmer} \quad j = \frac{nFAk_0}{j_0} (C_{\text{ox}}(0,t) e^{-\alpha f\eta} - C_{\text{red}}(0,t) e^{(1-\alpha)f\eta})$$

9.2 Cyclic Voltammetry

Offers information on the mechanism of the ec reactions occurring at an electrode.

- May be irreversible
 \rightarrow upper peaks \neq lower peaks
 \rightarrow irreversible reaction fast
- Sweep rate
 \rightarrow irreversible reaction slow

Water electrolysis High potentials/volt's
 \rightarrow affects I (disturbance, bad)

9.3 Amperometric Sensors

9.3.1 Clark (Oxygen) Electrode

→ Measure O_2

• test solution $\xrightarrow{\text{O}_2 \text{ passes membrane}} \text{Pt cathode} \xrightarrow{\text{reduction}} \text{current}$

• Ag anode is in KCl solution (\rightarrow "enough" Cl^- for oxidation)

9.3.2 1st and 2nd Generation

analyte of interest ... $\xrightarrow{\text{catalyze}} \text{redox enzyme} \xrightarrow{\text{P1}} \text{mediator} \xrightarrow{\text{P2}} \text{Clark Electrode}$

problem P1 (1st) O_2 may be consumed, when not measured

problem P2 (2nd) need to have "enough" of them

Mediator has to be • reversible • not toxic • no side reactions

9.3.3 3rd Generation

Immobilization/fixation of a redox enzyme on electrode surface

→ free-diffusing redox mediators are not necessary

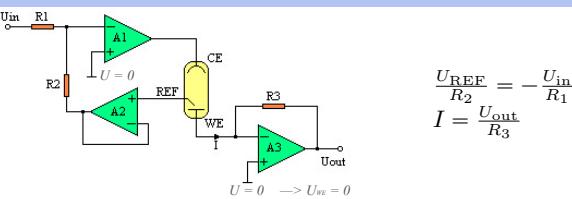
→ in vivo measurements allowed since immobilized

problem P3 Efficient electron transfer (Marcus theory)

→ may be overcome by mediators

→ minimize ET distance

9.4 Three Electrode Cell



10 Membranes and Transport

10.1 Diffusion

Concentration	$c(x, t)$ [mol/l = mol/ 10^3 cm 3]
Flux	$\phi(x, t)$ [mol/cm 2 s]
Fick's law	$\phi(x, t) = -D_n \frac{\partial c_n(x, t)}{\partial x} = \phi_0$ in steady state
	D_n : diffusion coeff [cm 2 /s]
Continuity eq.	$-\frac{\partial \phi_n(x, t)}{\partial x} = \frac{\partial c_n(x, t)}{\partial t}$
e.g. Delta initial condition	$c(x, t) _{t=0} = n_0 \delta(x)$
	$c(x, t) = \frac{n_0}{\sqrt{2\pi}\sigma} e^{-x^2/\sigma^2}$, $\sigma = \sqrt{2D_n t}$, $t_{1/2} = \frac{1}{D_n} x_{1/2}^2$

10.1.1 Diffusion across membrane

$\phi_n(t) = P_n(c_n^i(t) - c_n^o(t))$
with permeability: $P_n = \frac{D_n k_n}{d}$

10.2 Osmosis

Osmotic (back-)pressure $\pi(x, t) = RT \sum_n c_n(x, t)$ $c_\Sigma(x, t)$: osmolarity/total conc.

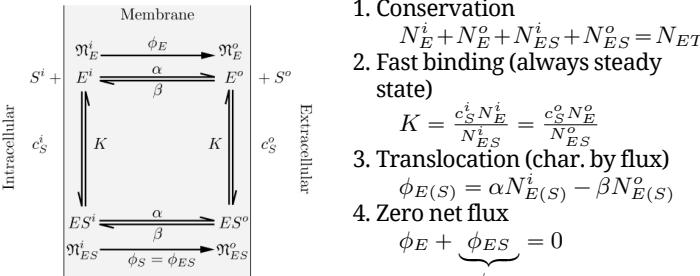
Zero pressure if $\pi_i - \pi_o = 0$

Volume of the cell $v_c(\infty) = v'_c + \frac{N_\Sigma^i}{c_\Sigma^o}$ v'_c : non-water volume

10.3 Carrier mediated Transport

- Hints for their existence
• Saturation of solute trsp. (∇ Fick's law)
• Competitive inhib.
• Structure specificity

4-state carrier model



Net flux out of cell $\phi_S = \frac{\alpha \beta}{\alpha + \beta} N_{\text{NET}} \left(\frac{c_S^i}{c_S^i + K} - \frac{c_S^o}{c_S^o + K} \right)$ $(\phi_S)_{\text{max}} = \frac{\alpha \beta}{\alpha + \beta} N_{\text{NET}}$

10.4 Ion Transport

Continuity eq. $\frac{\partial J_n(x, t)}{\partial x} = -z_n F \frac{\partial c_n(x, t)}{\partial t}$ z_n : valency

Poisson eq.

i.e.

$$\frac{\partial^2 \psi(x, t)}{\partial x^2} = -\frac{1}{\epsilon} \sum_n z_n F c_n(x, t)$$

electric field potential = local charge density

Nernst-Planck eq.

u_n : molar mobility

$$J_n(x, t) = -z_n F D_n \frac{\partial c_n(x, t)}{\partial x} - u_n z_n^2 F^2 c_n(x, t) \frac{\partial \psi(x, t)}{\partial x}$$

Debye Length "depletion width": $\lambda_D \simeq 1 \text{ nm}$ within $\tau_r \simeq 1 \text{ ns}$

Nernst Equi. Pot.

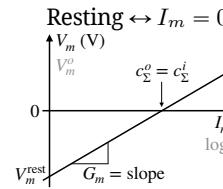
$$V_n = \frac{59 \text{ mV}}{z_n} \log_{10} Q \quad \text{with} \quad Q = \frac{c_n^o}{c_n^i}, \quad \frac{D_n}{u_n} = RT$$

$$V_K \simeq -75 \text{ mV}, \quad V_{Na} \simeq 55 \text{ mV}$$

Donnan equil.

$$V_m = V_n \Rightarrow I_n = 0 \quad \left(\frac{c_n^o}{c_n^i} \right)^{\pm \frac{1}{z_n}} = e^{\frac{F V_m}{RT}}, +: \text{anodic}$$

10.4.1 Resting (membrane) potential



3-ion model

permeable to K, Na and some others

Resting potential

$$V_m^{\text{rest}} = \frac{V_K G_K}{G_{\text{tot}}} + \frac{V_{Na} G_{Na}}{G_{\text{tot}}} + \frac{V_o G_o}{G_{\text{tot}}} \quad G_{\text{tot}} \equiv G_m = \text{slope}$$

$$J_m = J_K + J_{Na} + J_o = 0 \quad \text{where} \quad J_n \neq 0 \quad (\text{only momentarily rest})$$

10.5 Active Transport

Rest is only momentarily \rightarrow maintain conc. grad with act. transport

- Ions moving against its conc. gradient \rightarrow ATP needed
- Active pumps for $J_m = 0$ (rest) and $J_{n,in} + J_{n,out} = 0$ (quasi equilib.)

11 Action Potential & Hodgkin-Huxley Model

11.1 Current Clamp

Fix current I_m and measure membrane potential

\rightarrow Good for observing AP
(since voltage can change)

11.3 2-state ion channel model

two states

close $\xrightarrow{\alpha}$ open with gate charge Q

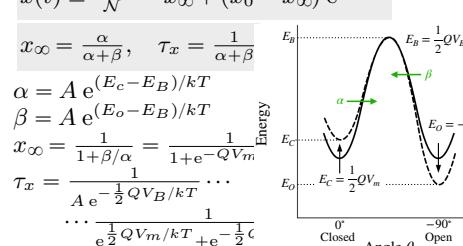
#open states

$$\frac{dn(t)}{dt} = \alpha(\mathcal{N} - n(t)) - \beta n(t)$$

Prob. being open

$$x(t) \simeq \frac{n(t)}{\mathcal{N}} = x_\infty + (x_0 - x_\infty) e^{-t/\tau_x}$$

Boltzmann law



$$\alpha = A e^{(E_C - E_B)/kT}$$

$$\beta = A e^{(E_o - E_B)/kT}$$

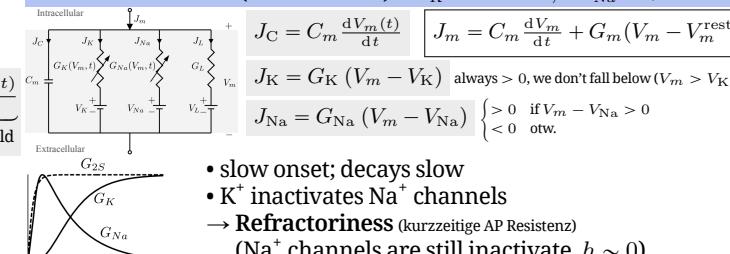
$$x_\infty = \frac{1}{1 + \beta/\alpha} = \frac{1}{1 + e^{-QV_m}}$$

$$\tau_x = \frac{1}{A e^{-\frac{1}{2} QV_B/kT}} \dots$$

$$\dots \frac{1}{e^{\frac{1}{2} QV_m/kT} + e^{-\frac{1}{2} QV_m}}$$

11.4 Circuit Model (Conductance)

$$V_K \simeq -75 \text{ mV}, \quad V_{Na} \simeq +55 \text{ mV}$$



- slow onset; decays slow
- K^+ inactivates Na^+ channels
- \rightarrow Refractoriness (kurzzeitige AP Resistenz)
(Na^+ channels are still inactivate, $h \sim 0$)

11.5 Multiple states gate

open $n_Q(V_m, t)$ big/small $Q \rightarrow$ fast/slow dynamics

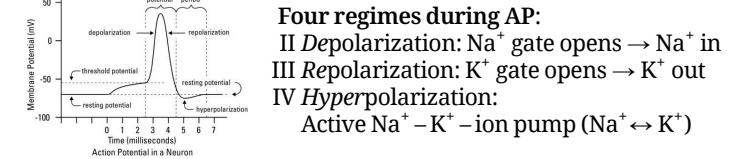
Let's write $[h] = n_{-Q}$ "slow", $[m] = n_{2Q}$ "fast", $[n] = n_Q$
The lower T , the bigger the diff. between them.

11.6 Hodgkin-Huxley (HH) model

Experimentally you may fit the K^+ and Na^+ current into

$$\text{Conductance} \quad G_K(V_m, t) = \bar{G}_K N^4$$

$$G_{Na}(V_m, t) = \bar{G}_{Na} m^3 h$$



11.7 Decrement-free conduction

11.7.1 Core - Conductor Model

$$R_i = r_i dz \quad \leftarrow dz: \text{per unit length}$$

$$R_o = r_o dz \quad \leftarrow \text{may use HH-model}$$

$$I_m = k_m dz \quad \leftarrow \text{if } 0 \rightarrow I_o = -I_i$$

$$\text{Core-Conductor eq.} \quad \frac{\partial^2 V_m(z, t)}{\partial z^2} = (r_o + r_i) K_m(z, t) - \frac{r_o K_e(z, t)}{dz}$$

$$\text{wave eq.} \quad = \frac{1}{v^2} \frac{\partial^2 V_m(z, t)}{\partial t^2} \quad \text{with } v = \frac{W}{\Delta t}$$

$$K_m = \frac{K_m a}{2\rho_i} \quad \text{for } r_i \gg r_o \quad \text{i.e. } v \propto \sqrt{a}$$

11.7.2 Cable model - Core-Conductor with HH-model inside

Linearize (1st order) timescale for membrane voltage changes $\tau_m = \frac{C_m}{G_m}$
Cable equation

$$v_m + \tau_m \frac{\partial v_m}{\partial t} - \lambda_C^2 \frac{\partial^2 v_m}{\partial z^2} = r_o \lambda_C^2 K_e \quad \lambda_C = \frac{1}{\sqrt{g_m(r_o + r_i)}}$$

= 0 time indep.

11.7.3 Saltatory Conduction Hypothesis

\rightarrow explain discrete manner in steps
velocity \sim axon diameter D
total delay $\sim N(\# \text{nodes}) \sim (\text{axon length})/L$
velocity $\sim \frac{\text{total delay}}{\text{axon length}} \sim D$

