



Master in Electrical and Electronics Engineering

EE-517: Bio-Nano-Chip Design

Lecture #10

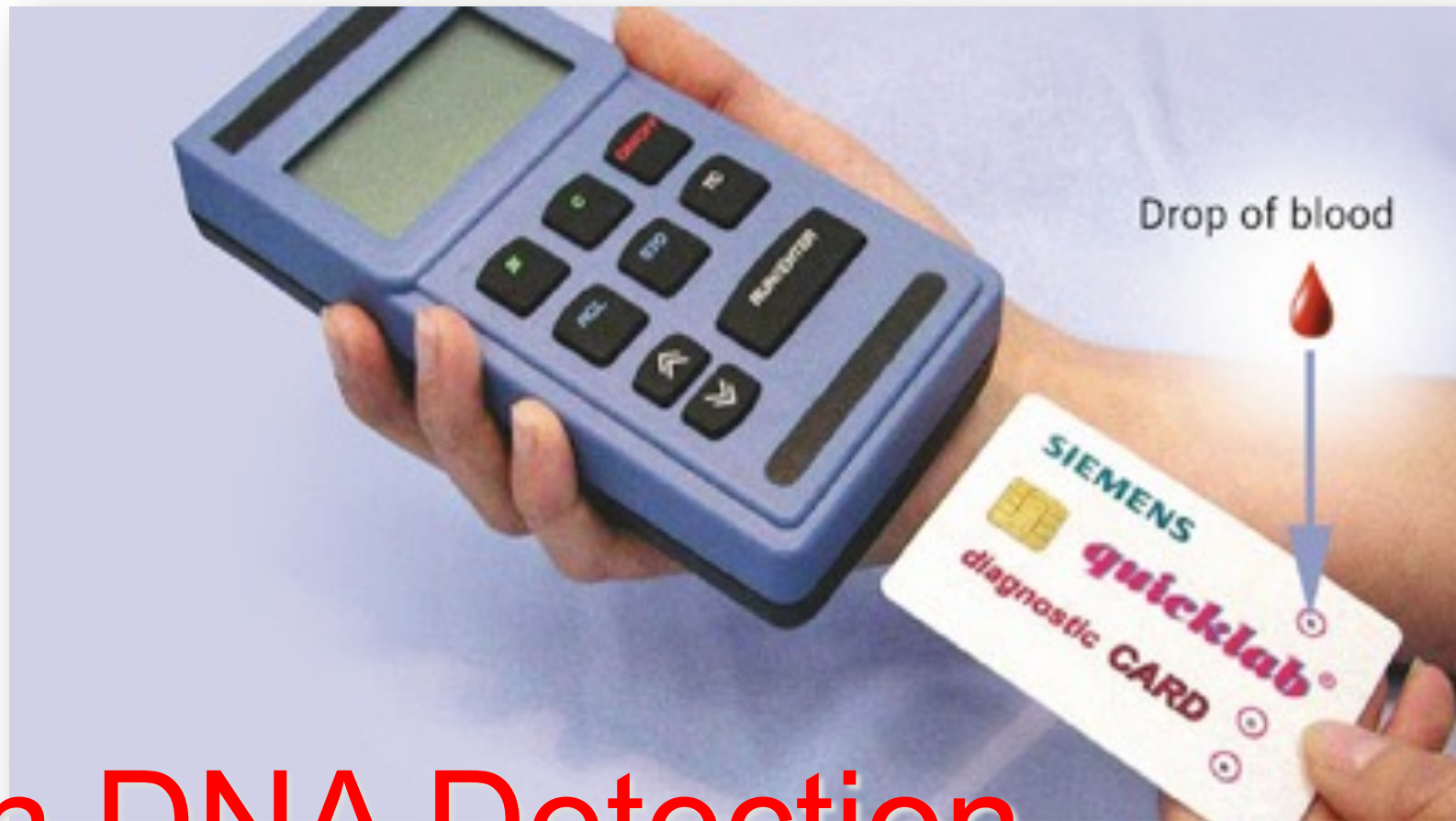
CMOS Building Blocks

Lecture Outline

(Book Bio/CMOS: Appendix B & Chapter' paragraph 8.9.3, 9.1.1, 9.2)

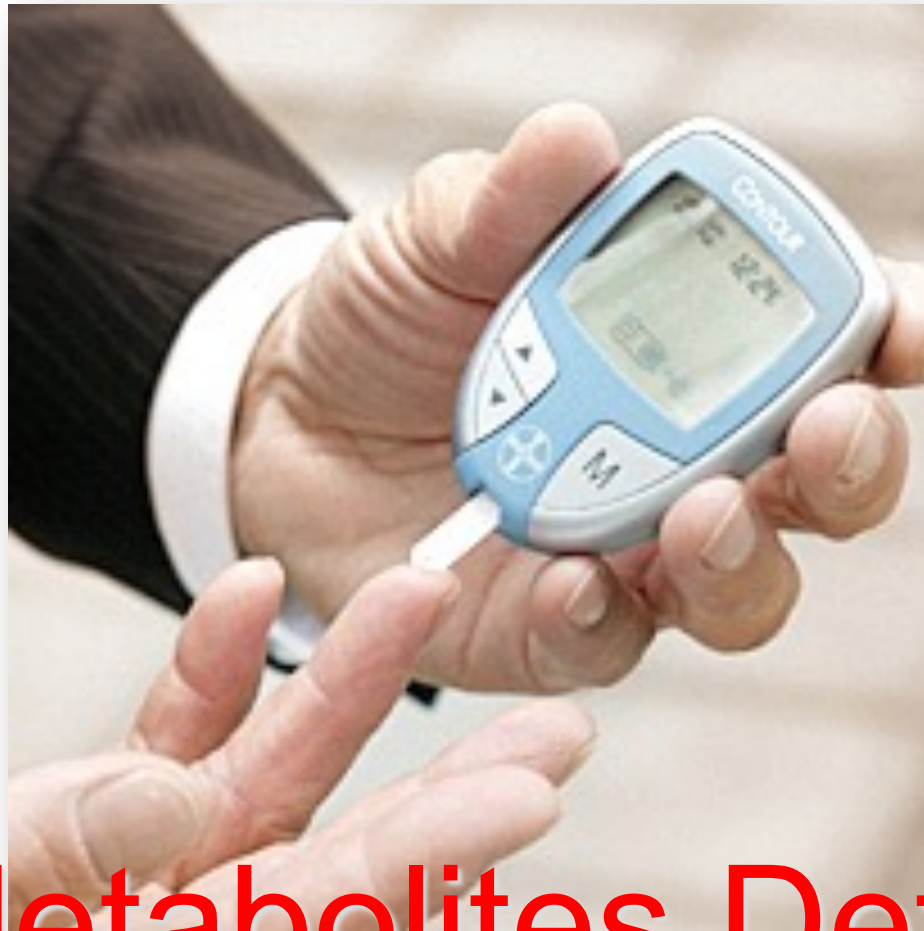
- CMOS design to drive the electrochemical cell
- Electrical properties of the electrochemical cell
- Basic Configuration of the cell: Grounded Counter
- Noise of the electrochemical interface

CMOS architectures for Portable



in DNA Detection

CMOS architectures for Portable

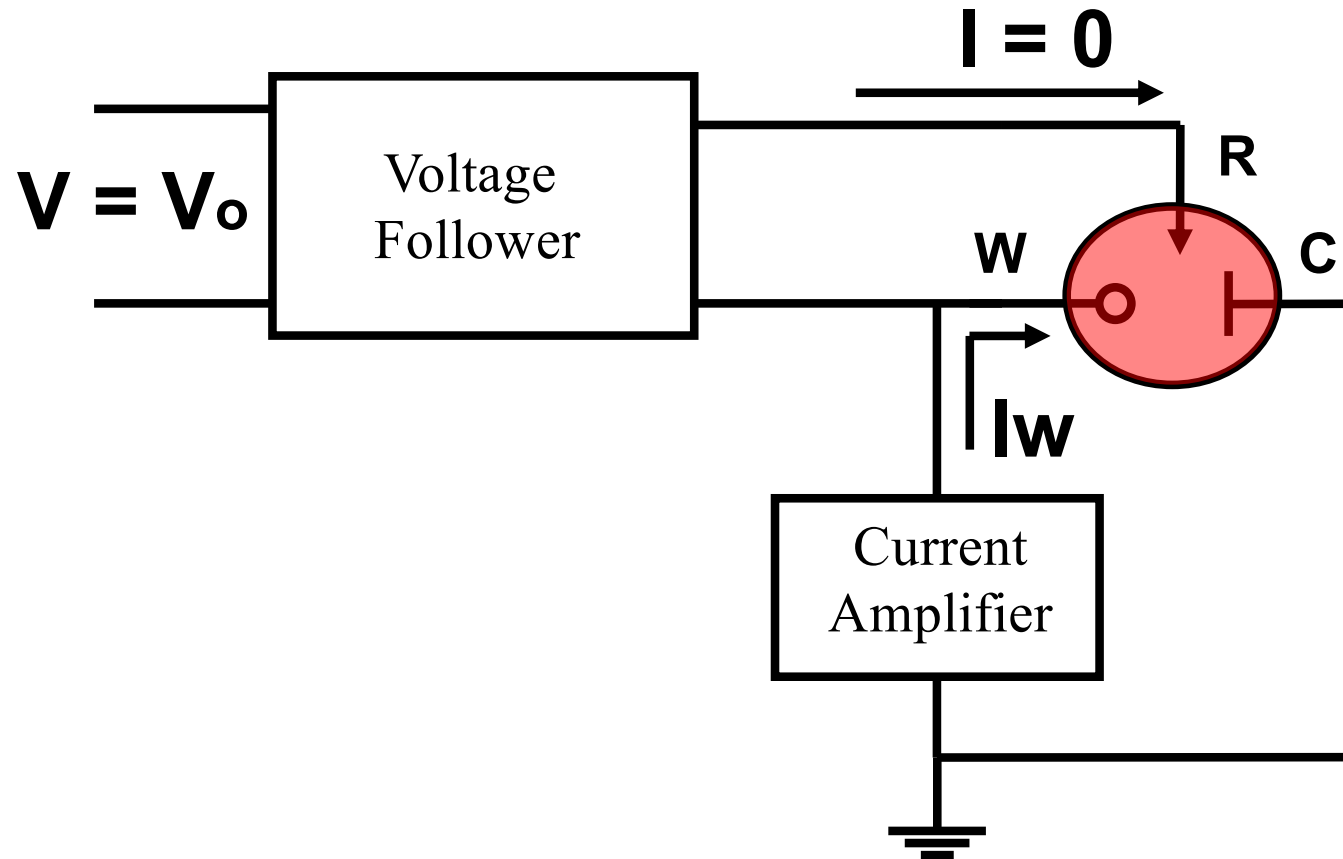


in Metabolites Detection

CMOS architectures for iPhone



Required Blocks



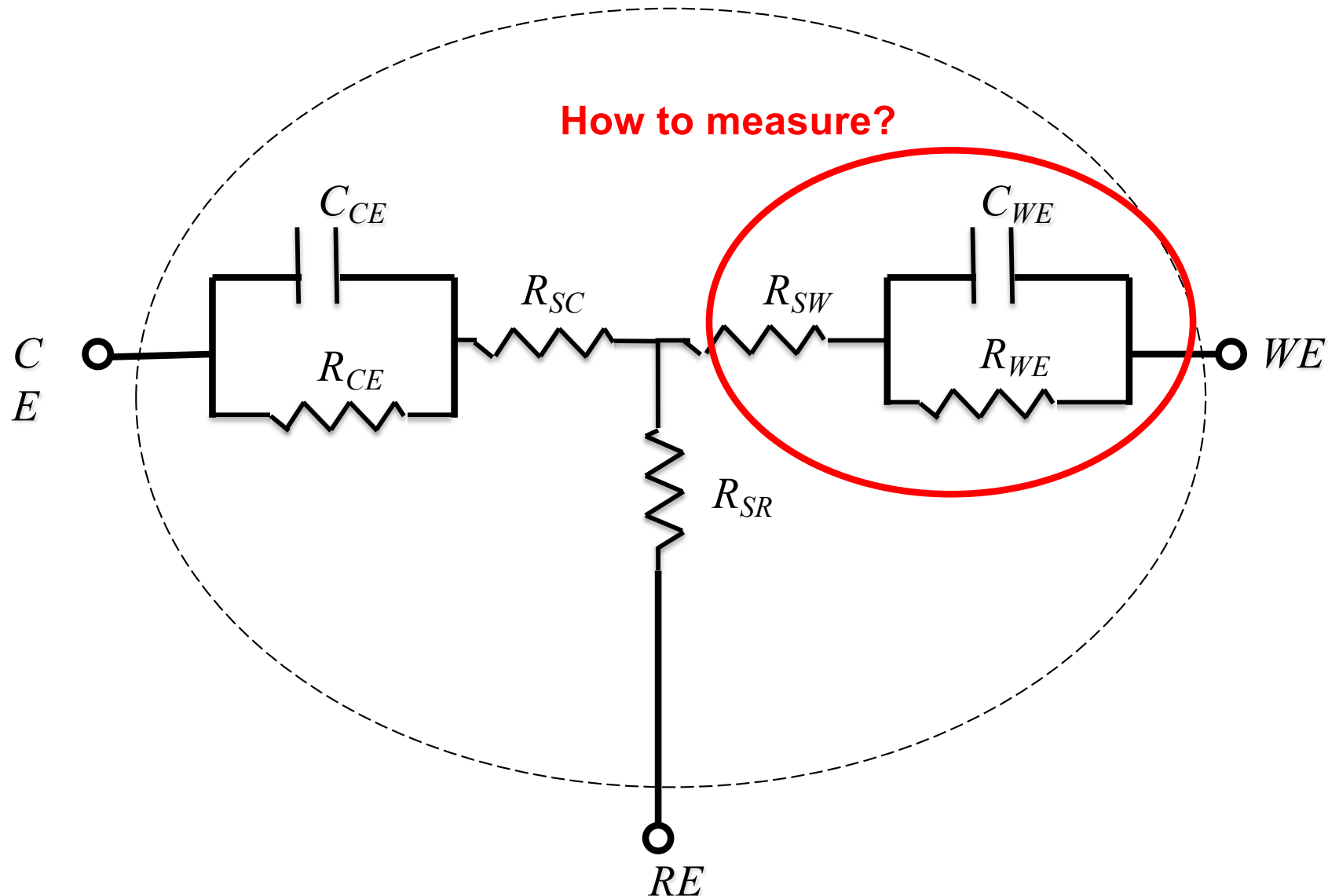


Q1

Why the electrochemical cell needs three electrodes?

- A. Because we need redundancy to improve the measure
- B. Because we need to measure a current, a voltage, and a flux
- ☒ C. Because we need to measure a current, while applying a precise voltage
- D. Because we need to measure a voltage, while supplying a precise current
- E. Because the cell is a node with three entering currents

Equivalent circuit: passive model



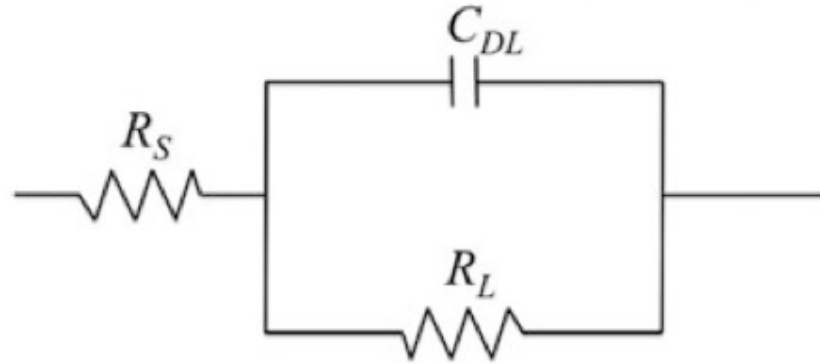


Q2

How to measure the equivalent circuit of an electrochemical cell?

- A. Impossible to measure, that's just a theoretical model
- B. Possible but very difficult to measure since it contains too many parameters
- C. Possible but not very useful since that's just a theoretical model
- ☒ D. That's enough to perform a measure of impedance

Equivalent Impedance



$$Z_{//} = Z = C_{DL} // R_L \quad \left\{ \begin{array}{l} Z = \frac{R_L}{j\omega C_{DL} R_L + 1} \xrightarrow{\omega \rightarrow 0} R_L \\ Z = \frac{R_L}{j\omega C_{DL} R_L + 1} \xrightarrow{\omega \rightarrow \infty} 0 \end{array} \right.$$

The Layering effects result in the impedance in parallel

Equivalent Impedance

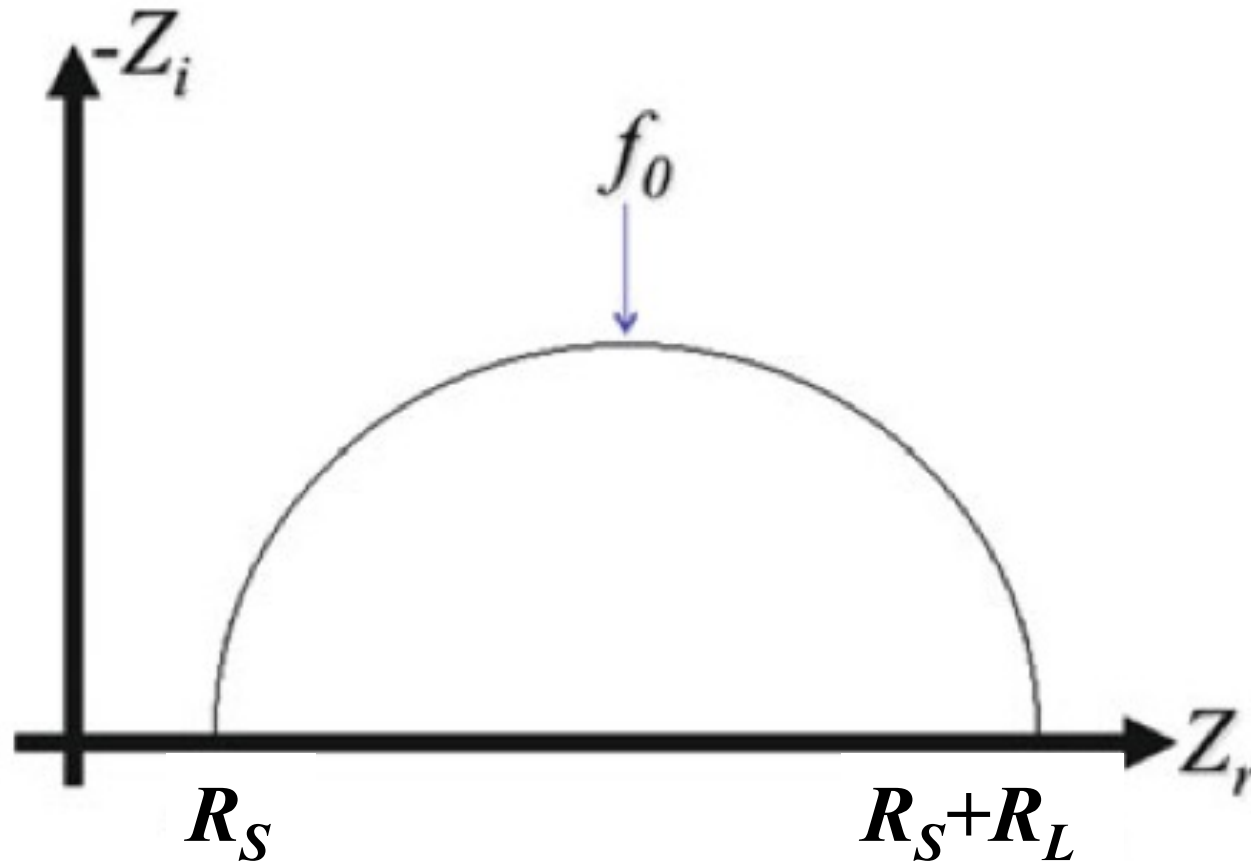
$$Z = \frac{R_L}{j\omega C_{DL}R_L + 1} \cdot \frac{1 - j\omega C_{DL}R_L}{1 - j\omega C_{DL}R_L}$$

$$Z = \frac{R_L - j\omega C_{DL}R_L^2}{1 + (\omega C_{DL}R_L)^2}$$

$$Z = \frac{R_L}{1 + (\omega C_{DL}R_L)^2} - j \frac{\omega C_{DL}R_L^2}{1 + (\omega C_{DL}R_L)^2} \quad \left\{ \begin{array}{l} Z_{\text{Re}} = \frac{R_L}{1 + (\omega C_{DL}R_L)^2} \\ Z_{\text{Im}} = - \frac{\omega C_{DL}R_L^2}{1 + (\omega C_{DL}R_L)^2} \end{array} \right.$$

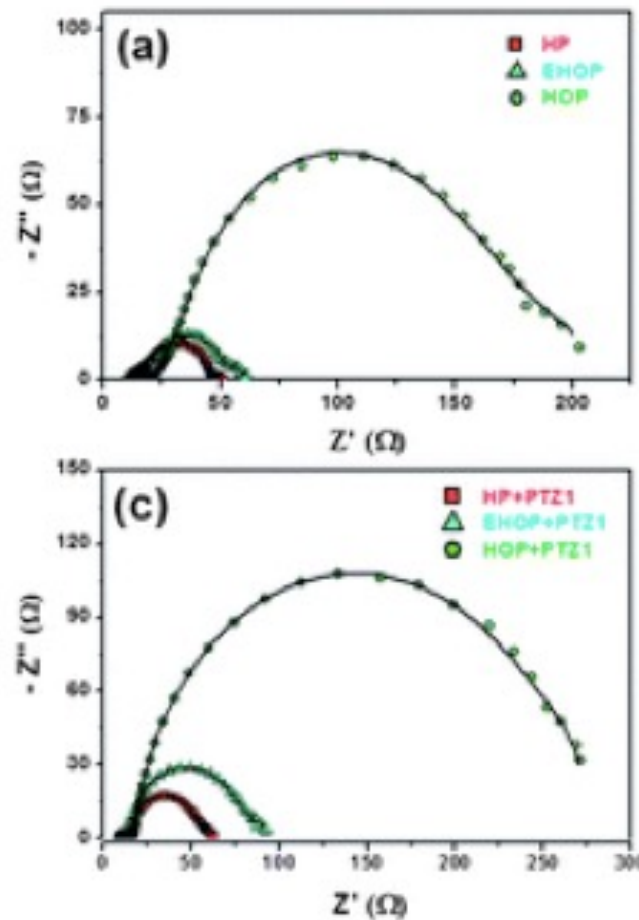
This impedance presents both resistive and reactive components

Nyquist Plot



The Nyquist plot is also a mean to fit data about a specific electrochemical cell

Nyquist Plot



The Nyquist plot is also a mean to fit data about a specific electrochemical cell



Q3

In real cases, are layering phenomena correctly described by capacitors?

- A. Yes, of course!
- B. Impossible to correctly model the layering
- C. Possible but very difficult to correctly model the layering
- D. Possible but not very useful since that's just a theoretical model
- ☒ E. Not really

Capacitance vs Frequency

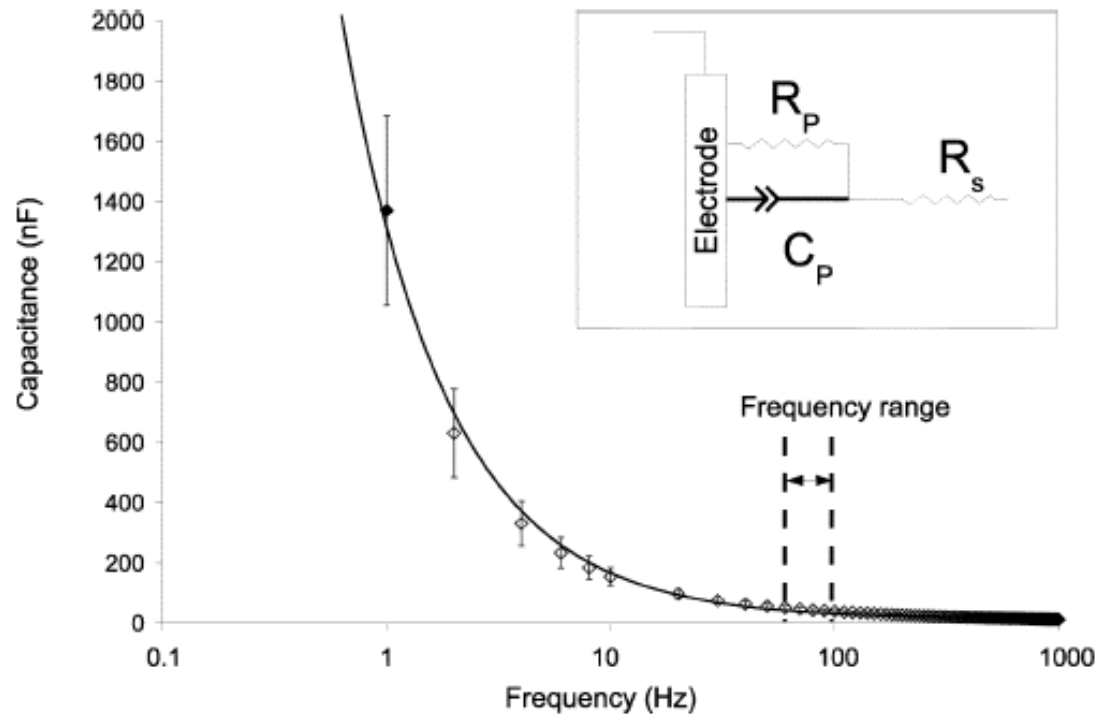
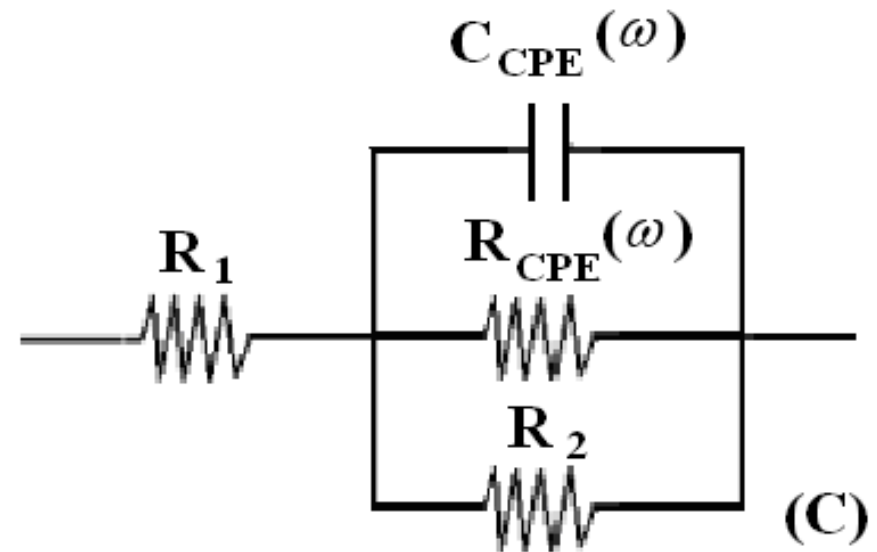
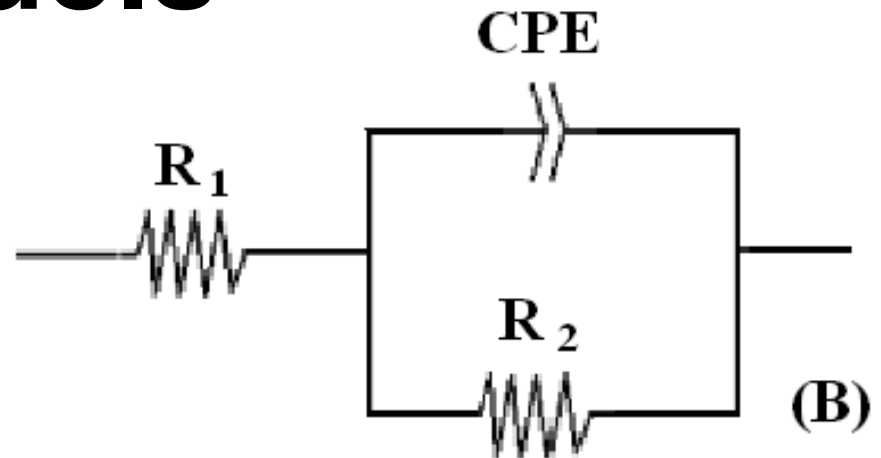
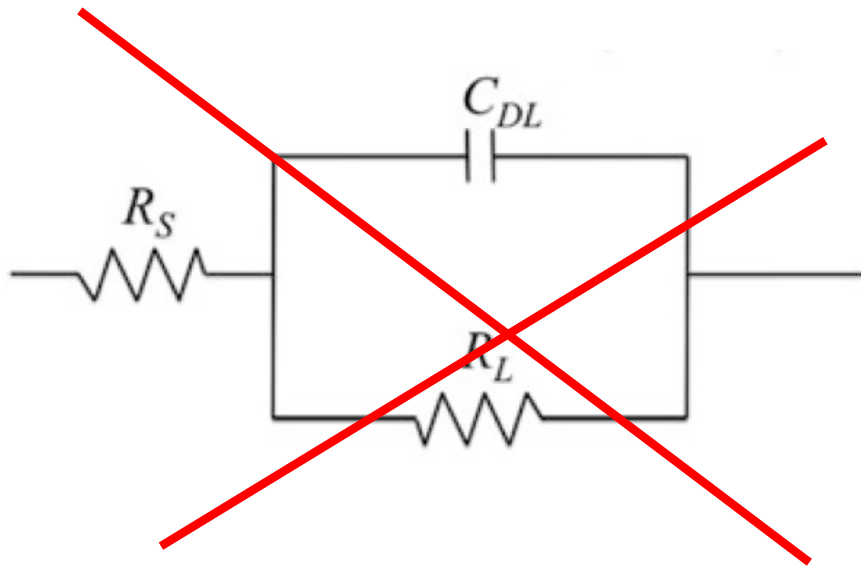


Fig. 9. Measured capacitance versus charge/discharge frequency on clean gold electrodes. The continuous line shows the fitting.

Some times, the Layering effect corresponds to non-ideal capacitances

Interface models



Equivalent circuits for non-ideal layering effects

CPE element

$$Z_{CPE} = \frac{1}{C_p(j\omega)^\alpha} = \frac{\cos\left(\frac{\pi}{2}\alpha\right)}{C_p\omega^\alpha} - j\frac{\sin\left(\frac{\pi}{2}\alpha\right)}{C_p\omega^\alpha}$$

$$Z_{CPE} \cong \frac{1}{\omega^\alpha C_p} \sqrt{1 - \alpha^2} + \frac{1}{j\omega^\alpha C_p} \alpha$$

The Constant Phase Element (CPE)
as Equivalent Component

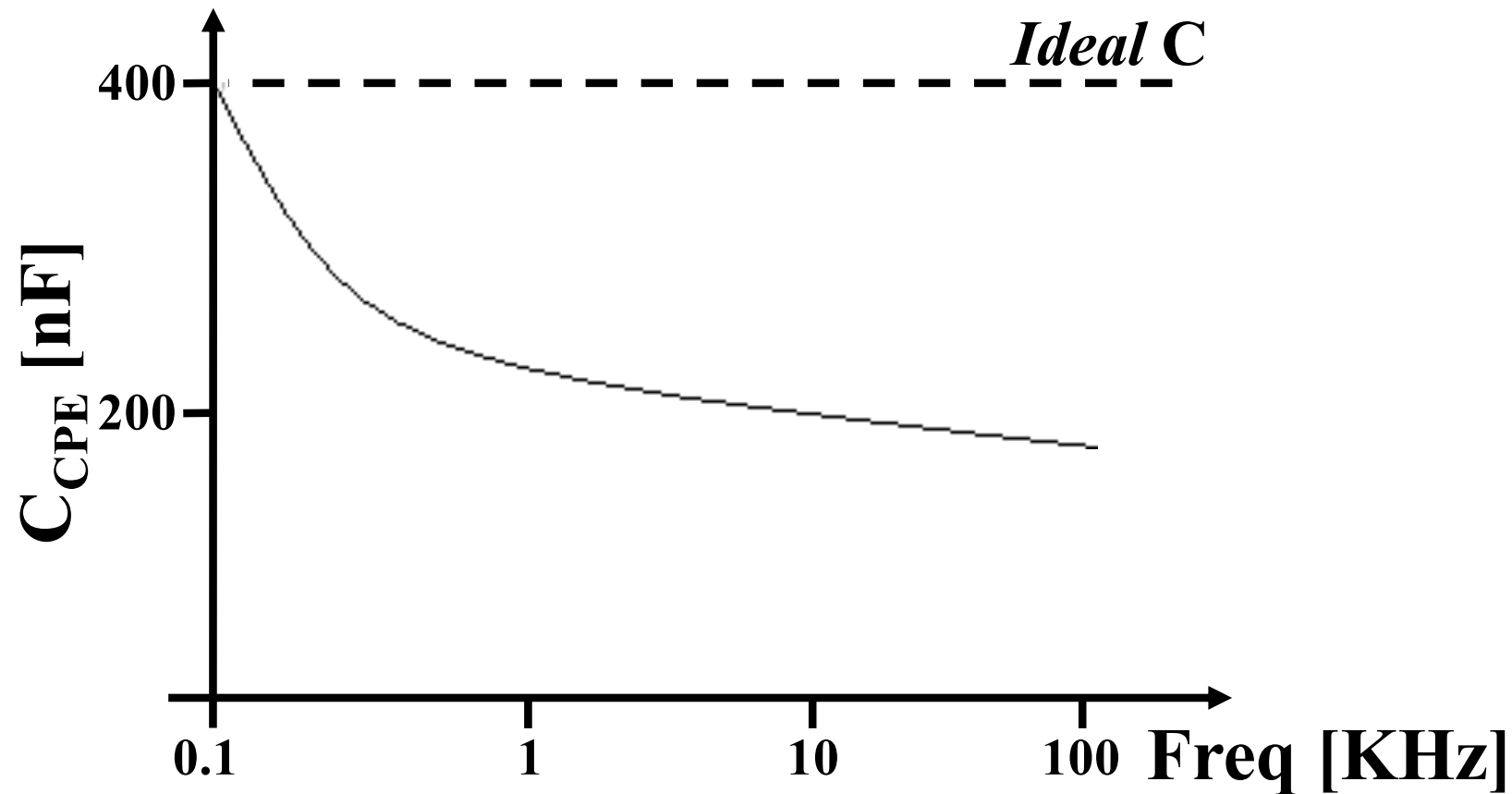
CPE element

$$Z_{CPE} \begin{cases} R_{CPE} \cong \frac{1}{\omega^\alpha C_p} \sqrt{1 - \alpha^2} \\ X_{CPE} \cong \frac{1}{\omega^\alpha C_p} \alpha \end{cases}$$

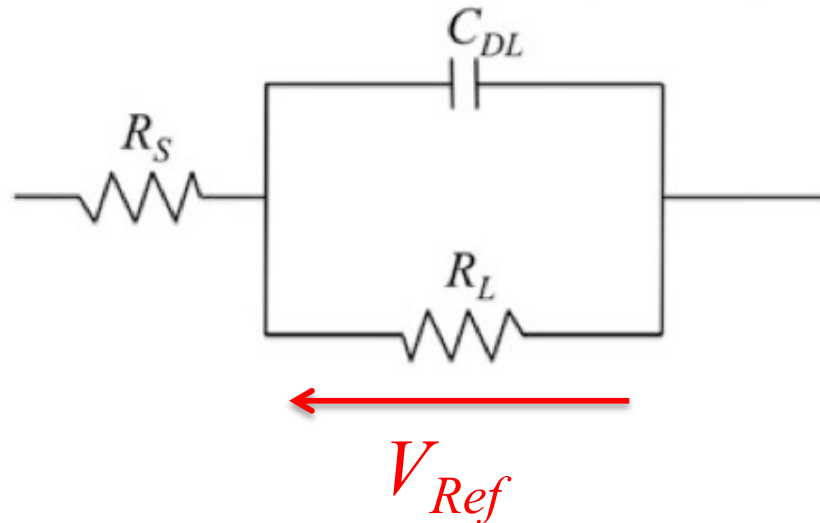
$$|X_{CPE}| \cong \frac{1}{\omega^\alpha C_p} \alpha = \frac{1}{\omega^{\alpha-1} \omega C_p} \alpha = \frac{1}{\omega \left(\frac{C_p}{\alpha \omega^{1-\alpha}} \right)}$$

$$C_{CPE} \cong \frac{C_p}{\alpha \omega^{1-\alpha}}$$

Equivalent Capacitance vs frequency



Non-Faradaic Current



$$I_{non-F} = \frac{V_{ref}}{Z} = \frac{1 + j\omega C_{DL}R_L}{R_L} V_{ref}$$

Non-Faradaic currents are also circulating in the cell

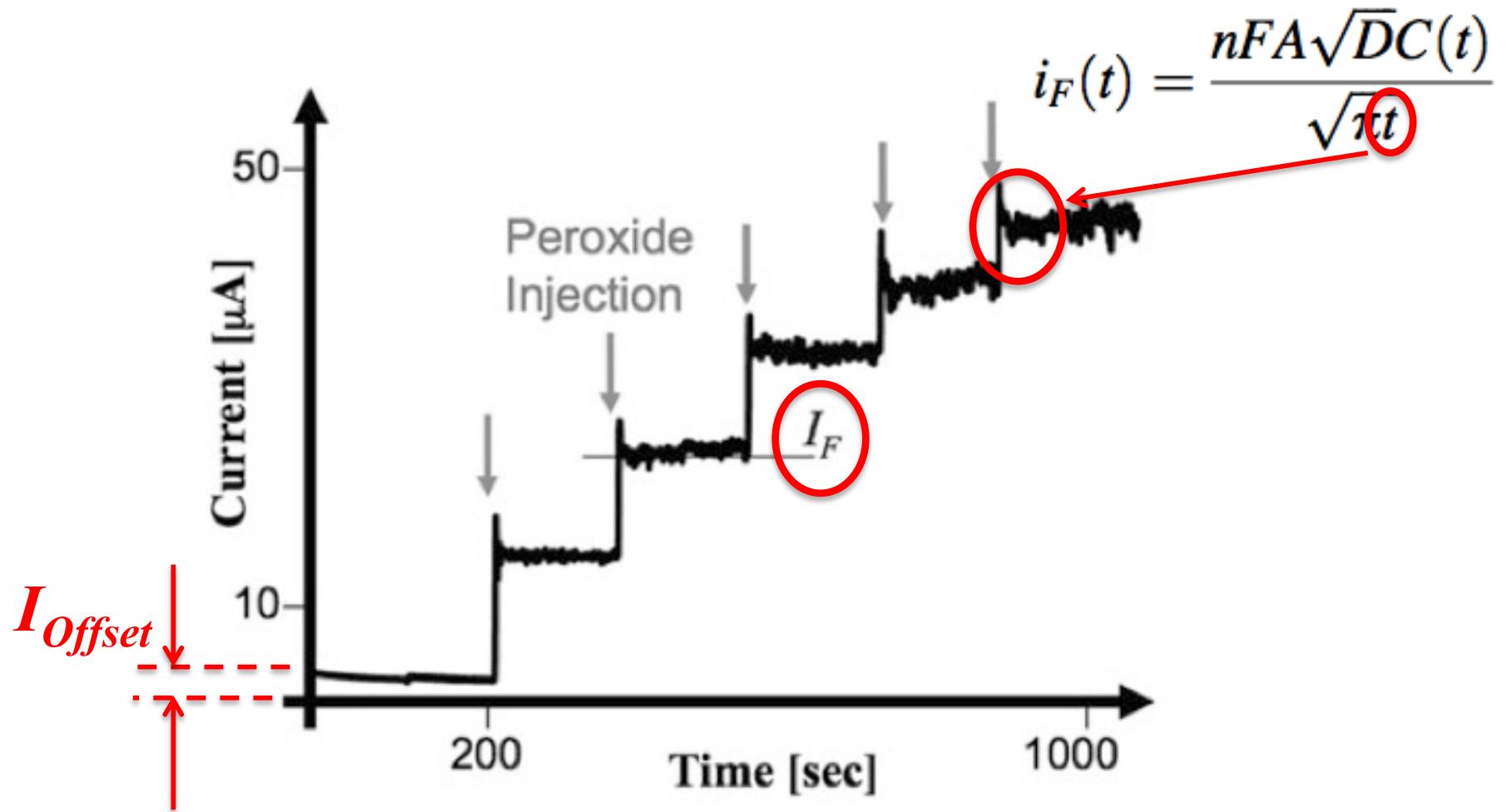


Q4

Why $C_{DL} // R_L$ do not correctly model Faradaic currents ?

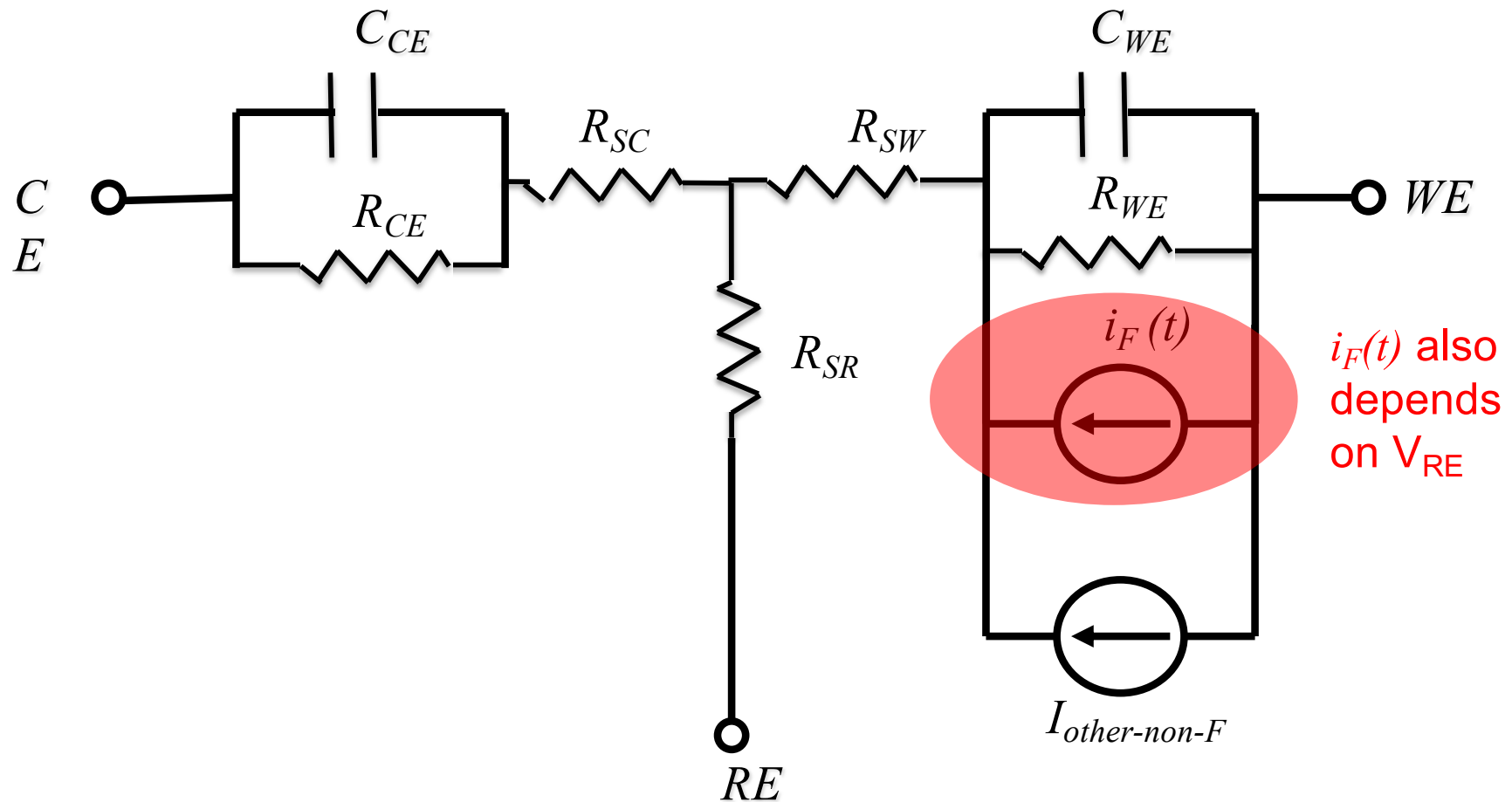
- A. Since Faradaic currents do not follow Ohm law
- B. Since Faradaic currents also depend on species' concentration
- C. Since it is not possible to correctly model the Faradaic currents
- D. Since it is very difficult to correctly model the Faradaic currents

Faradaic Current

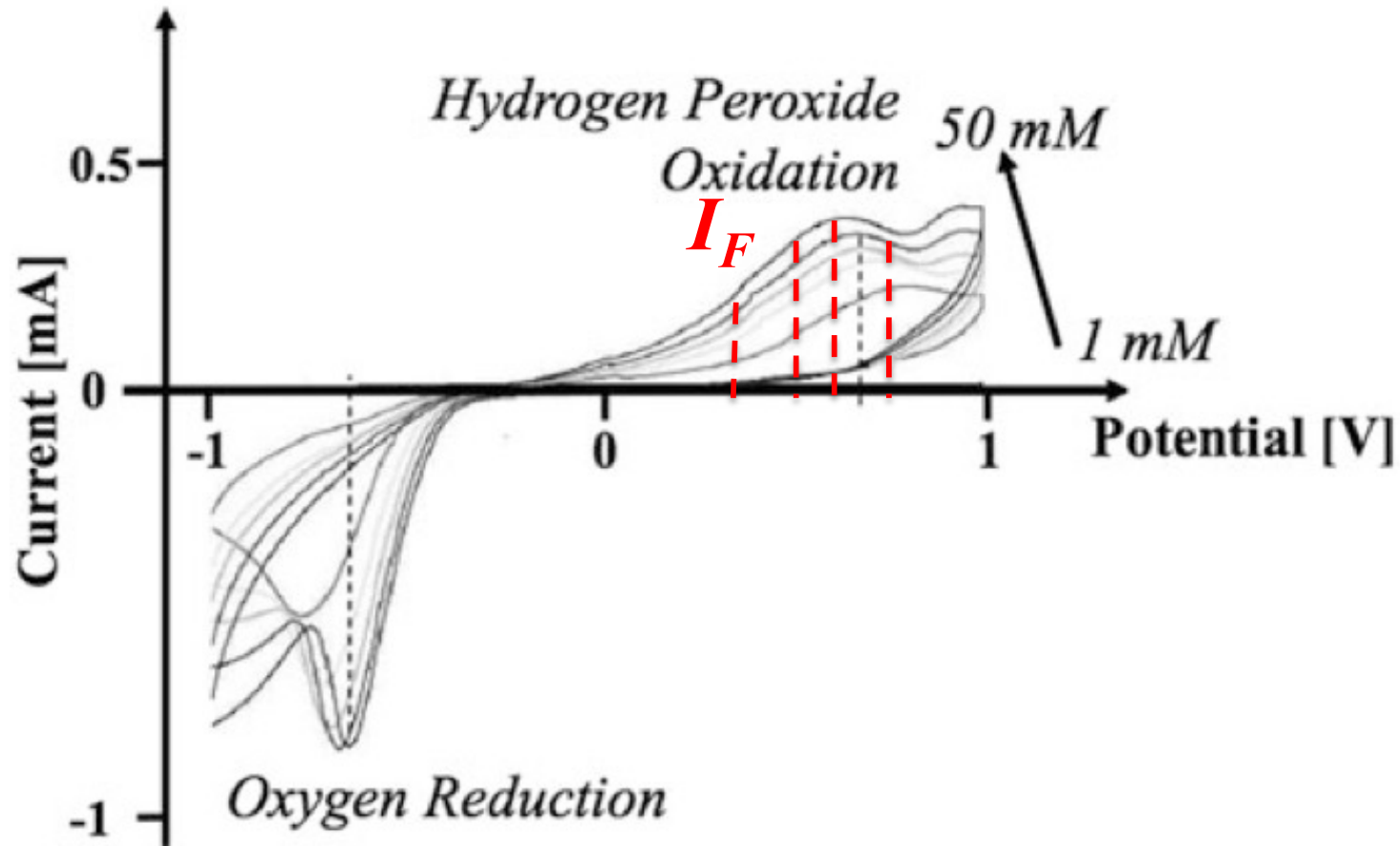


Typical curve in chronoamperometry

Equivalent circuit: active model

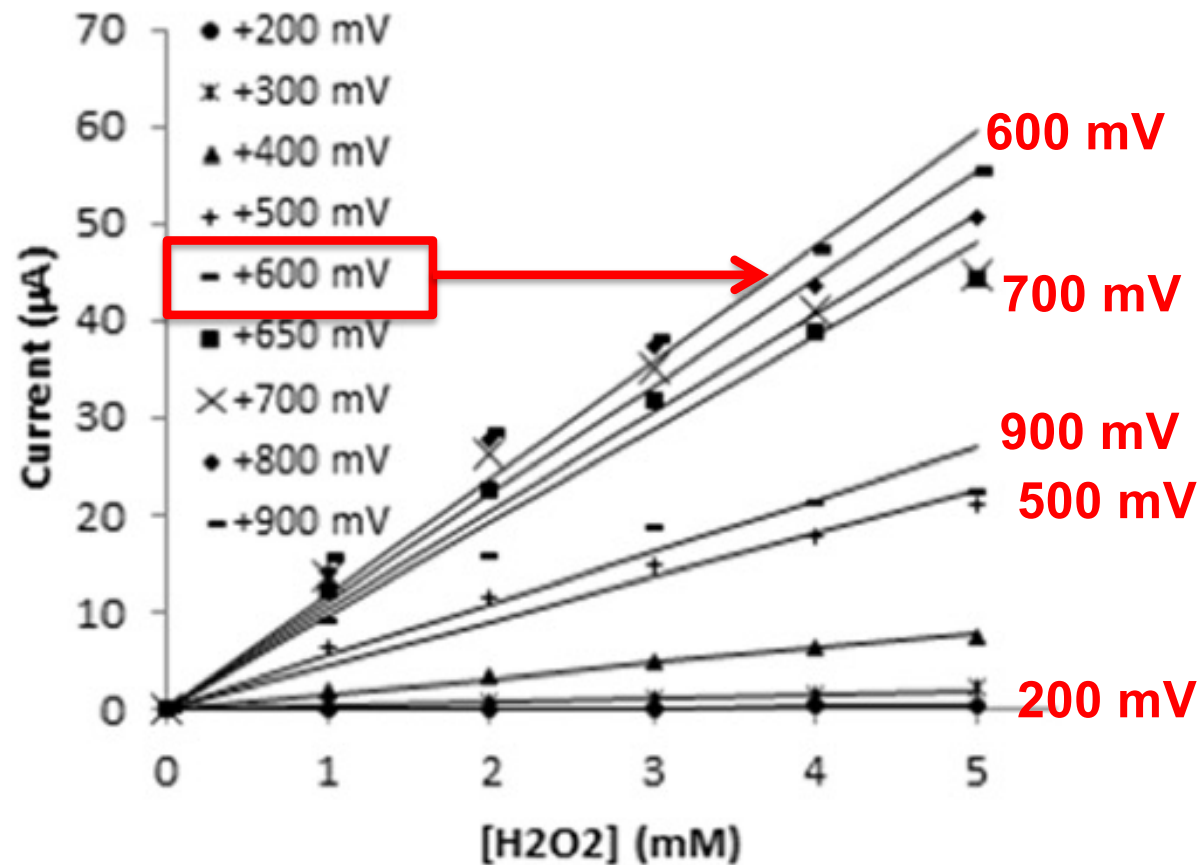


Redox with hydrogen peroxide



O_2 reduction and H_2O_2 oxidation observed by potential sweeping


Faradaic Current Generator



The sensitivity depends on the Reference Potential

Faradaic Current Generator

$$I = SC + I_{Offset}$$


$$I_{Offset} = 0$$

$$I = SC$$

$$I(t, V) = S(V)C(t) \qquad S(V) = S_0 e^{-\frac{(V-V_0)^2}{\sigma}}$$

The sensitivity depends on the Reference Potential



Q5

How to correctly apply the right Reference Potential (to RE)?

- A. In closed loop
- B. In open loop
- C. With a power supplier
- ☒ D. Without current supply
- E. Without changes in frequency

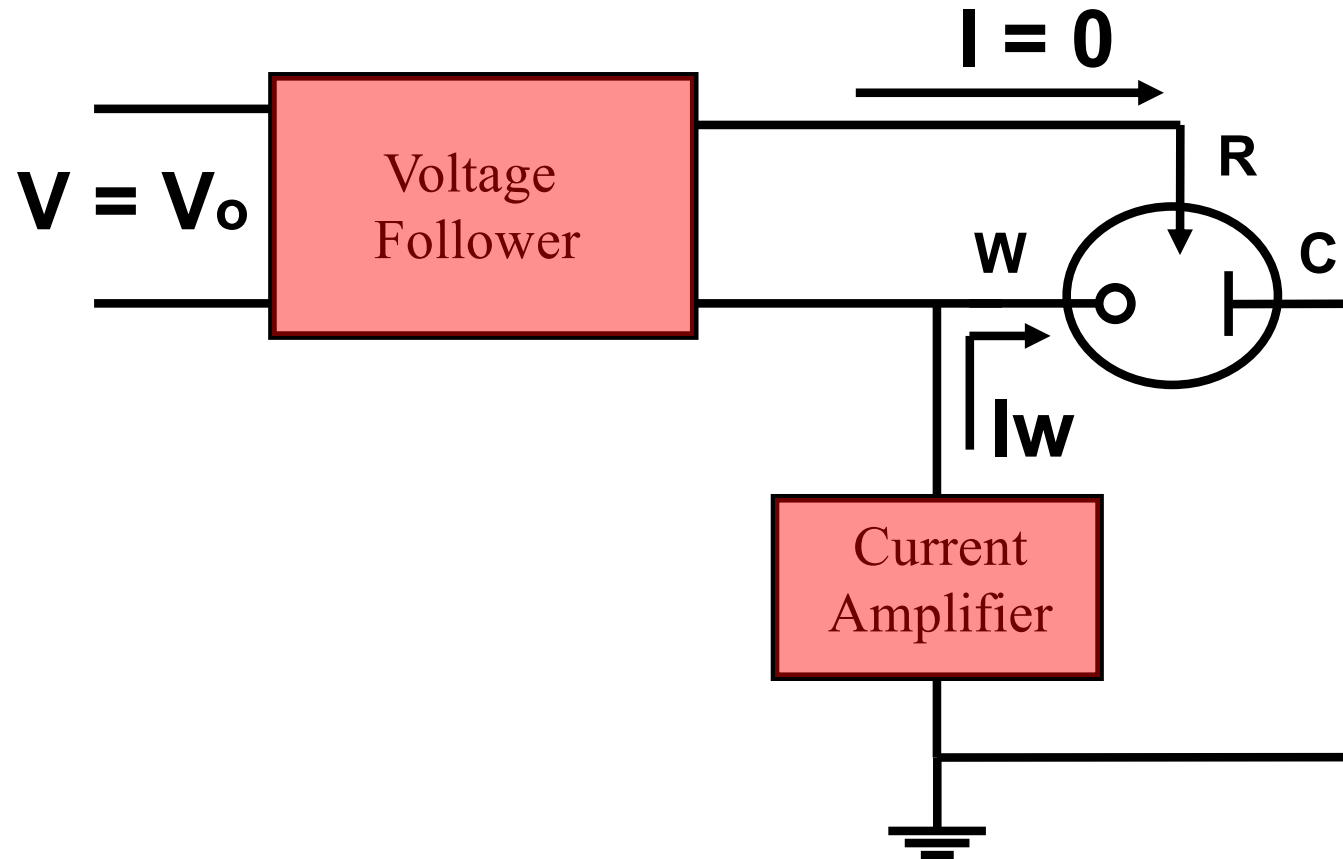


Q6

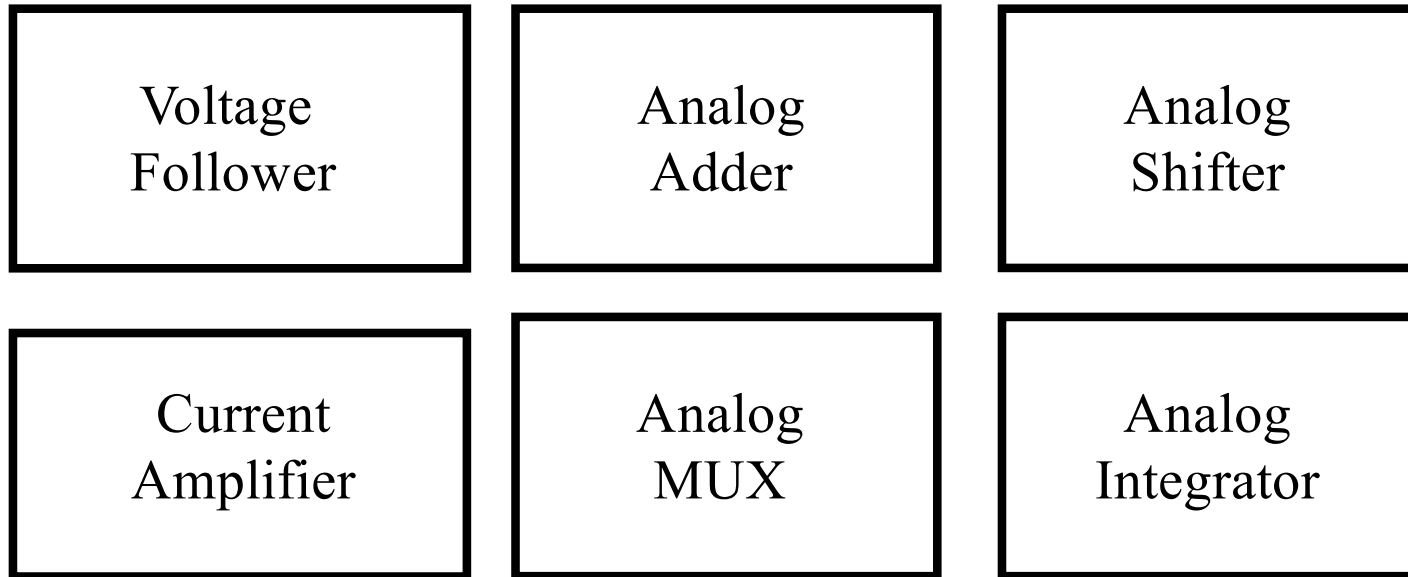
How to apply the Reference Potential without current supply?

- ☒ A. Designing a proper voltage supplier
- ☐ B. Designing a proper current supplier
- ☐ C. Designing a proper frequency supplier
- ☐ D. Designing a proper electrochemical cell

Required Blocks



Required Building Blocks



Basic Configurations of Operational Amplifiers

(Book Bio/CMOS: Appendix B)



Q7

What is an Operational Amplifier?

- A. A normal Differential Amplifier
- ☒ B. A special Differential Amplifier
- C. A differential Amplifier Operating at special frequency
- D. An Amplifier Operating differently



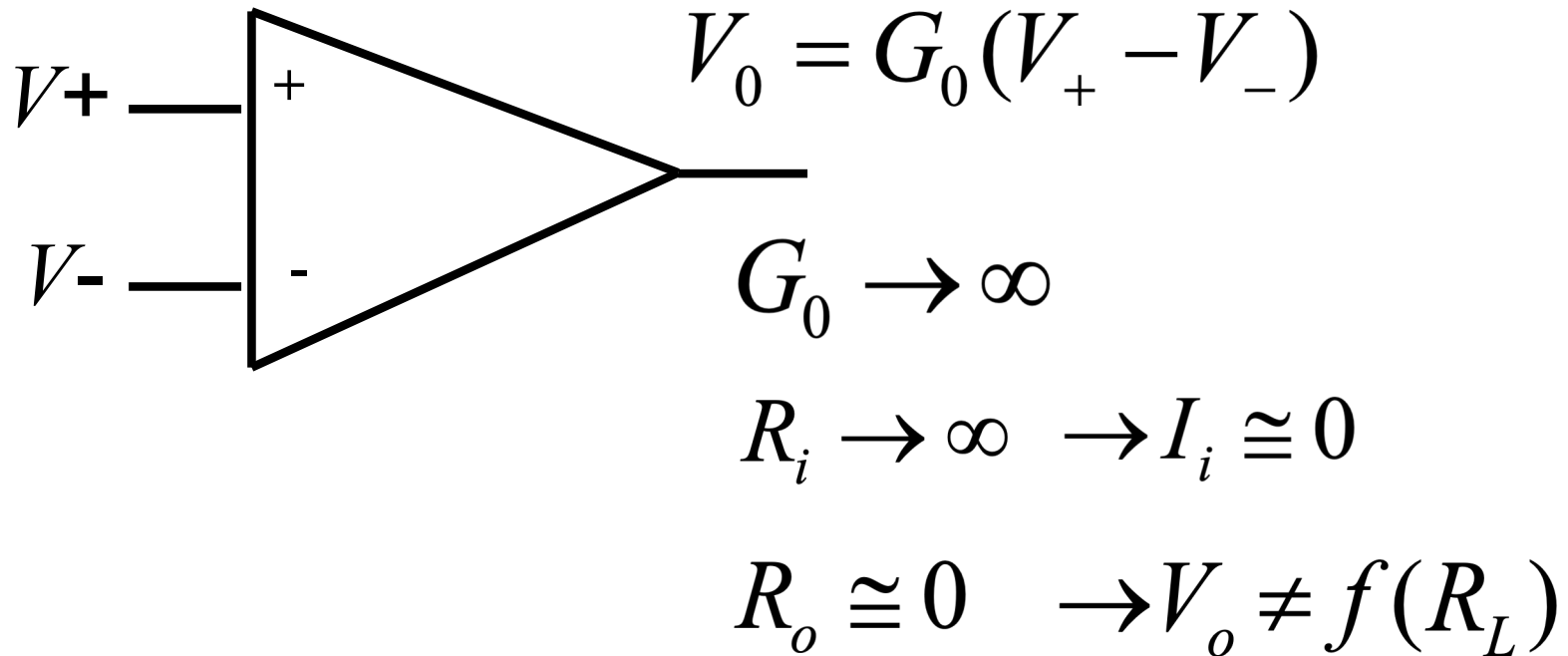
Q8

Why an Operational Amplifier is a Special Differential Amplifier?

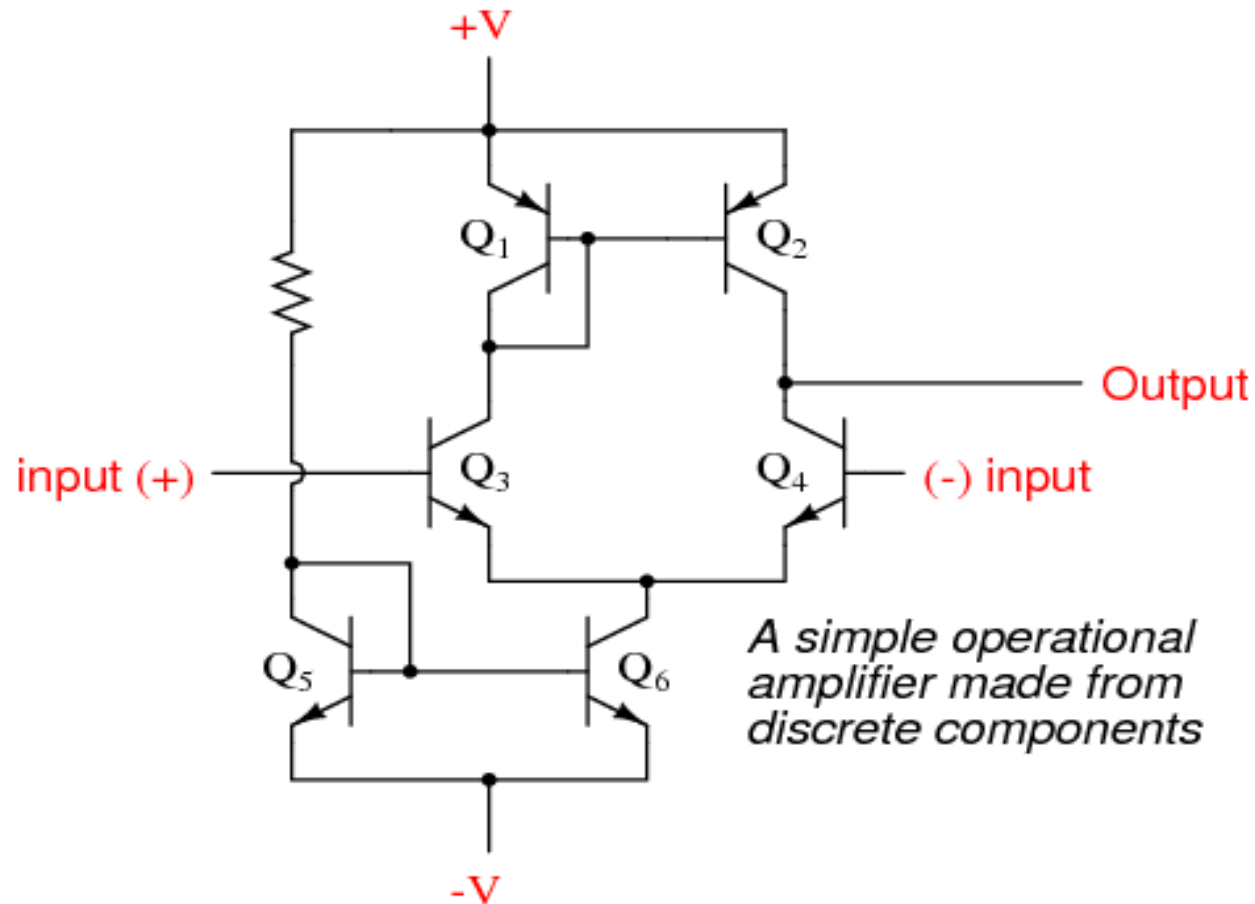
- ☒ A. Since it has an enormous gain
- ☒ B. Since it has enormous input impedance
- ☒ C. Since it has negligible output impedance
- ☒ D. Since it has several special features

What's an Op. Amp.?

DIFFERENTIAL AMPLIFIER

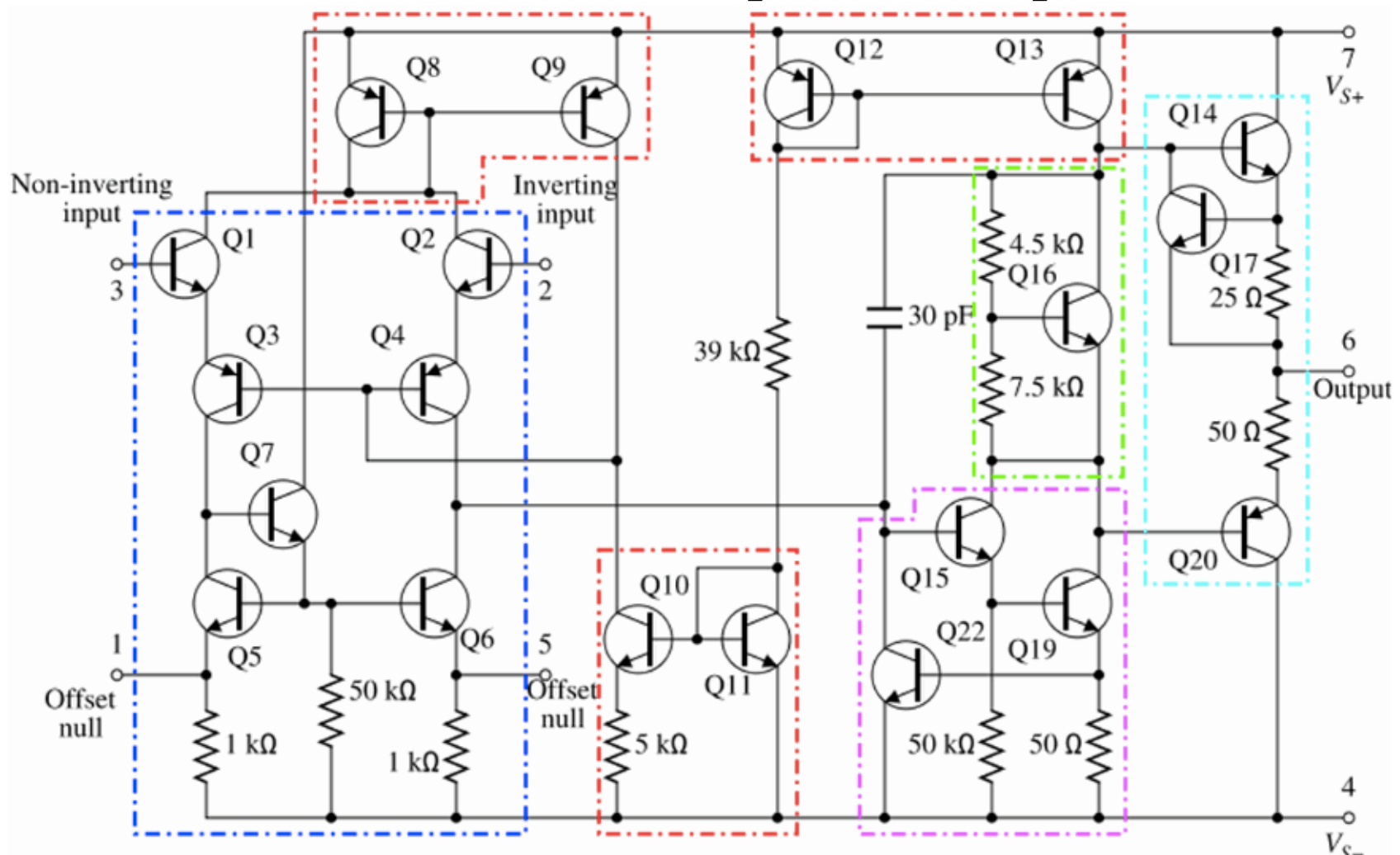


What's an Op. Amp.?



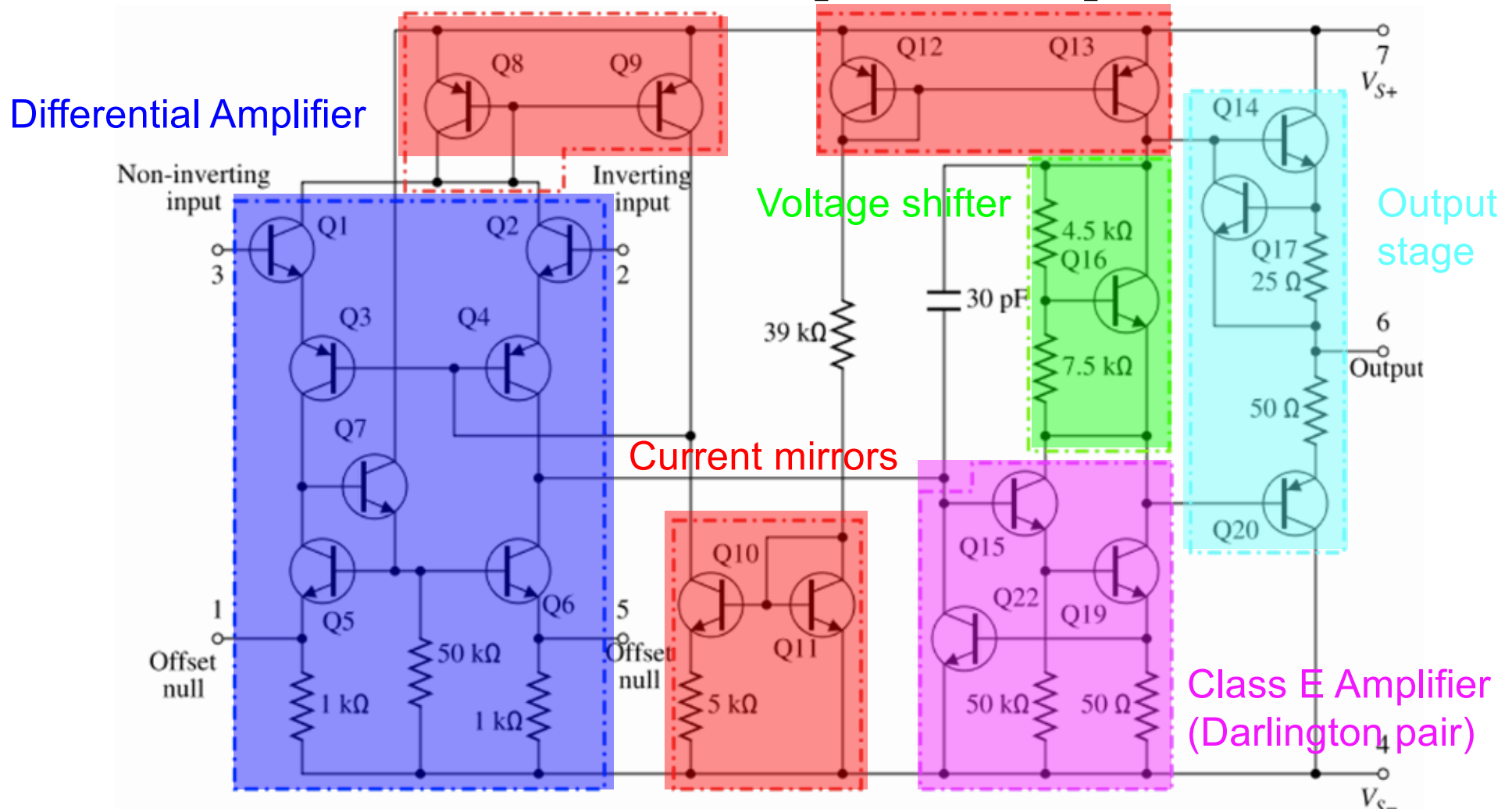
A simple scheme of a differential amplifier at transistor level

What's an Op. Amp.?



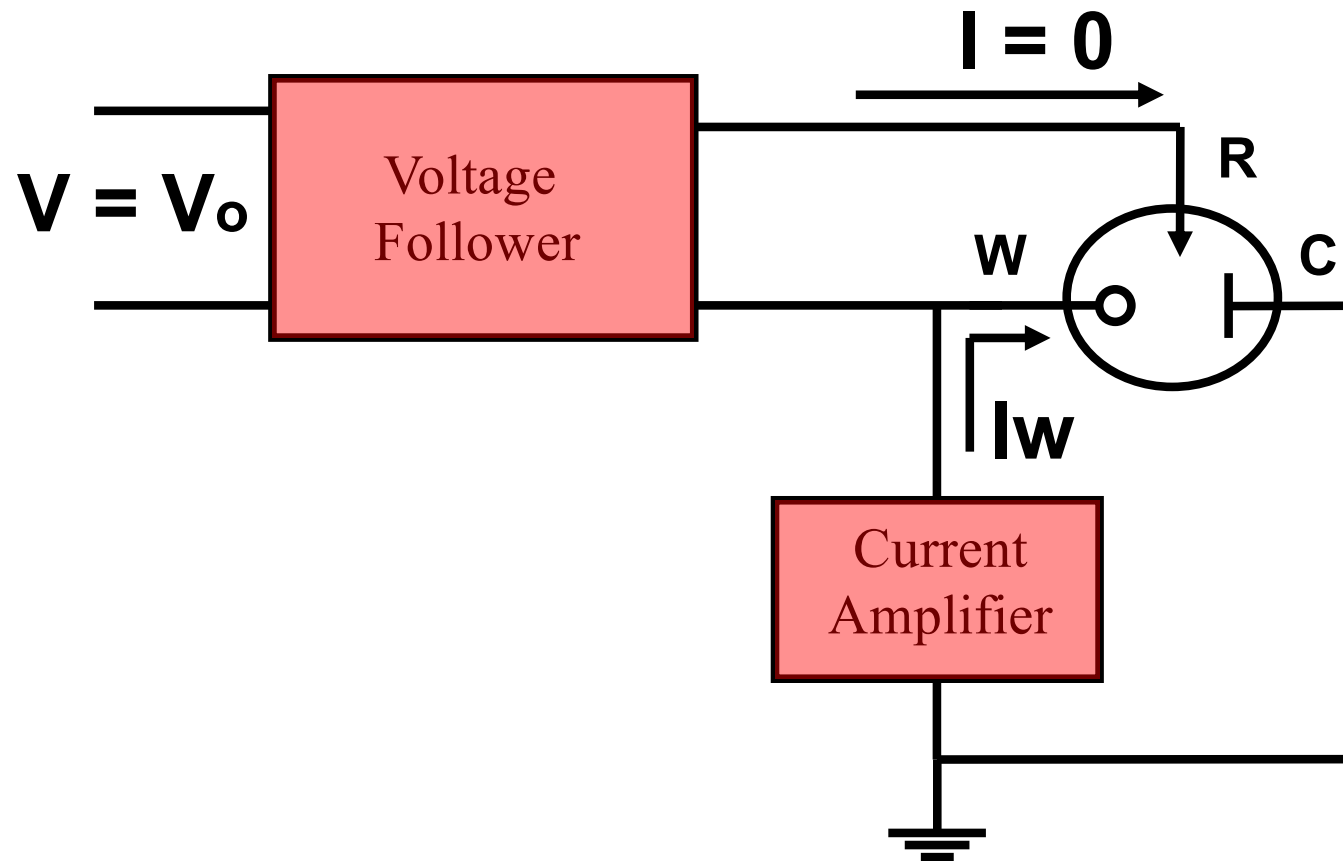
A more complex architecture of an Operational Amplifier (the common 741)

What's an Op. Amp.?

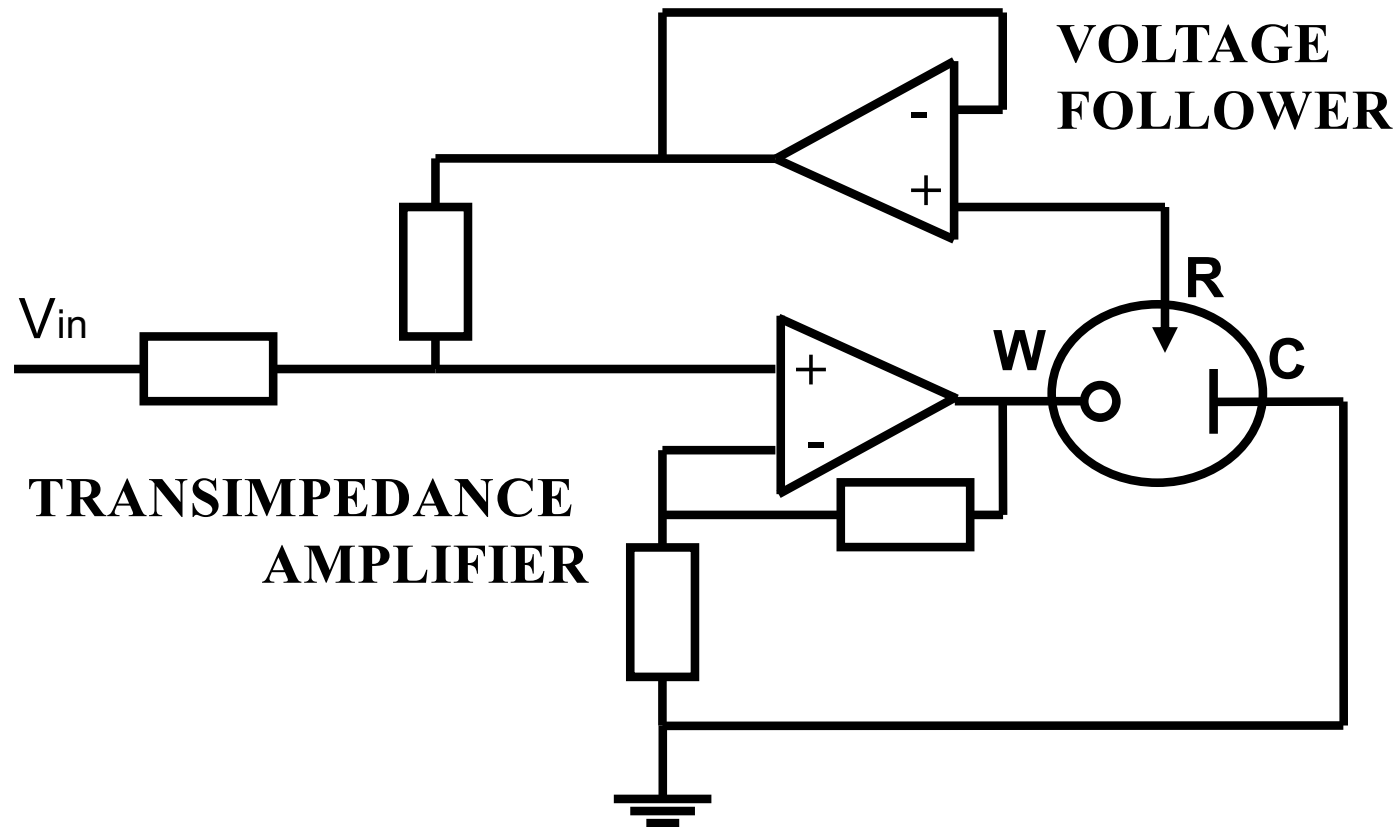


A more complex architecture of an Operational Amplifier (the common 741)

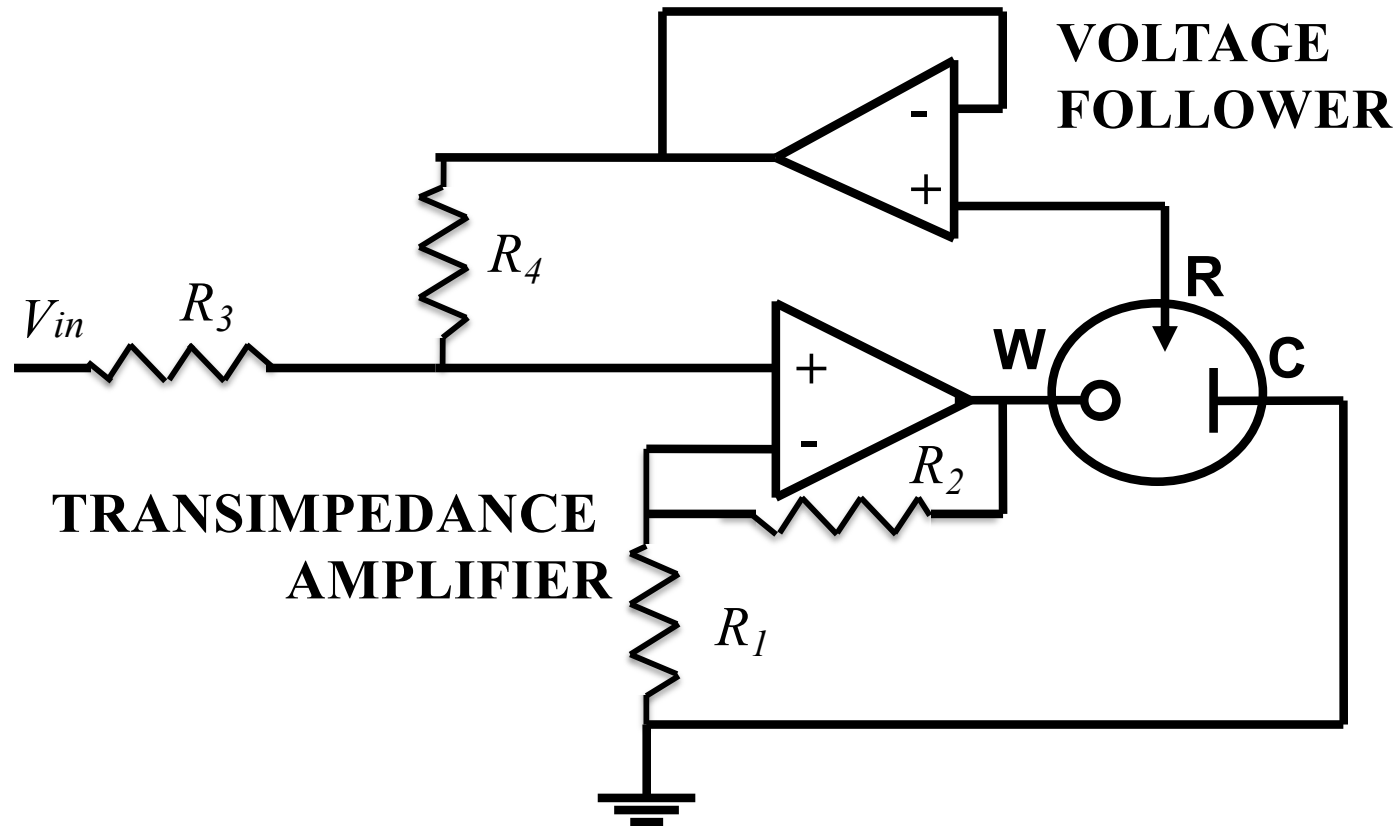
CMOS for Redox



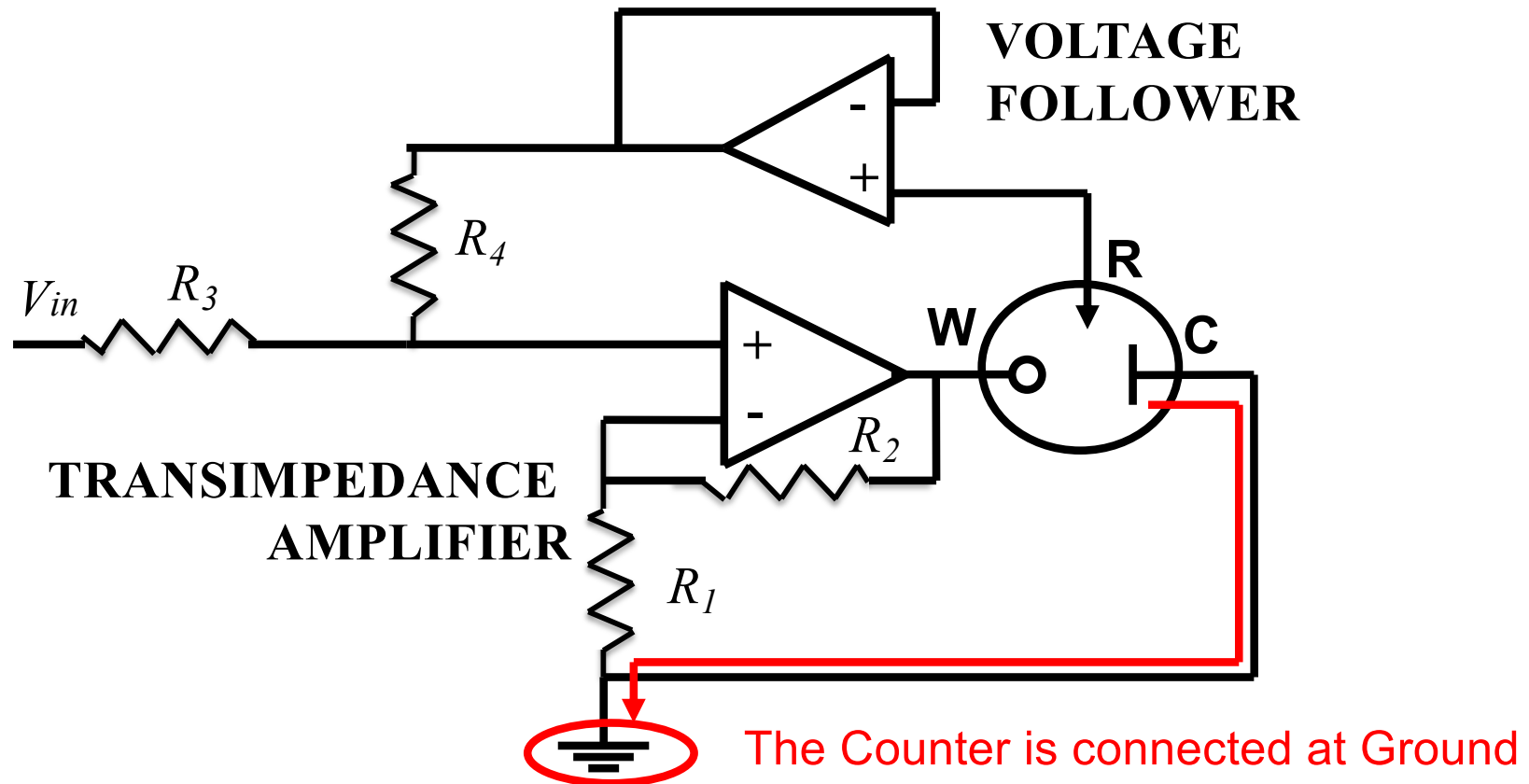
The basic CMOS for Redox



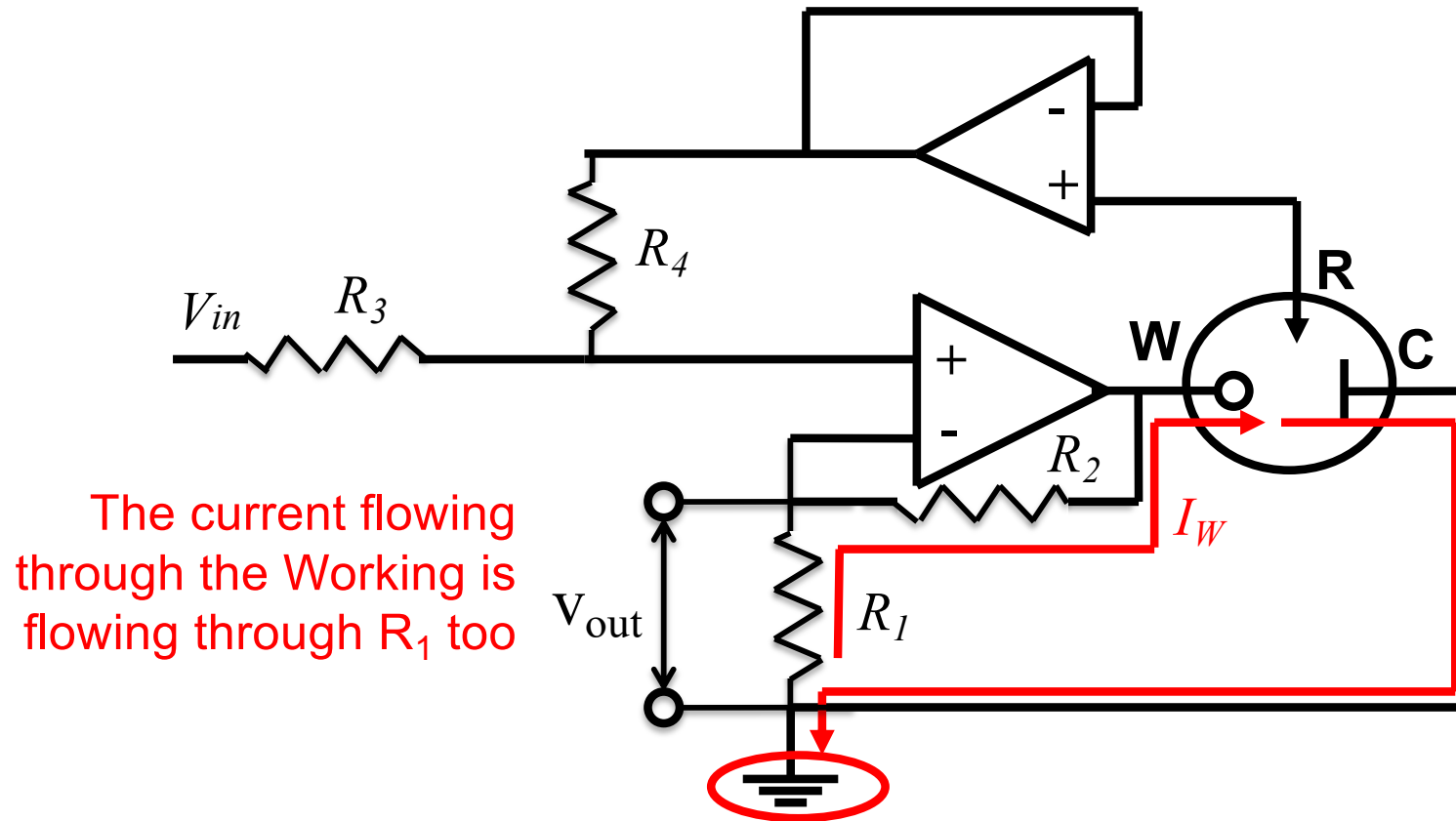
The basic CMOS for Redox



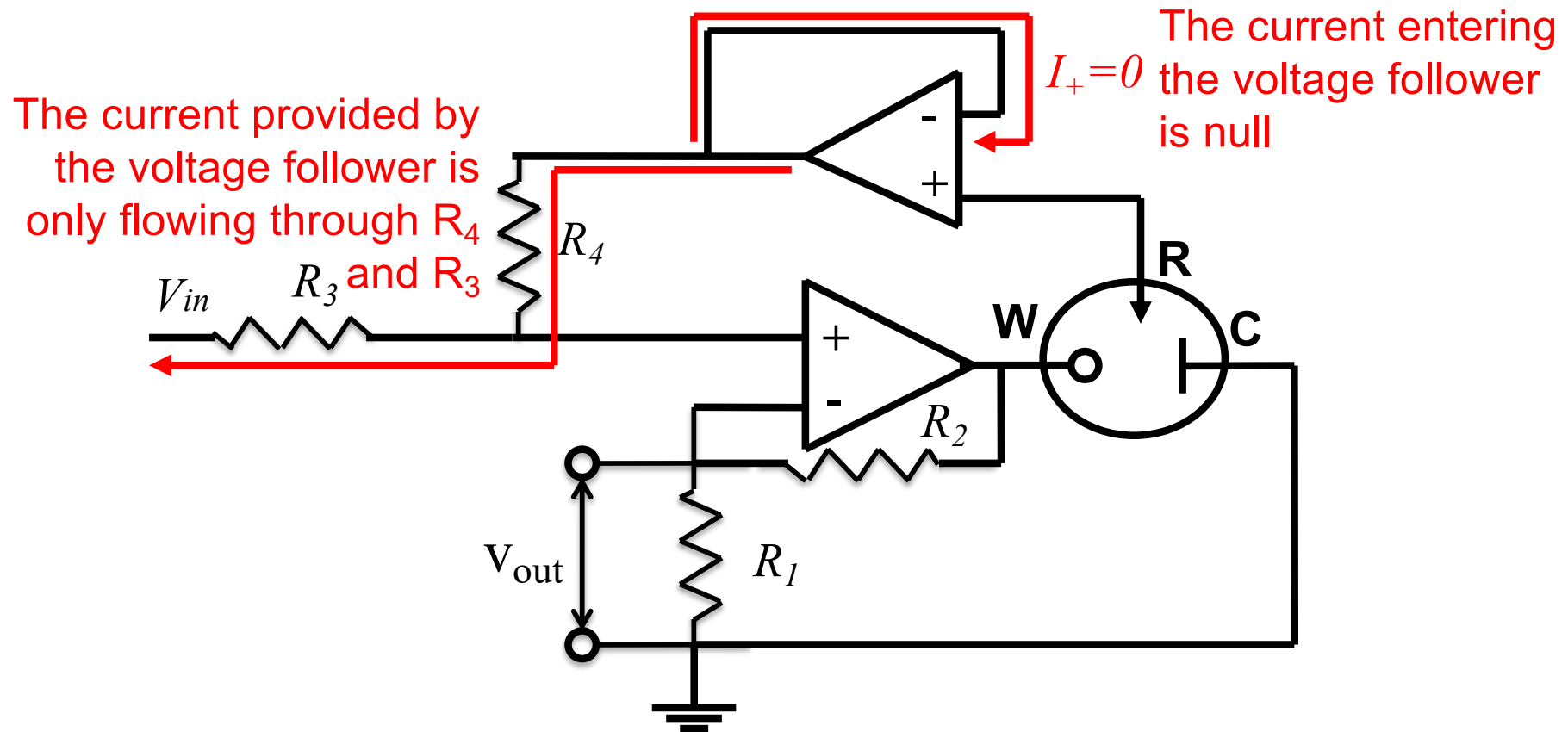
Grounded Counter



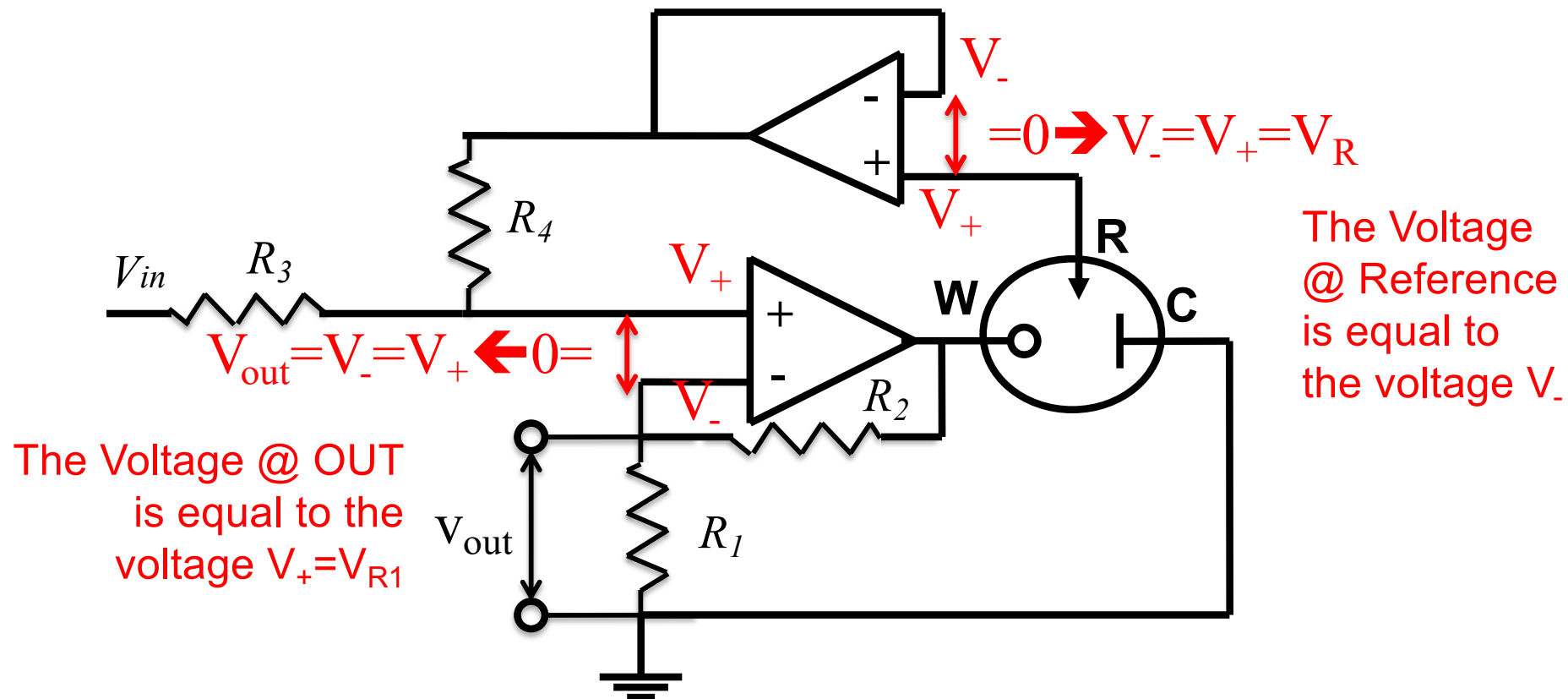
Grounded Counter



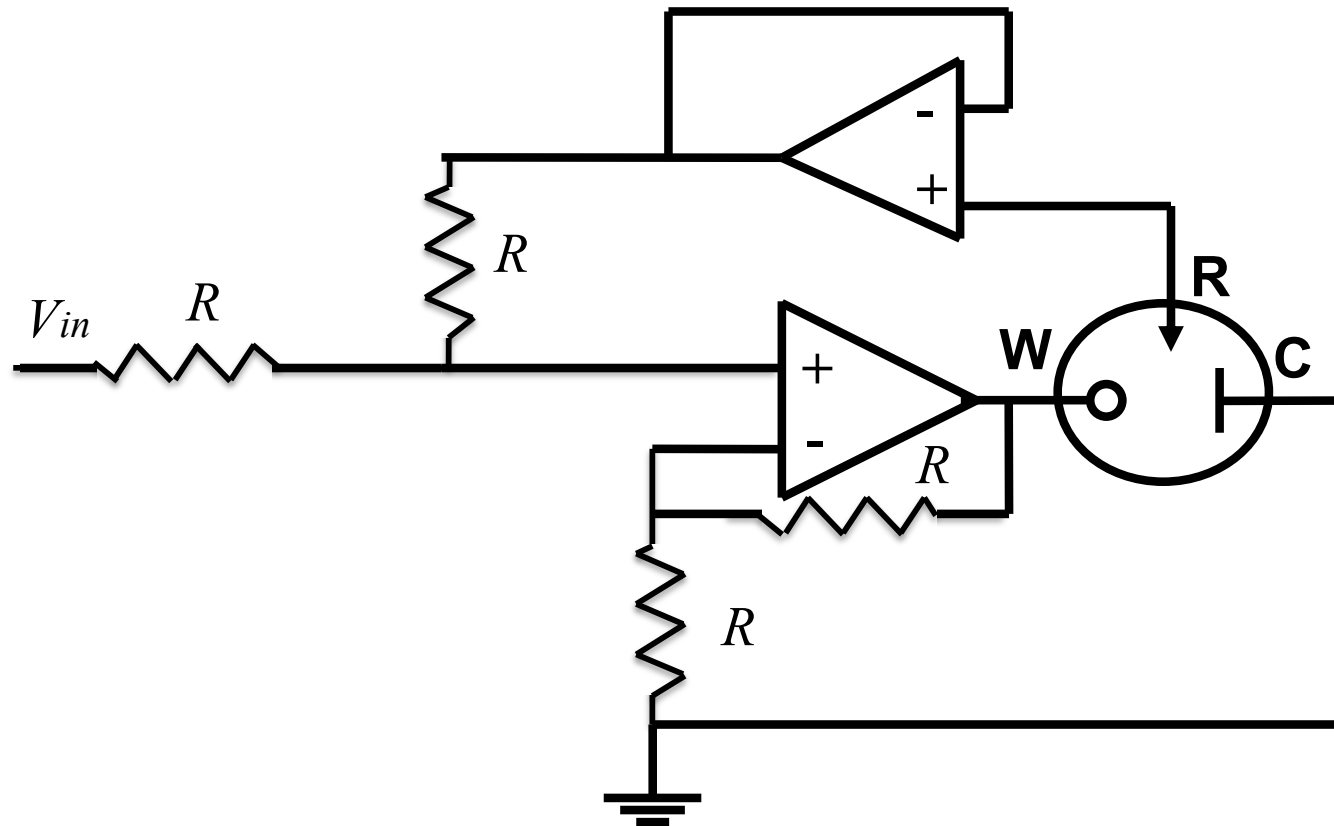
Grounded Counter



Grounded Counter

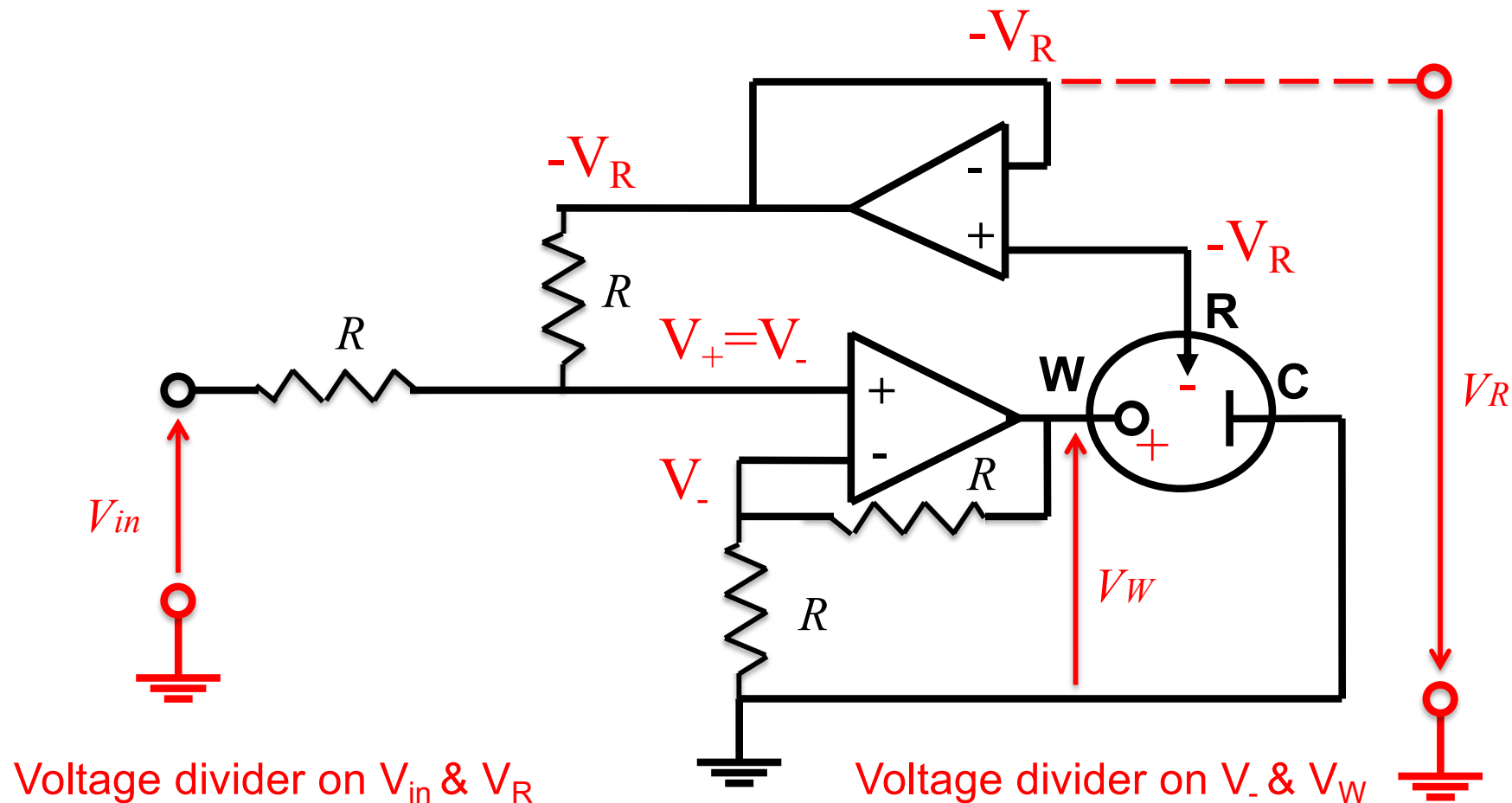


Grounded Counter



$$R_1 = R_2 = R_3 = R_4 = R$$

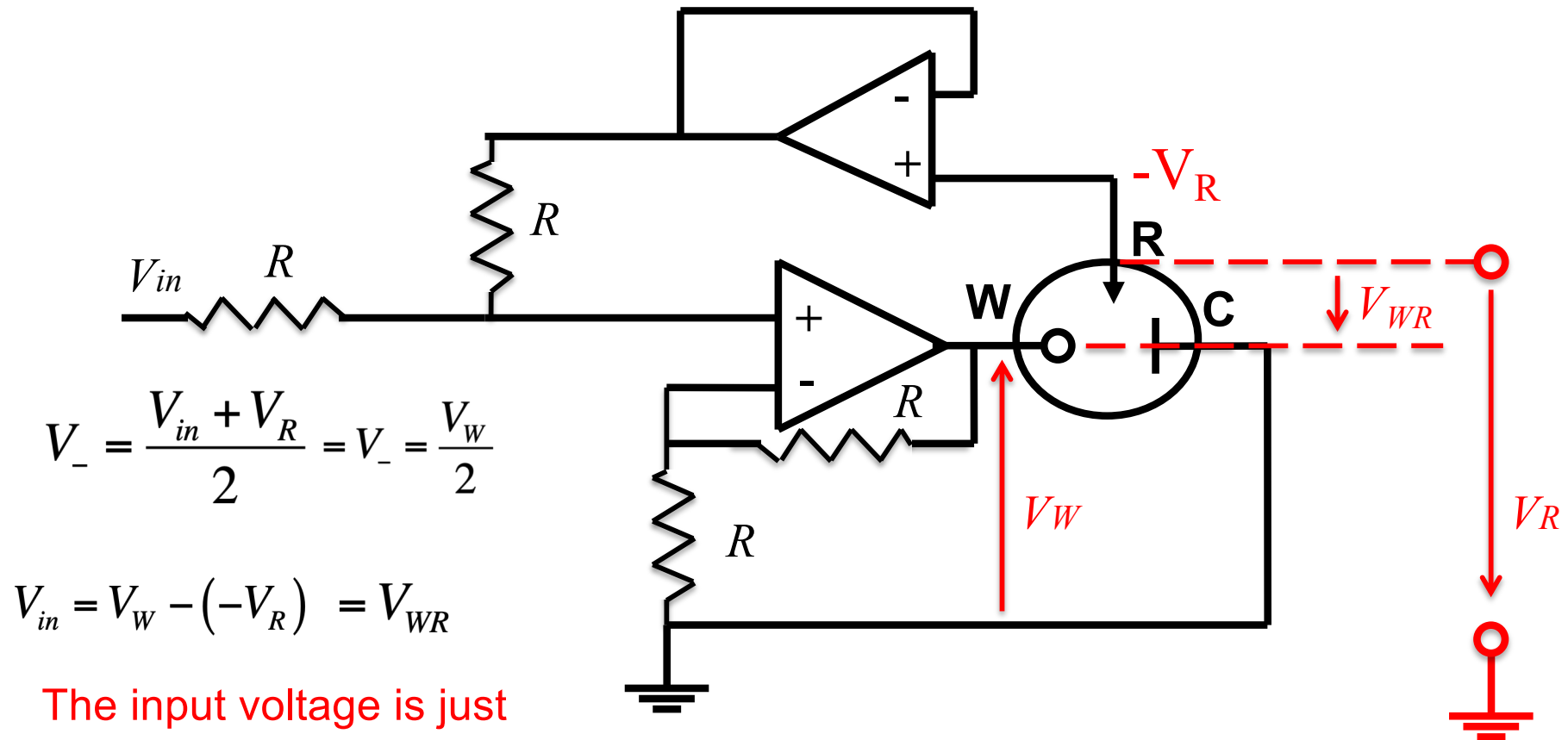
Grounded Counter



$$V_- = (V_{in} + V_R) \frac{R}{R + R} = \frac{V_{in} + V_R}{2}$$

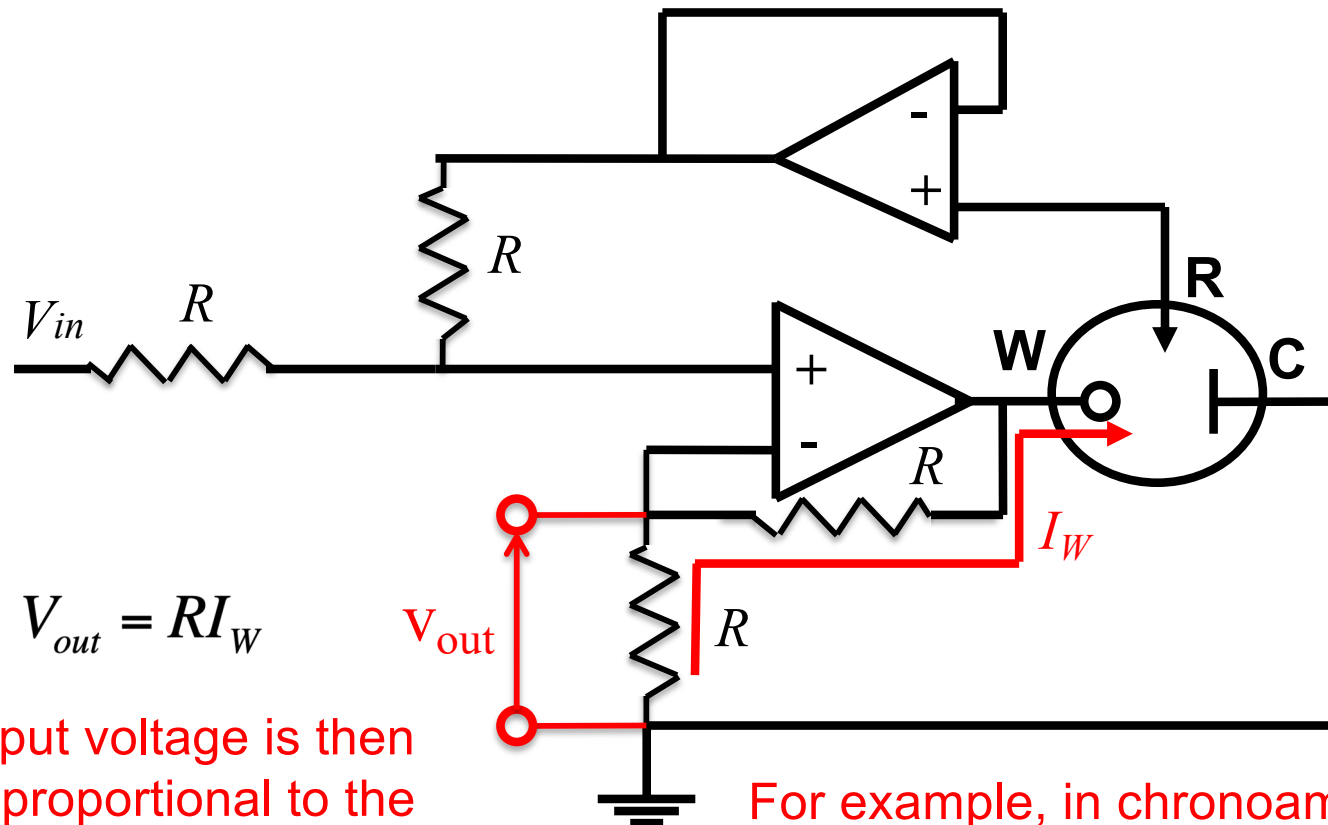
$$V_- = V_W \frac{R}{R + R} = \frac{V_W}{2}$$

Grounded Counter



The input voltage is just applied between the Reference and the Working

Grounded Counter



The output voltage is then directly proportional to the Faradaic current generated by the redox occurring at the working electrode

For example, in chronoamperometry

$$V_{out} = R \frac{nFA\sqrt{D}}{\sqrt{\pi t}} C_R$$

Concentration
of Redox specie

Noise issues!

$$V_{out} = RI_F = R \frac{nFA\sqrt{D}}{\sqrt{\pi t}} C_R$$

This is only the Faradaic contribution

↓

$$V_{out} = RI_W = I_F + I_C + I_n$$

Total noise in the output signal

$$I_n = I_{thermal} + I_{shot} + I_{flicker}$$

Usual sources of noise in electronics

White noise

$$I_{thermal} \rightarrow PSD = \frac{4kT}{R}$$

Johnson-Nyquist thermal noise current

$$I_{shot} \neq \Phi(T, f)$$

Originates from the discrete nature of electric charge. Shot noise is temperature and frequency independent

$$I_{flicker} = \frac{A}{f}$$

Flicker noise, which has a spectral density that decreases with the frequency. It is the dominant noise source at low frequencies

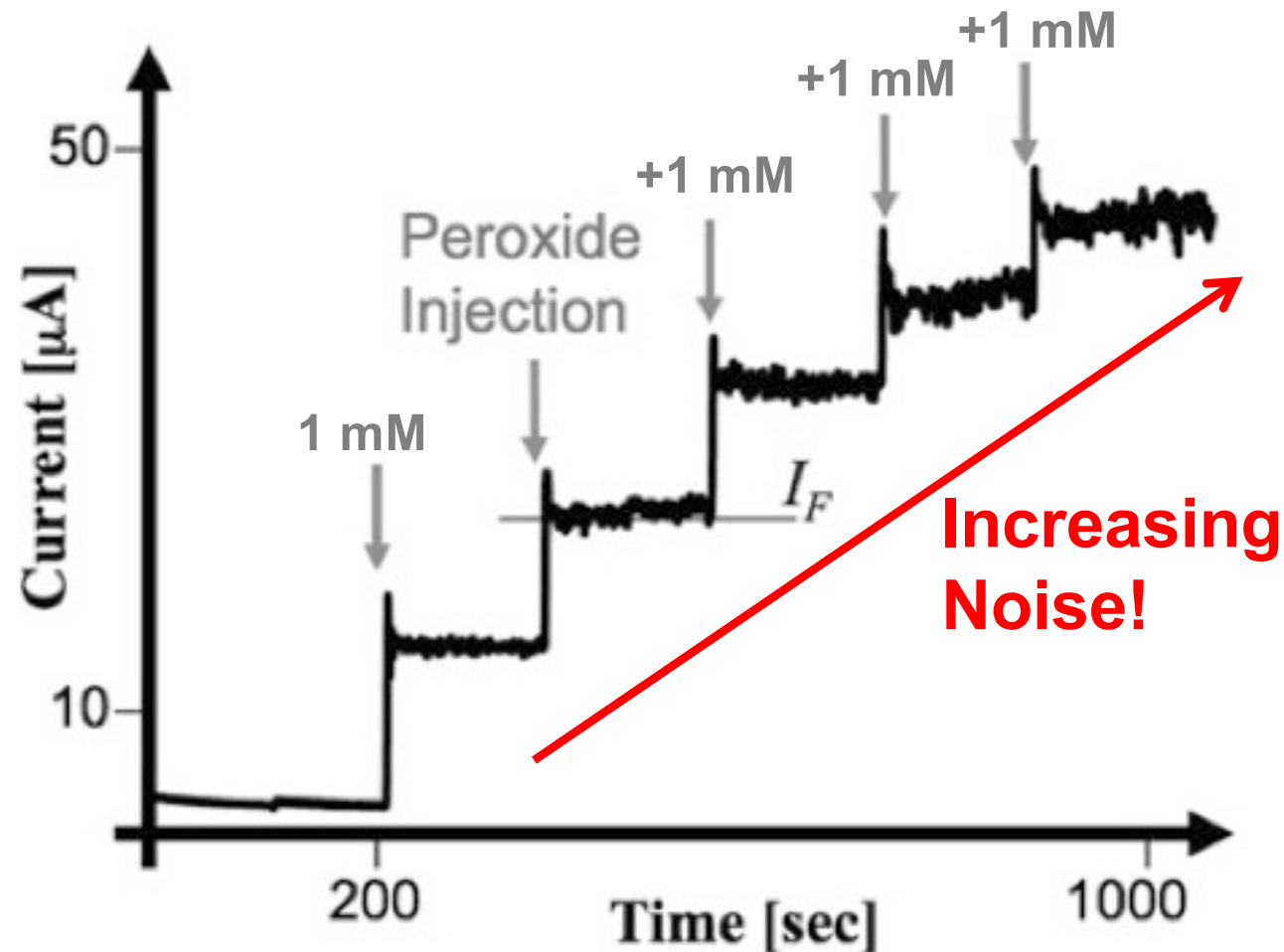


Q9

**Does the electronic noise
is the only one in the system?**

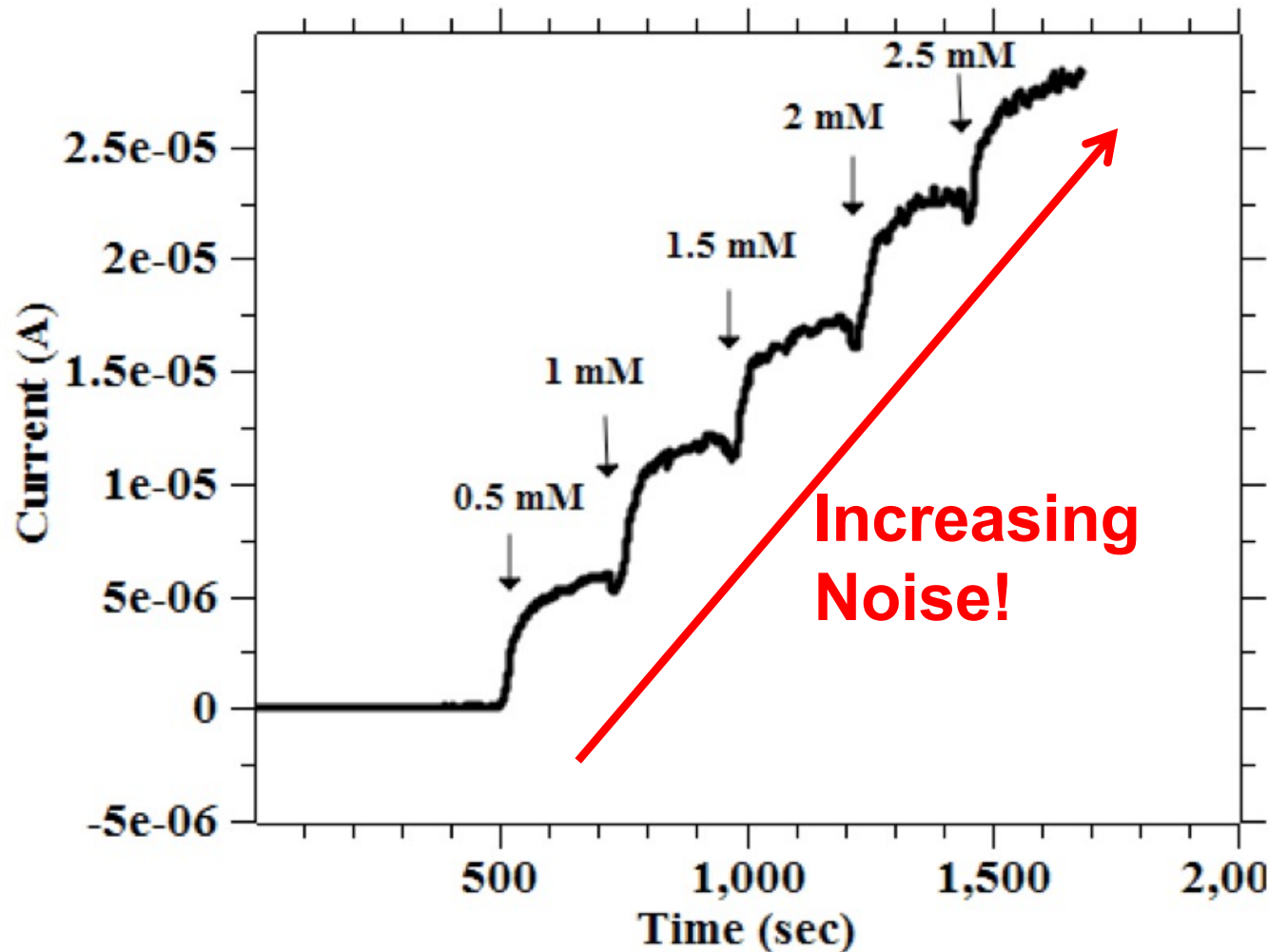
- A. Yes, of course!
- B. Almost, since it is the dominant one
- ☒ C. No, since it is not the dominant one
- D. Not Really

Noise @ the Bio-interface



Typical chronoamperometry (650 mV) on hydrogen peroxide

Noise @ the Bio-interface



Typical chronoamperometry (300 mV) on Ferrocyanide

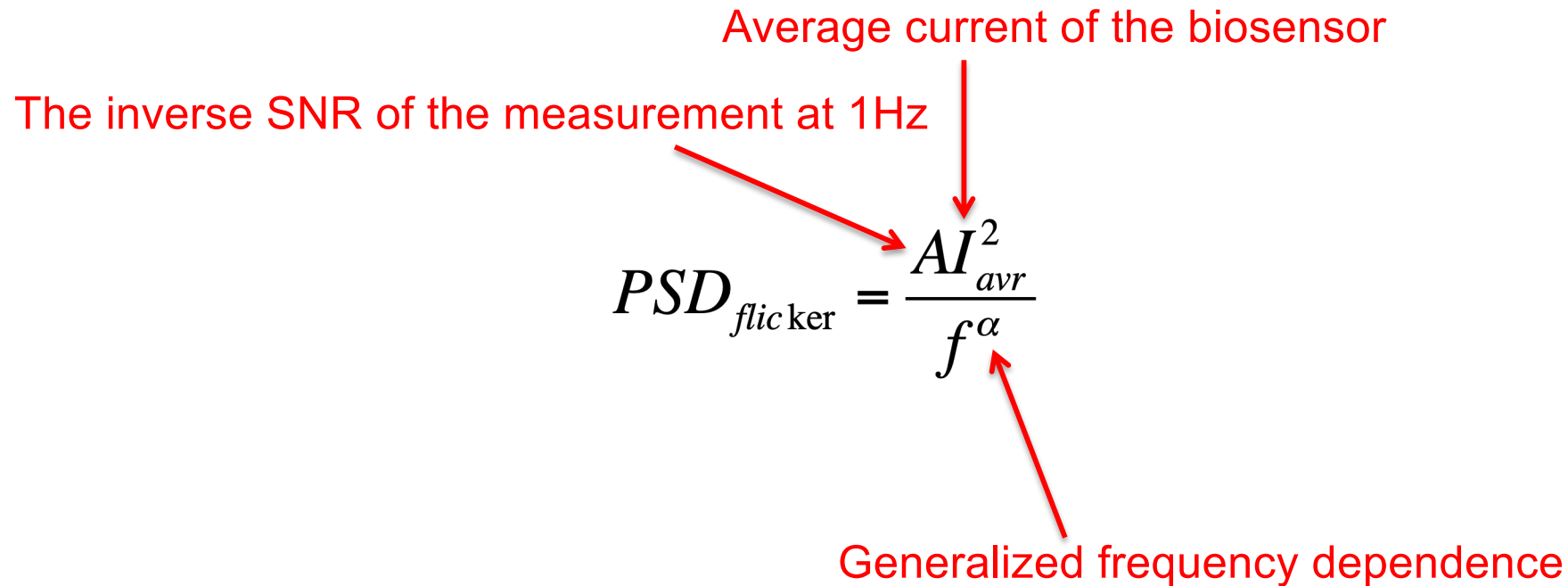
Noise Power Spectra Density

Average current of the biosensor

The inverse SNR of the measurement at 1Hz

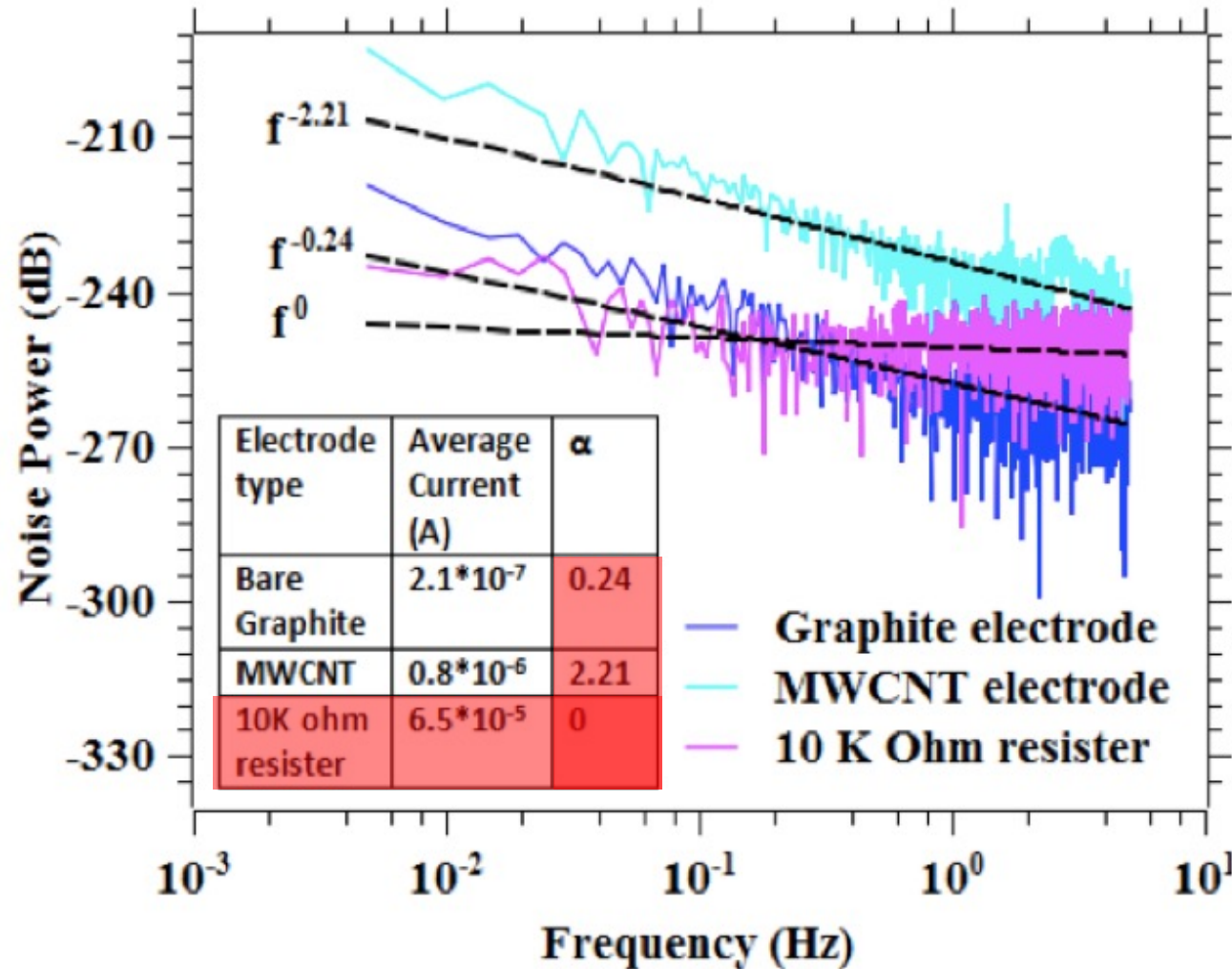
$$PSD_{flicker} = \frac{AI_{avr}^2}{f^\alpha}$$

Generalized frequency dependence

The diagram illustrates the components of the flicker noise formula. A red arrow points from the text 'Average current of the biosensor' to the term I_{avr}^2 in the numerator. Another red arrow points from 'The inverse SNR of the measurement at 1Hz' to the entire fraction $\frac{AI_{avr}^2}{f^\alpha}$. A third red arrow points from 'Generalized frequency dependence' to the term f^α in the denominator.

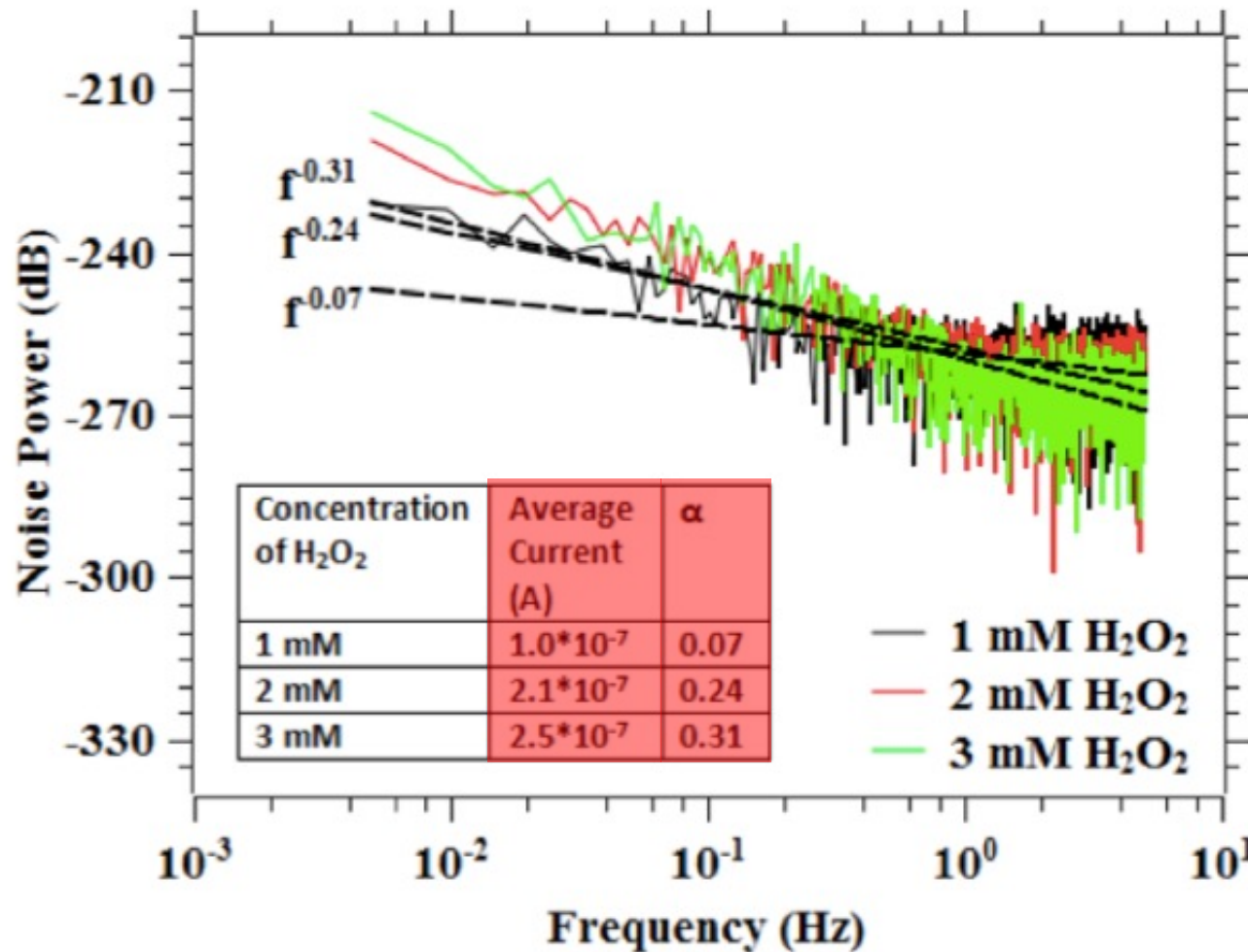
Generalized flicker formula to extract the values of noise coefficients by fittings on the electrochemical interface

Power Spectra Density



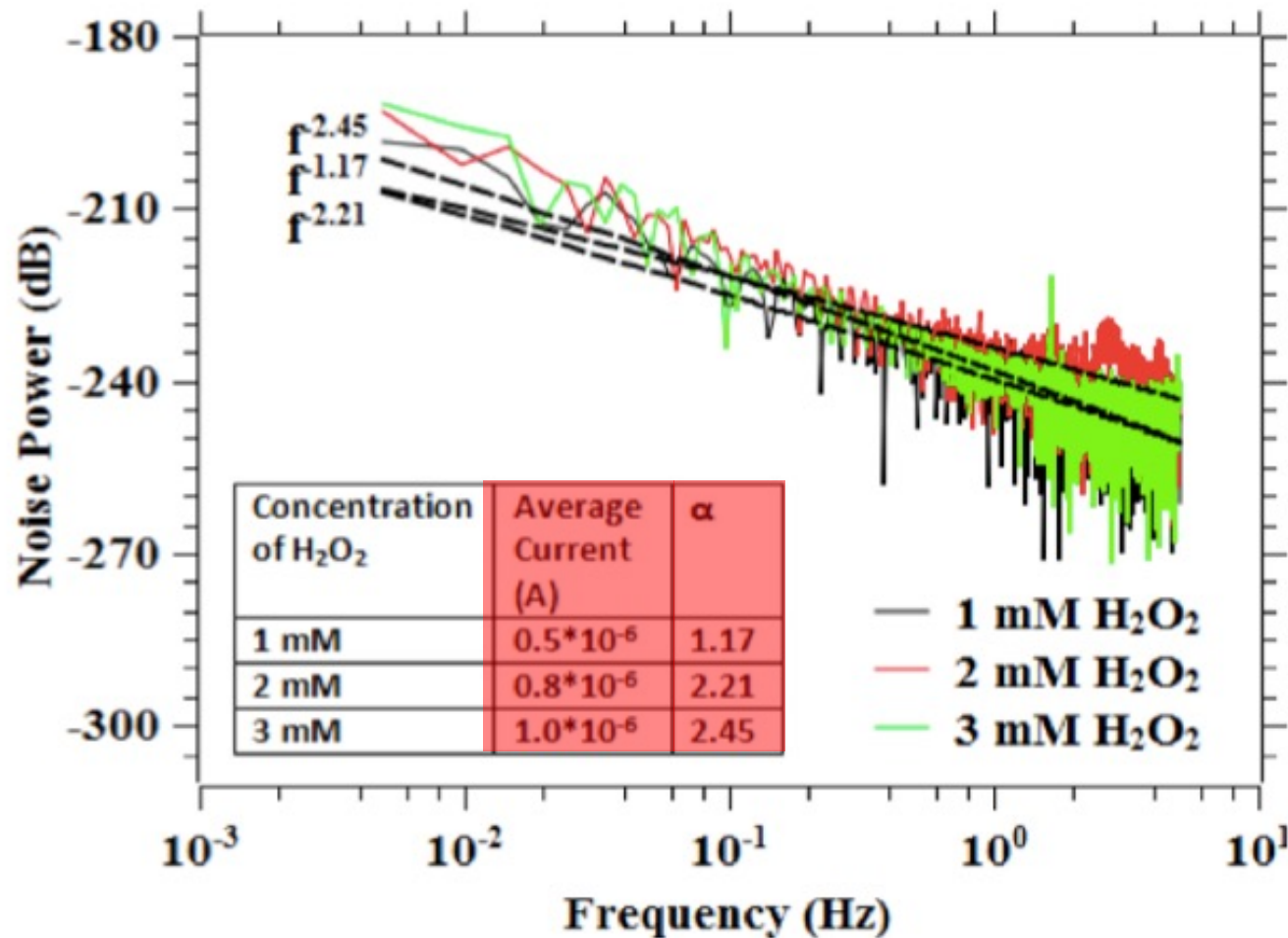
Noise PSD in chronoamperometry measurements with bare and MWCNT electrodes and a 10 k Ω resistor

Noise PSD on Bare



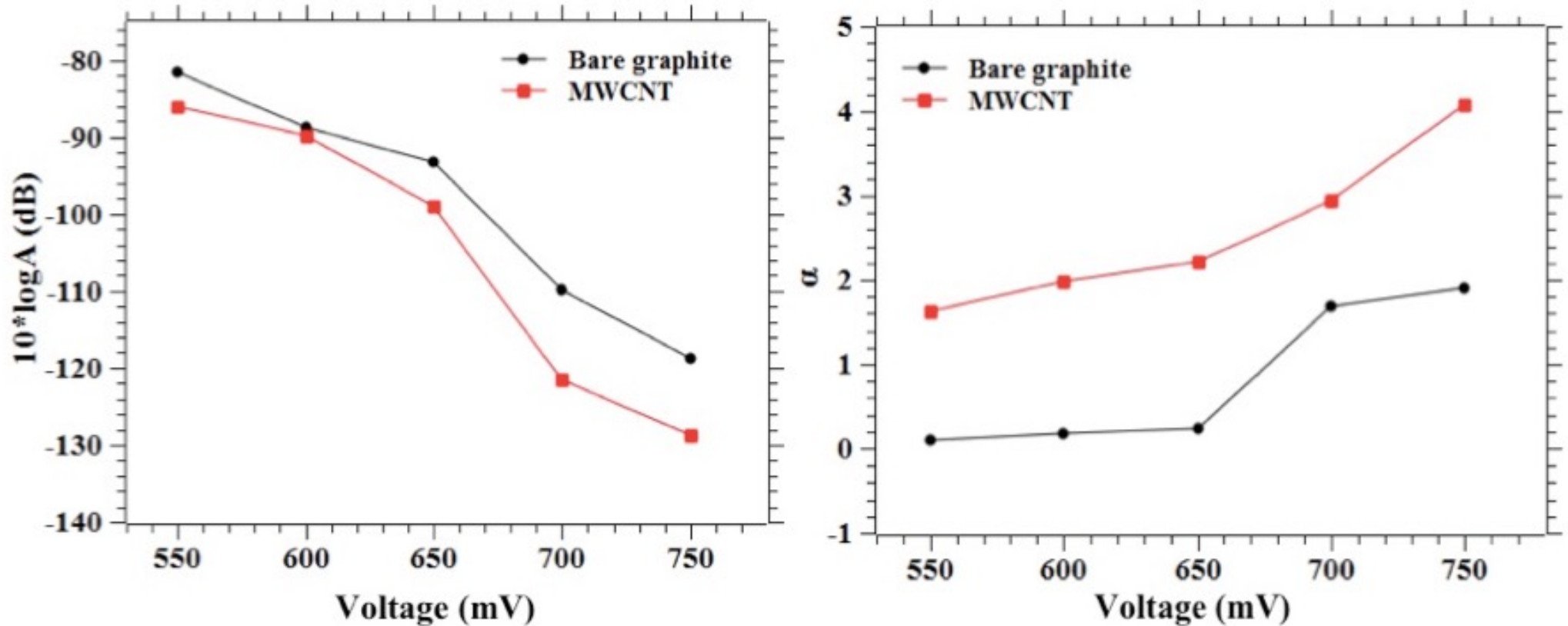
Noise PSD in chronoamperometry measurements (650 mV) of H₂O₂ with bare screen-printed electrode

Noise PSD on MWCNT



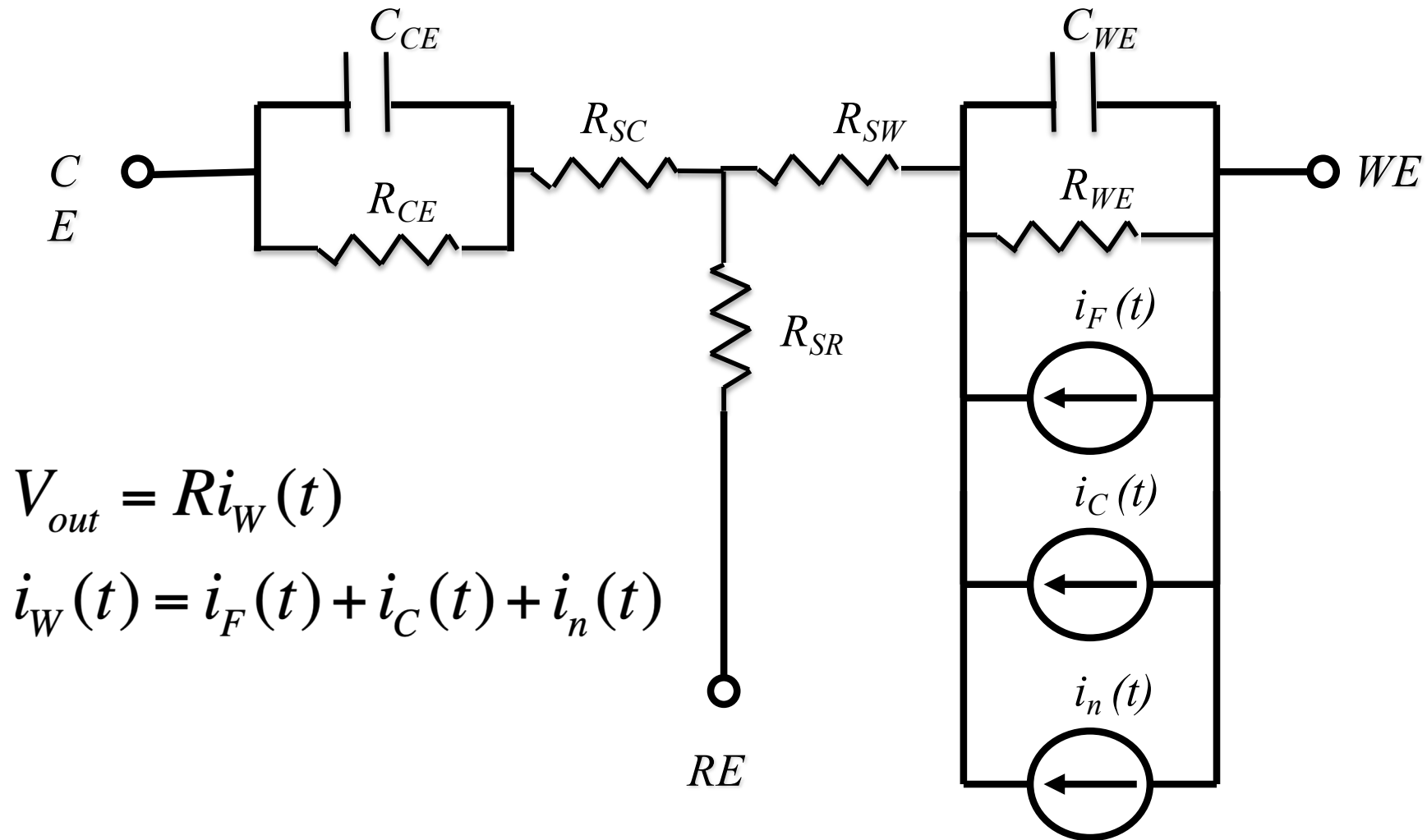
Noise PSD in chronoamperometry measurement (650 mV) of H₂O₂ with MWCNT structured electrode

Dependence by the Voltage



Values of parameters A (left) and α (right) versus the applied voltage, estimated on 2mM of H_2O_2

Equivalent circuit with all the current sources



$$V_{out} = Ri_W(t)$$

$$i_W(t) = i_F(t) + i_C(t) + i_n(t)$$