

Week2 Optical Biosensor

1. Structure of Biosensor:

Light source -> sensor -> light analyzer

2. Key Parameters of Biosensors:

Specificity: what is the analyte being measured
Sensitivity: the quantity (or concentration) of the analyte (LOD) (=slope)

Detection limit / Limit of detection (LOD)

$$LOD = 3 \times s/m$$

3. Light sources: (Lasers, LED, lamps)
-
- | s: standard deviation;
-
- m: slope;
-
- ceil

CW: continuous wave

4. General requirements on sources:

Spatial coherence

Low noise (RIN)

Adequate power output (SNR)

5. Light as Waves - The EM Wave Model:

$$E(t, z) = E_0 \cos(\omega t - kz)$$

angular frequency: $\omega = 2\pi\nu$ wavelength: $\lambda = c/\nu$ wave vector: $k = 2\pi/\lambda$ speed of light: $c = 3 \times 10^8 \text{ m/s}$

6. Light as Particles - The Particle Model

Energy is delivered in photons (光子).

Energy of one photon: $E = h\nu = 1239.8/\lambda [\text{nm}]$ Planck's constant: $h = 6.63 \times 10^{-34} \text{ Joule}\cdot\text{s}$

$$1W = 1/s \quad 1\text{eV} = 1.602 \times 10^{-19} \text{ J}$$

Photon momentum (动量): $p = h/\lambda$

7. Refractive Index

 $n = \text{Speed in Vacuum} / \text{Speed in medium}$ Snell's Law: $n_i \sin(\theta_i) = n_s \sin(\theta_s)$ Total internal Reflection: $\theta_c = \sin^{-1}(n_s/n_i)$

8. Evanescent Wave Field

Penetration depth: $d = \lambda_0 / 4\pi\sqrt{n_i^2 \sin^2 \theta_i - n_s^2}$

(assuming incident angle = 90°)

Light intensity: $I(d) = \exp(-d/L_0)$

9. Light-matter Interactions

Incident = Reflected + Transmitted + Absorbed

Absorption / A+Luminescence / Scattering

10. Absorption spectroscopy

Absorbance: $A = \epsilon CL = -\log_{10}(I/I_0)$

$$I(\lambda) = I_0 \cdot e^{-\epsilon'(\lambda)CL}, \epsilon' = \epsilon / 2.303$$

 ϵ : molar absorption coefficient ($M^{-1}cm^{-1}$)c: molar concentration (M)L: optical path length (cm)

11. Fluorescence Lifetime & Quantum Yield:

$$\Phi = N_{\text{em}}/N_{\text{absorb}} = k_e / (k_e + k_{nr}) = k_e \tau_s$$

 k_e : fluorescence rate constants

12. Scattering (no absorption):

Elastic scattering: no energy change

Inelastic scattering: energy change

Frequency change, Vibration, Raman

13. Raman scattering

stokes: $E \downarrow f \downarrow$; anti-stokes: $E \uparrow f \uparrow$ wavenumber: $\bar{v} = 1/\lambda (\text{cm}^{-1})$

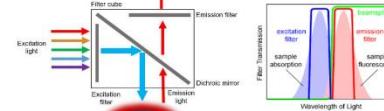
$$\text{Raman shift} [\text{cm}^{-1}] = \frac{10^7}{\lambda_{\text{ex}} [\text{nm}]} - \frac{10^7}{\lambda [\text{nm}]}$$

14. Grating

Dispersion: $d \sin \theta = m \cdot \lambda$ Resolving Power: $R = \lambda/d\lambda = mN$ $\Delta\lambda$: resolution m : diffraction order Ceil(N)

Week3 Optical Biosensor (2)

1. Fluorescence Biosensors-(Dye) Labeled Sensors:



1) Excitation of a fluorophore through the absorption of light energy. 2) A transient excited lifetime with some loss of energy. 3) Return of the fluorophore to its ground state, accompanied by the emission of light.

2. Selecting Filters:

3. Label-Free Sensor Working Principle

Sensitivity: $S[\text{nm}/RIU] = (\lambda_2 - \lambda_1)/(n_2 - n_1)$ Resonant wavelength: $\lambda = 2\pi n_{\text{eff}}/m$ r: fiber radius n_{eff} : effective refractive indexFWHM = $x_2 - x_1$

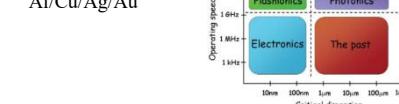
$$f(x_1) = f(x_2) = 0.5f_{\max}$$

Q-factor: $Q = f_0/\Delta f$ Δf by $0.5f_{\max}$ 决定 f_0 : Resonant/central frequencyFigure of Merit: FOM = Sensitivity/ Δf

Surface Plasmon Biosensor:

Materials:

Al/Cu/Ag/Au



Week4 Biomedical Imaging (1)

1. Light propagation in tissues:

attenuation coefficient: $\mu_a [\text{cm}^{-1}] = \mu_a + \mu_s$ μ_a : absorption coefficient μ_s : scattering μ_a ≡ probability of absorption / unit pathlength = inverse of the mean-free-path for absorptionlight function: $I(x) = I_0 \cdot e^{-\mu_a x} = I_0 \cdot e^{-(\mu_a + \mu_s)x}$

loss of incident light: dl=absorption+scattering

2. Fresnel reflection coefficients (normal incident):

$$R = ((n_1 - n_2)/(n_1 + n_2))^2, n_1$$
 incident

3. Property of thin lens:

thin lens equation: $(1/S_1) + (1/S_2) = (1/f)$ Magnification: $M = S_2/S_1$ S_1 : object distance, f : focal length

4. Diffraction Limit:

Resolution: $\Delta d = 0.61\lambda/\text{NA}$ Numerical aperture: $NA = n_{\text{solution}} \sin \theta$

Width of the central band of the Airy disk:

$$D = 1.21\lambda/(n \sin \theta)$$

In practice: $M \Delta d / \Delta x = 2.3 \sim 3$ Δx : the pixel size of the detector

5. Two-photon excited fluorescence

Excited energy: hv_0

6. Optical Coherence Tomography (OCT)

light path difference: $2L$ Phase difference: $(2\pi/\lambda) \cdot 2L$

intensity of interference:

$$I = I_1 + I_2 + 2\sqrt{I_1 I_2} \cdot \cos(4\pi L/\lambda)$$

7. Confusion Matrix

Sensitivity = TP / (TP+FN)

Specificity = TN / (FP+TN)

Data on slanted line are large -> good model

Receiver Operator Characteristic (ROC)

Area Under Curve = 1 -> perfect

Week5 Optical Bioimaging and Devices

1. Physics of Ultrasound:

$$p = p_0 e^{-\alpha x} \cos(\omega t - kx)$$

angular frequency: $\omega = 2\pi\nu$ propagation constant: $k = 2\pi/\lambda$ α : attenuation coefficientAttenuation = $\alpha (dB/(MHz \text{ cm})) \cdot l[\text{cm}]$ $\cdot f[\text{MHz}]$

1. 是往返总路程

intensity of the acoustic wave: $I(t) = p^2(t)/Z$ $[W/m^2], p(t)$: pressure, Z : impedance

2. Confusion Matrix

Sensitivity = TP / (TP+FN)

Specificity = TN / (FP+TN)

Data on slanted line are large -> good model

Receiver Operator Characteristic (ROC)

Area Under Curve = 1 -> perfect

Week6 Electrochemical Biosensor

1. Electrochemical Calculation
Coulomb Calculation Formula: $Q = I \times t$
 Q : Coulombs(C); I : Current (A, amps); t : time(s)
Faraday Constant Formula:

$$1 \text{ mol of electrons} = 1F = 96485 \text{ C/mol}$$

Avogadro's Num: $N_A \approx 6.02 \times 10^{23} \text{ particles/mol}$ Moles of electrons: $n_e[\text{mol}] = Q/F$ Moles of element: $n_{\text{element}}[\text{mol}] = n_e/n$

n: electrochemical equivalent

Mass: $m_{\text{element}} = n_{\text{element}} \cdot M_{\text{element}} = \rho \cdot V$ M_{element} : Molar mass of silver

2. Randle equivalent circuit:

 R_s : active electrolyte resistance R_{ct} : charge transfer R C_{dl} : double-layer capacity Z_w : faradaic reaction Z

x-axis: resistance (real part)

y: reactance (imaginary)

origin: $\omega \rightarrow \infty$

$$Z_{c_{dl}} = 1/j\omega C_{dl}$$

$$Z_w = (1-j)\sigma / \sqrt{\omega}$$

3. Bode plot:

x-axis: logarithmic scale of the frequency

y-axis: logarithm of the impedance Z & phase shift Φ

$$\omega = 2\pi f$$

Week12 Bioelectricity and Biopotential

1. Ionic concentrations and channels

Current: $I_K = g_K(V_m - E_K)$

$$V_m = V_{in} - V_{out} < 0$$

$$E_K = (RT)/(zF) \cdot \ln([K^+]_{out}/[K^+]_{in})$$

 g_K : conductance, 电阻的倒数 E_K : Equilibrium potential for potassium R : Universal gas constant (J/mol·K); T : Temperature (K); z : 离子电荷数(K+>-1) F : Faraday's constant $[K^+]_{out}$: Concentration of K^+ outside the cell

2. five steps on the cell membrane:

Time(ms)

Membrane potential (mV)

Resting potential

Depolarization

Action potential

Re polarization

Hyperpolarization

Threshold potential

3. Biopotential at Tissue Level:

1 V₁, 2 V₂, 3 V₃, 4 V₄, 5 V₅, 6 V₆, 7 V₇, 8 V₈

EEG (Brain)

EMG (Muscles)

ECG (Heart)

$$V_I = V_2 - V_1 \text{ (lead I)}$$

$$V_{II} = V_3 - V_1 \text{ (lead II)}$$

$$V_{III} = V_3 - V_2 \text{ (lead III)}$$

4. The supplementary information:

$$R: V = I_R, Z = R$$

$$L: V = j\omega L, Z = j\omega L, X_L = \omega L$$

$$C: V = 1/j\omega C, Z = 1/j\omega C, X_C = 1/\omega C$$

$$Z(\omega) = |Z|e^{j\phi} = |Z|(\cos \phi + j \sin \phi)$$

$$Z(\omega) = Z' + jZ'', |Z| = \sqrt{(Z')^2 + (Z'')^2}$$

$$V_{A-B} = V_B - V_A$$

5. Analog Filter (没C2就没方框内的项)

Circuit diagram showing a low-pass filter with a 20 log(R2/R1) dB/octave roll-off.

20 log(R2/R1) dB/octave

-20 dB/octave

-40 dB/octave

-60 dB/octave

-80 dB/octave

-100 dB/octave

-120 dB/octave

-140 dB/octave

-160 dB/octave

-180 dB/octave

-200 dB/octave

-220 dB/octave

-240 dB/octave

-260 dB/octave

-280 dB/octave

-300 dB/octave

-320 dB/octave

-340 dB/octave

-360 dB/octave

-380 dB/octave

-400 dB/octave

-420 dB/octave

-440 dB/octave

-460 dB/octave

-480 dB/octave

-500 dB/octave

-520 dB/octave

-540 dB/octave

-560 dB/octave

-580 dB/octave

-600 dB/octave

-620 dB/octave

-640 dB/octave

-660 dB/octave

-680 dB/octave

-700 dB/octave

-720 dB/octave

-740 dB/octave

-760 dB/octave

-780 dB/octave

-800 dB/octave

-820 dB/octave

-840 dB/octave

-860 dB/octave

-880 dB/octave

-900 dB/octave

-920 dB/octave

-940 dB/octave

-960 dB/octave

-980 dB/octave

-1000 dB/octave

-1020 dB/octave

-1040 dB/octave

-1060 dB/octave

-1080 dB/octave

-1100 dB/octave

-1120 dB/octave

-1140 dB/octave

-1160 dB/octave

-1180 dB/octave

-1200 dB/octave

-1220 dB/octave

-1240 dB/octave

-1260 dB/octave

-1280 dB/octave

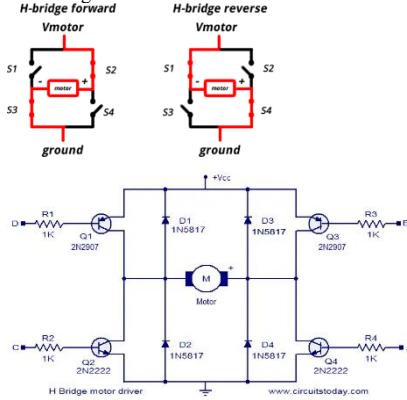
-1300 dB/octave

-1320 dB/octave

-1340 dB/octave

Week10

1. H-bridge driver



Hyperspectral Imaging 包含更丰富的光谱，全波长的信息（传统的只包含 RGB 三个波长的信息），扫描成像

Week 5 非光学成像技术

Ultrasound Imaging 基于反射，声波频率只有百 KHz，因此频率比光低，波长更大，身体不同组织对超声波的衰减是不同的，且与频率有关，深度定义也是信噪比为 1 的地方。但是超声波是反射的，要计算来回的距离。因此实际深度是一半。

声光成像 Photoacoustic Imaging 声和光的优势，声更深

laser pulse \rightarrow absorption \rightarrow thermal expansion \rightarrow acoustic waves \rightarrow ultrasound detection \rightarrow image formation

Week6 电化学传感器

化学氧化还原反应 Redox reaction 产生电子流，体液 blood, saliva, tears, urine, sweat

电压 Potentiometric, 电流 Amperometric, 阻抗 Conductometric 三种传感原理

电压是参考值，要有确定的 GND

Week7 人体电信号

对单个的 cell，可以用 patch electrode 直接插入细胞测试；也可以用微电极阵列 Multielectrode Array 测试细胞表面神经细胞的内外压差是 -70mv，由于钠钾泵，静息状态，内部 K 多，外部 Na 多

肌肉 EMG 电位用两个电极，测量两电极的差，有效降噪

心脏 ECG 的用三个电极，两臂和腿，由于心脏有吸血和泵血

脑电波 EEG 用 20 个电极在头的各个部位

LDO 用于低压降，纹波小，电阻分压原理

DCDC 用于高压降，纹波大，但是效率很高，PWM 分压

计算反馈电阻 $V_{out} = V_{ref} \cdot (1 + R_1/R_2)$ ，计算软启动时间 $Q = CV = it$ 恒流源给外部电容充电到 V_{ref} 所耗费的时间即软启动时间，10ms 左右；超级电容放电， $E = 0.5 \cdot C \cdot V^2$

H 跨驱动

二极管作用续流，电极可视为一个大电感，停转时候会有反向的巨大电压，防止烧毁

Week1

Sensor 定义

A sensor is a device that detects and responds to input (stimulus) from its physical environment.

Physical Changes \rightarrow Sensor \rightarrow Output Signals

Week 2 光学传感器 Optical Biosensor

.Fluorescence intensity is defined as the amount of photons emitted per unit time and per unit volume of solution

. Brightness

$$\text{Brightness} = \varepsilon \chi \Phi$$

光栅(grating) 角度分光能力 单位角度内有多少波长成分 d 角度/d 波长

分光能力越大越好，在一个角度内要包含更多的波长成分

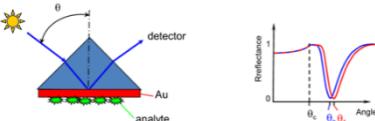
Week 3 Resonator 共振光学传感器

Surface Plasmon Resonance

纳米结构下的缝，会让光密度变大，用 Al, Ag, Cu, Au 生成 plasmonic，当激光照射金属表面，会吸收特定波长的光发热，形成一个波谷 dip dark signal 暗信号

改变外部浓度，比如特定病毒附着，dip 会发生偏移，可能是激光角度也可能是波长 Localized Surface Plasmons 把金属 film 变成细小颗粒

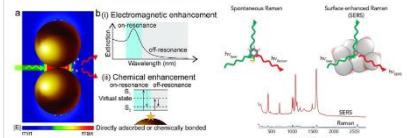
拉曼散射 SERS surface enhanced Raman Scattering



金属纳米颗粒靠近或化学键有自己的 bend 会发生共振，在某些波长下会出现 peak 或 dip，增强拉曼散射，使信号放大

Week4 成像技术

The enhancement factor can be as much as $\sim 10^6$ to $\sim 10^{12}$



Penetration depth 光信号深入人体组织深度后，信噪比为 1 的深度；红外对人体组织的穿透更深，用于计算心跳，血氧饱和度，利用血红蛋白携带氧气后的吸收差异

Optical Coherence Tomography OCT 主要用于眼科检测，发射后，距离的细微差异带来相位差，图像主要与反射率有关。是眼睛的纵切面成像