



Master in Electrical and Electronics Engineering

EE-517: Bio-Nano-Chip Design

# Lecture #10

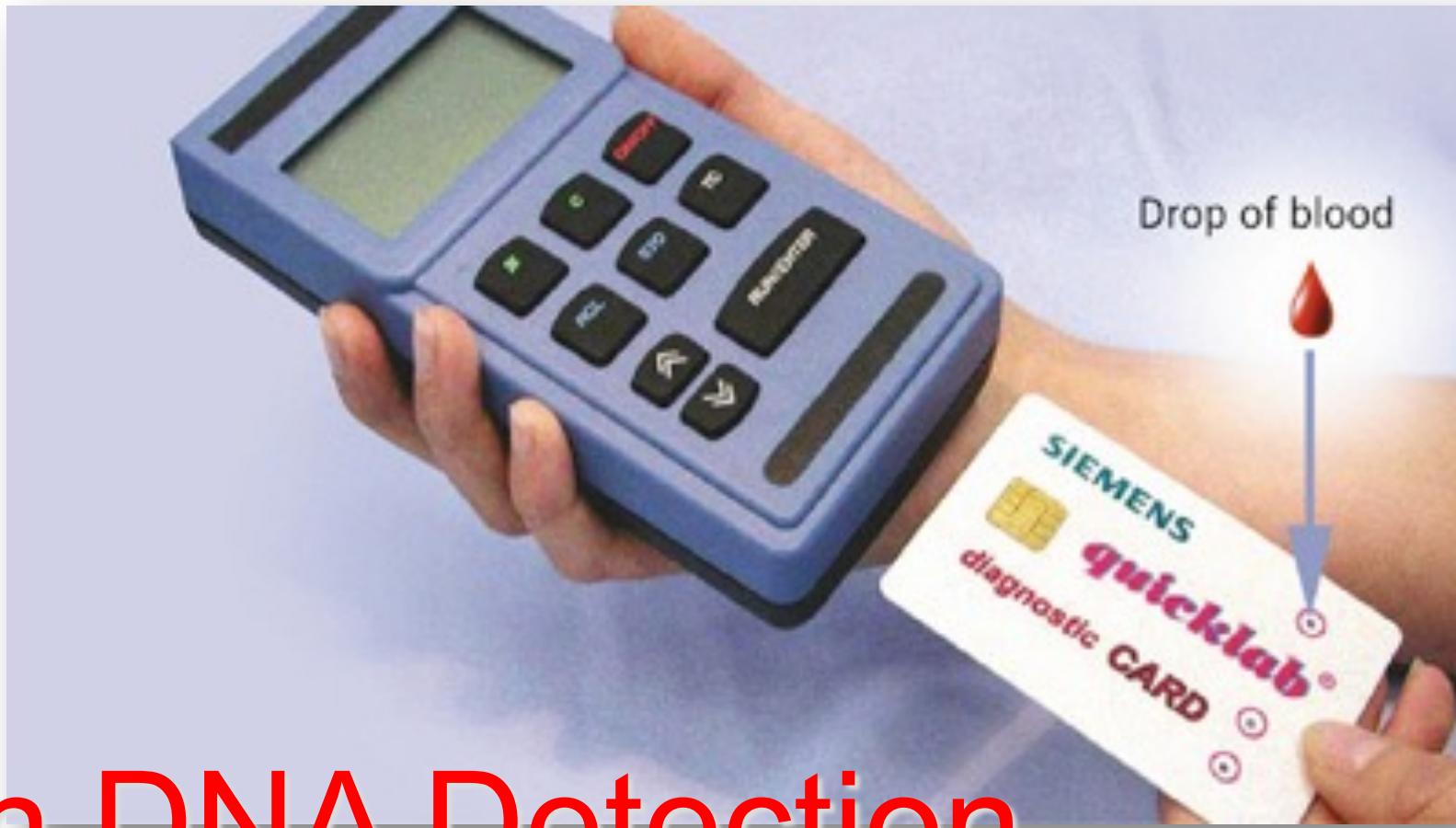
## CMOS Building Blocks

# Lecture Outline

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

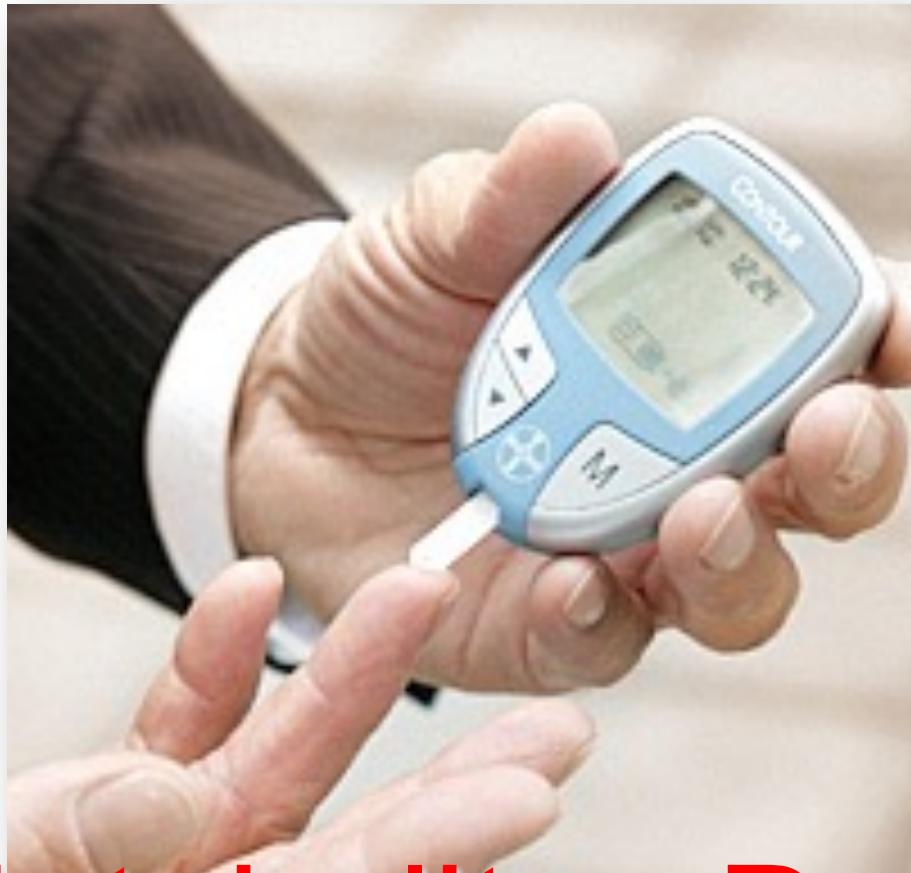
- CMOS design to drive the electrochemical cell
- Electrical properties of the electrochemical cell
- Basic Configuration of the cell: Grounded Counter
- Noise of the electrochemical interface

# CMOS architectures for Portable



in DNA Detection

# CMOS architectures for Portable

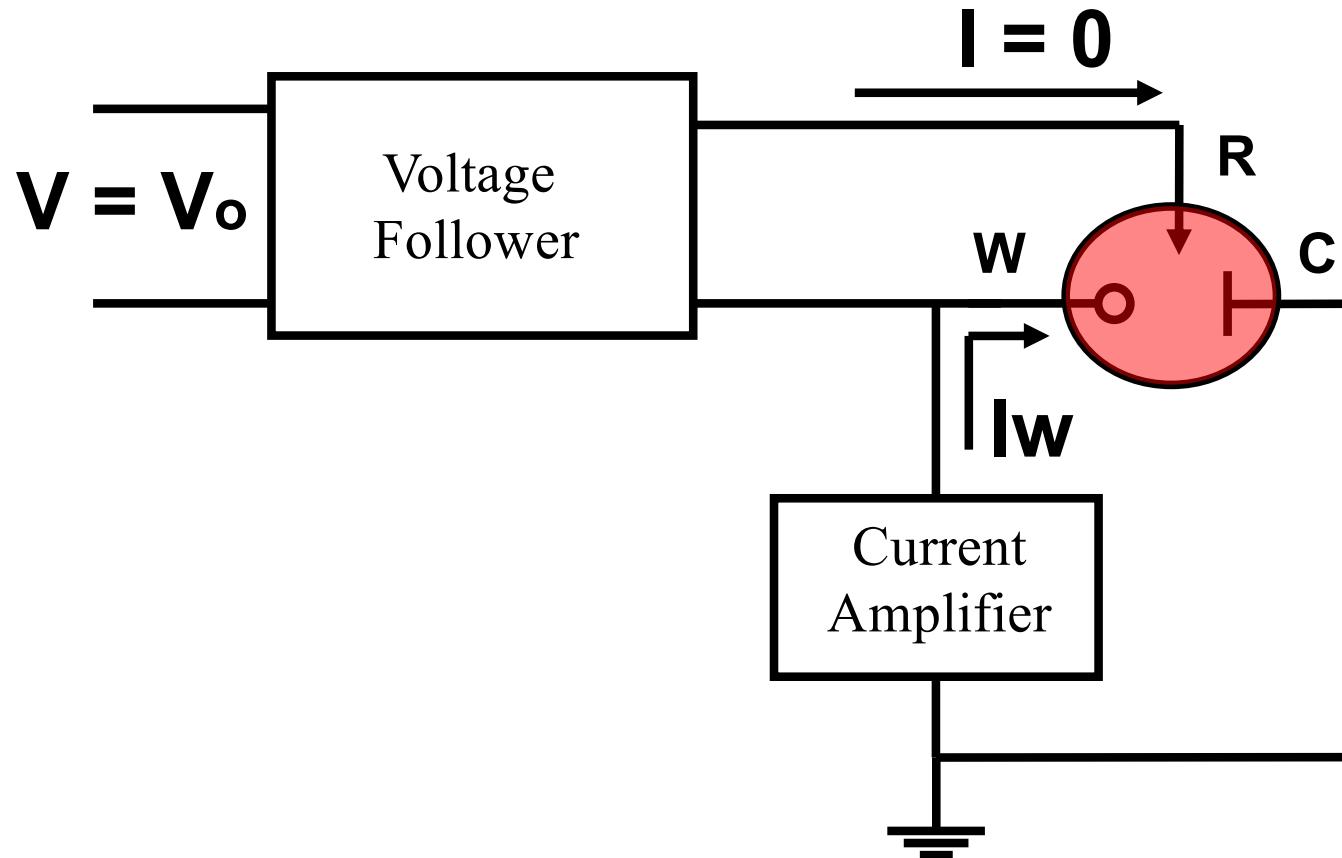


in Metabolites Detection

# CMOS architectures for iPhone



# Required Blocks



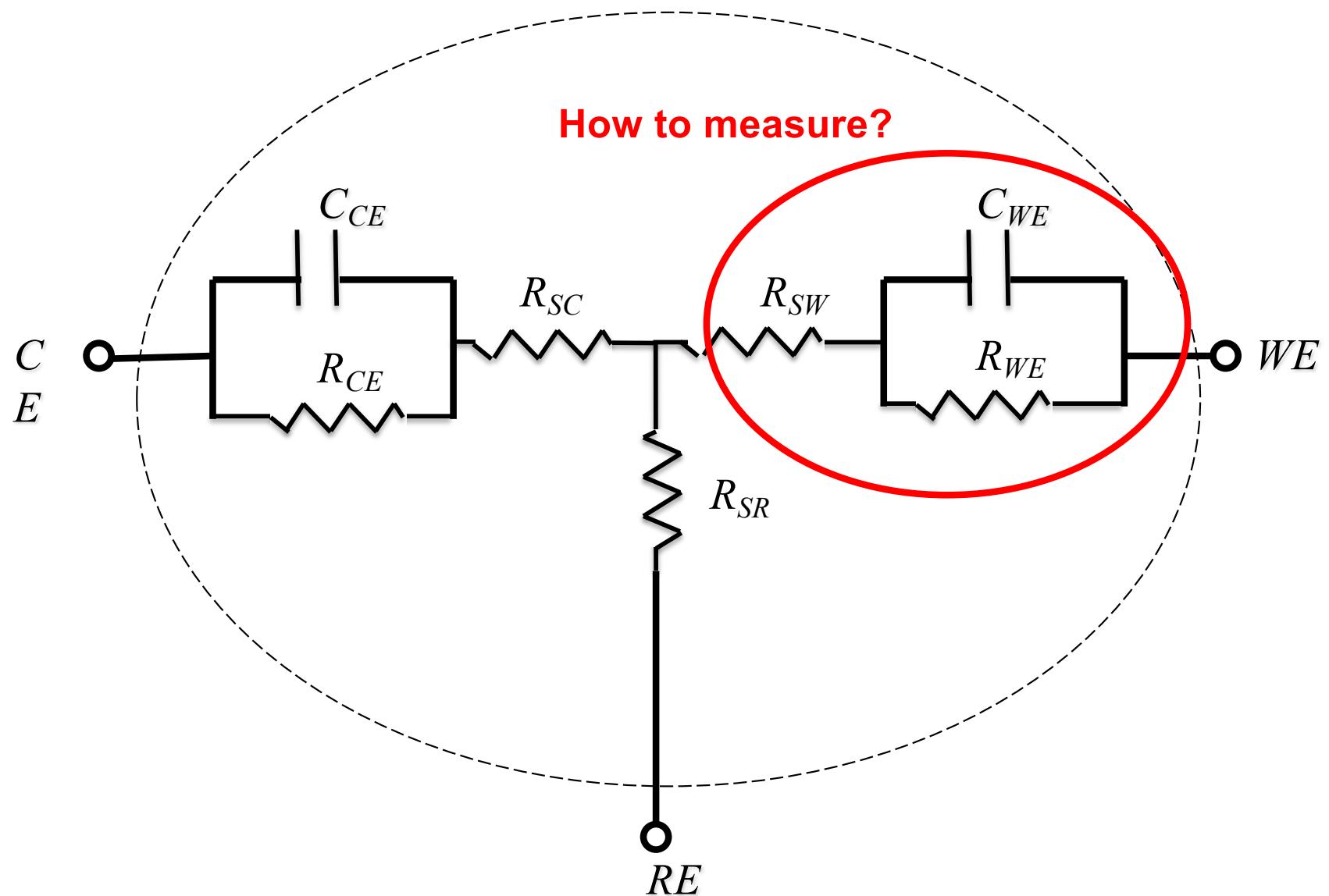


Q1

# 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



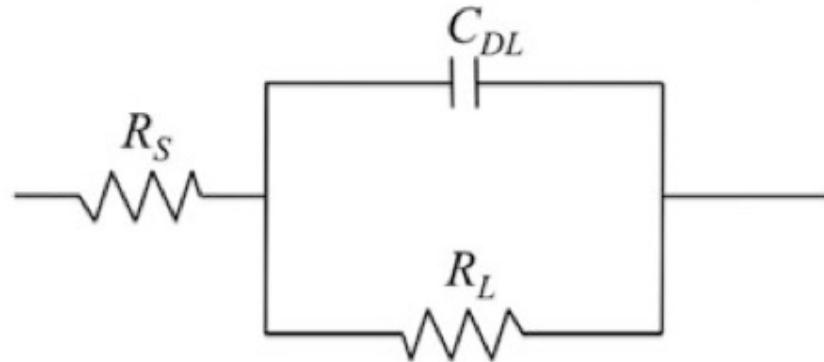


Q2

## 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

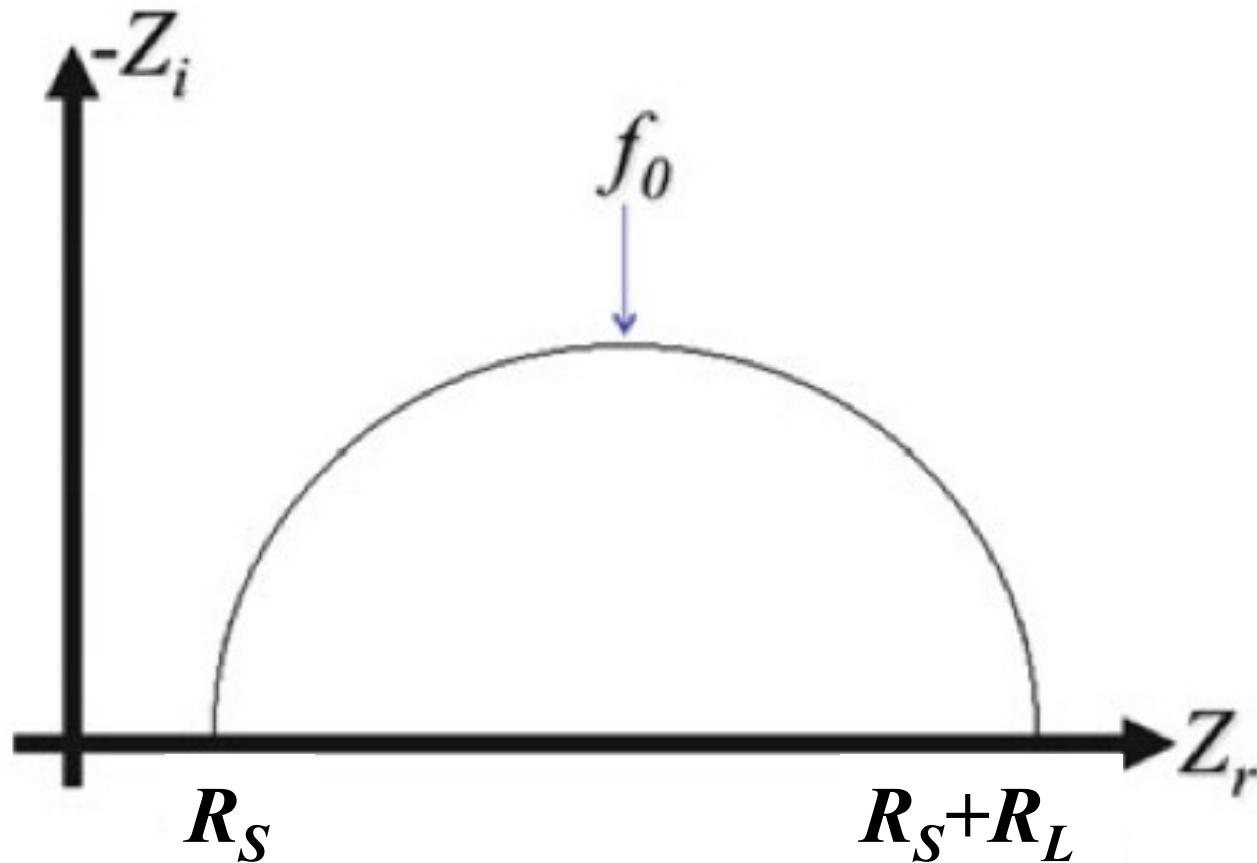
$$Z = \frac{R_L}{j\omega C_{DL}R_L + 1} \cdot \frac{1 - j\omega C_{DL}R_L}{1 - j\omega C_{DL}R_L}$$

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

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

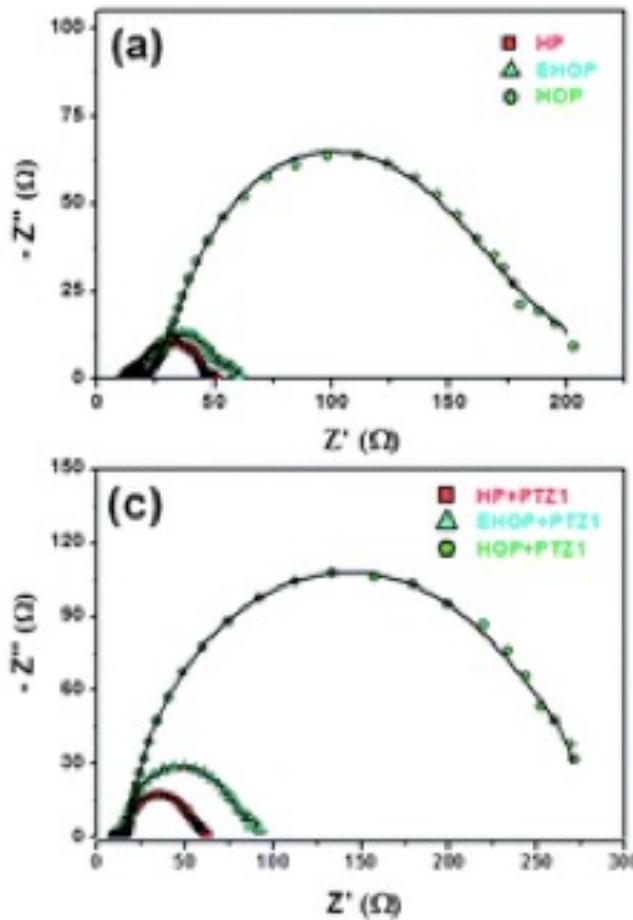
This impedance presents both resistive and reactive components

# 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

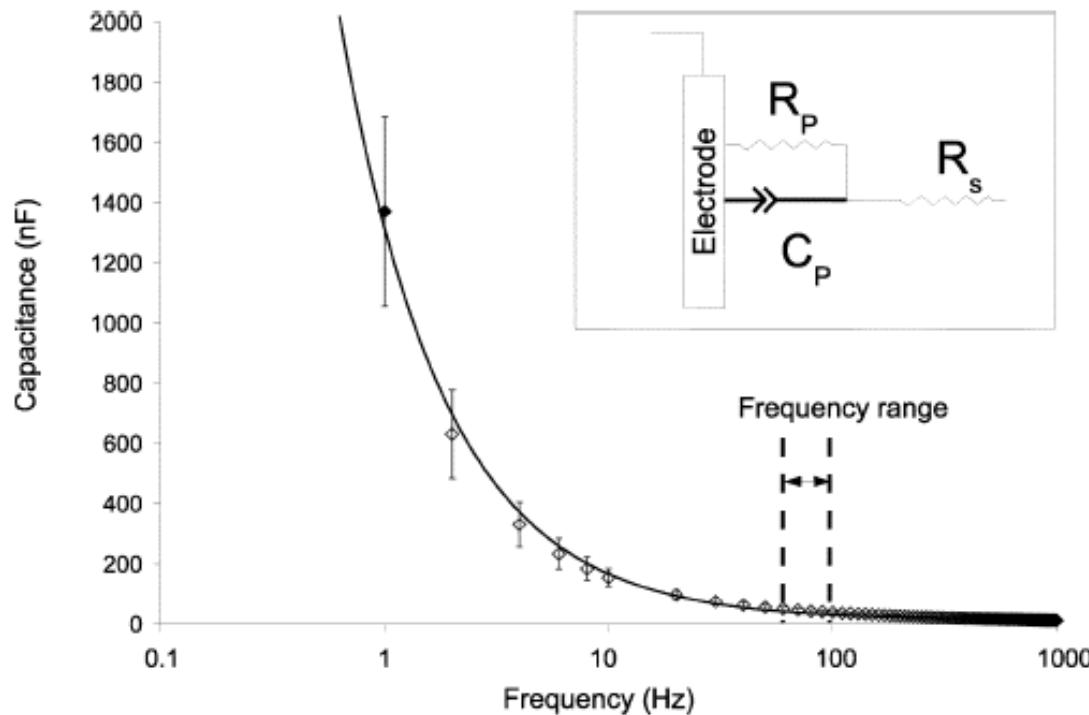
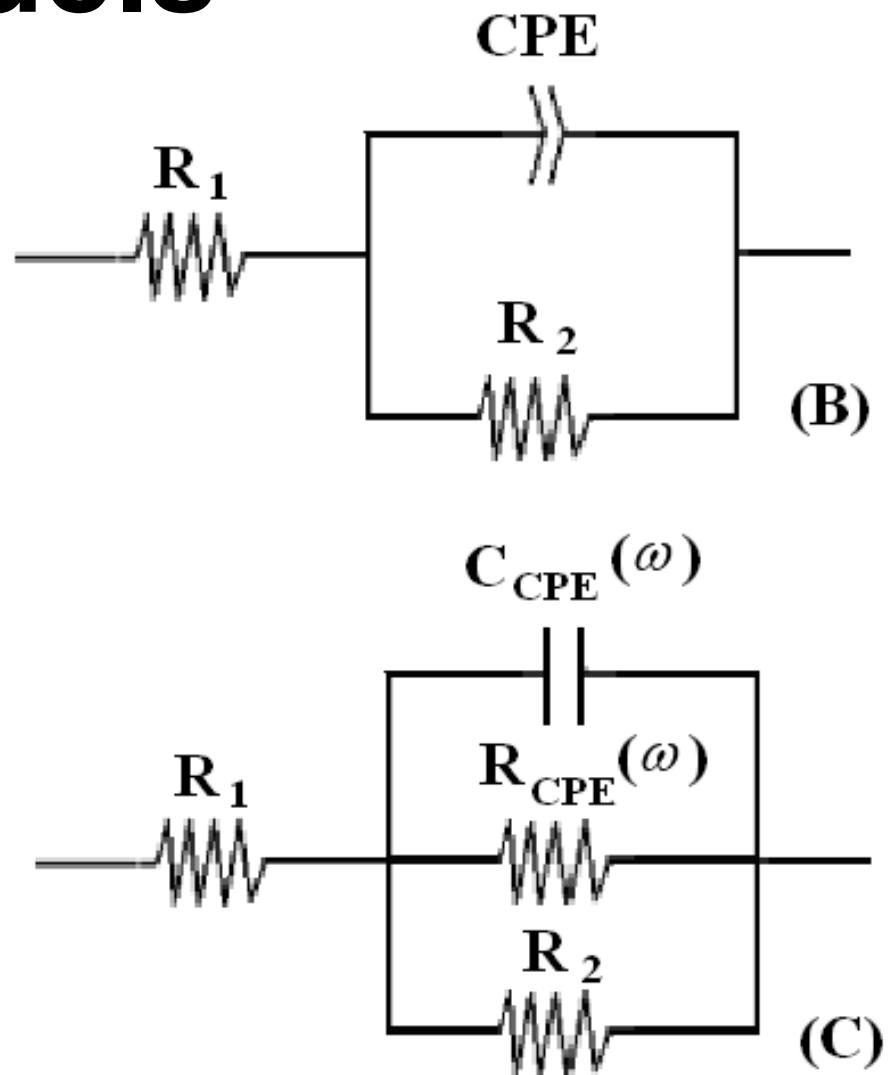
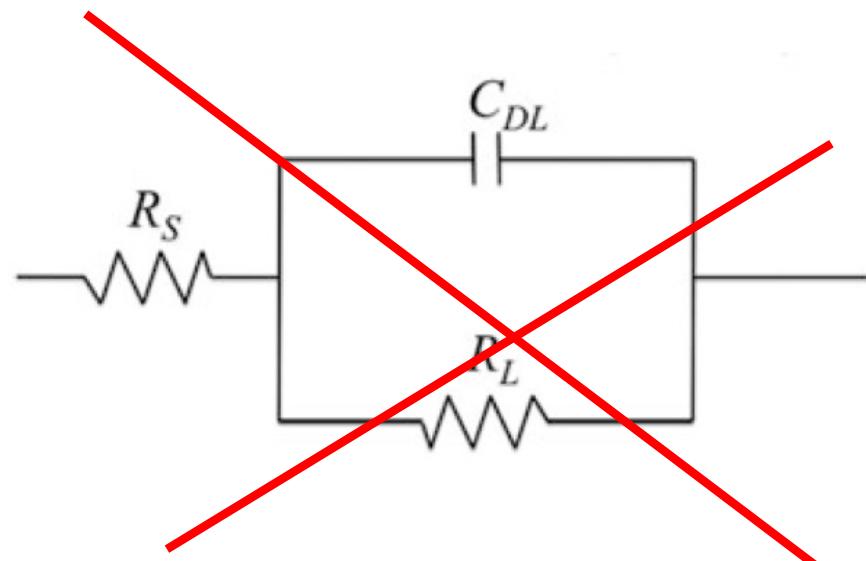


Fig. 9. Measured capacitance versus charge/discharge frequency on clean gold electrodes. The continuous line shows the fitting.

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

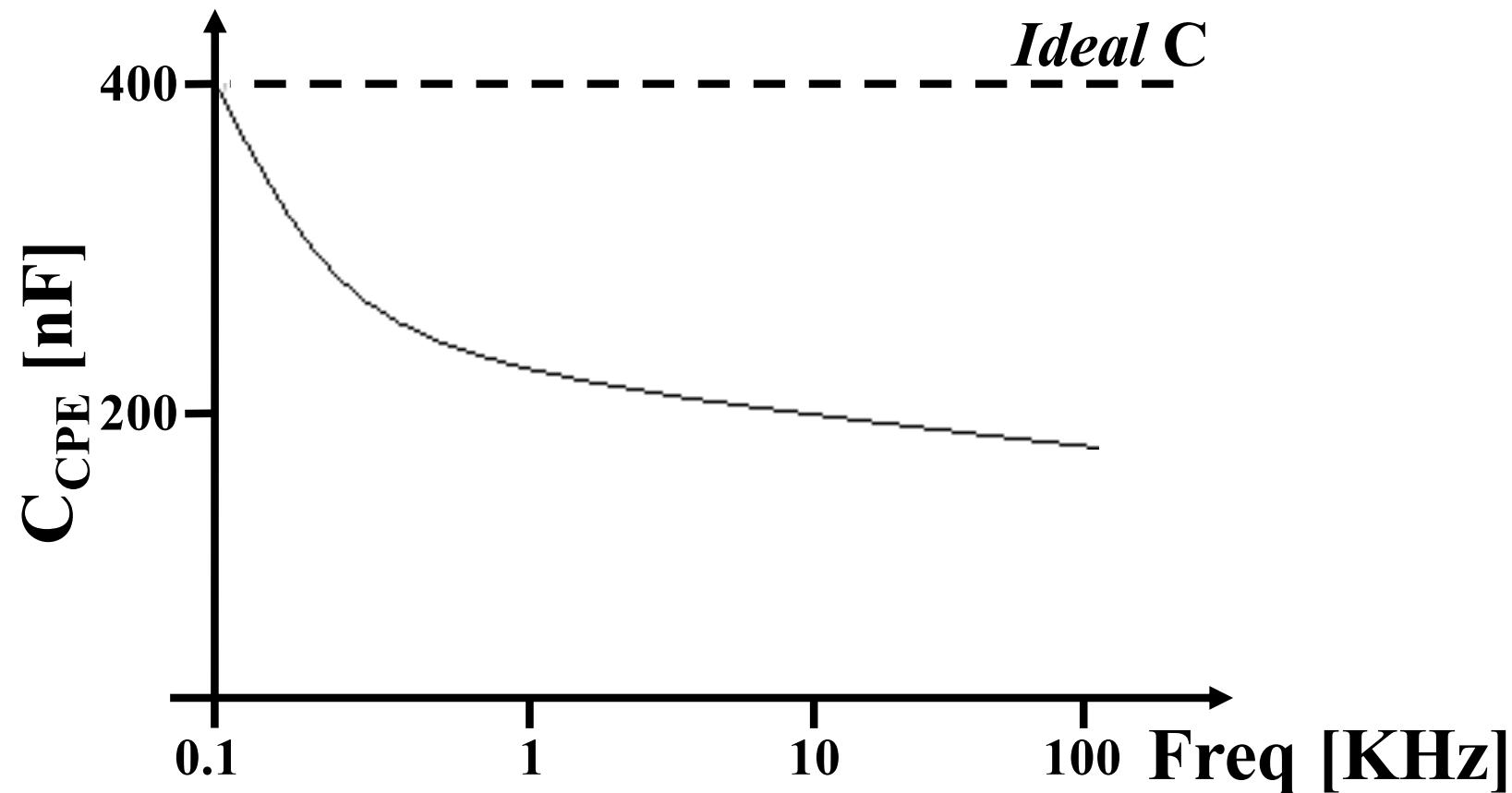
# CPE element

$$Z_{CPE} \left\{ \begin{array}{l} R_{CPE} \cong \frac{1}{\omega^\alpha C_p} \sqrt{1 - \alpha^2} \\ X_{CPE} \cong \frac{-1}{\omega^\alpha C_p} \alpha \end{array} \right.$$

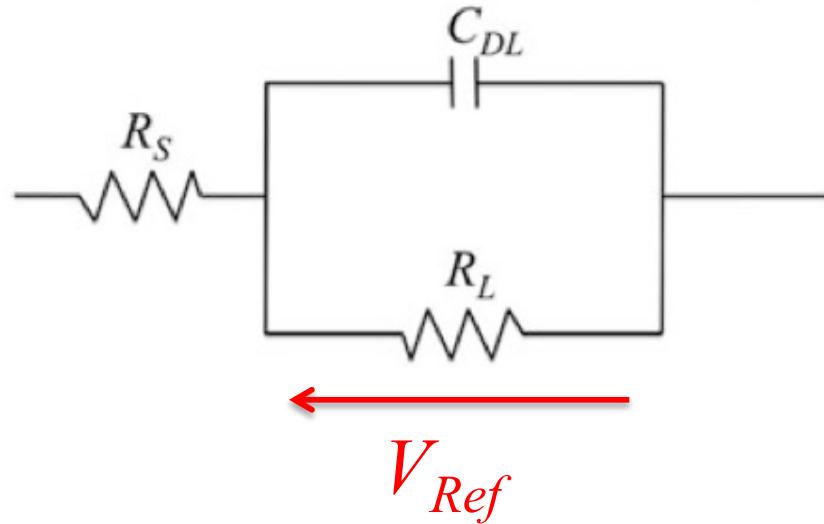
$$|X_{CPE}| \cong \frac{1}{\omega^\alpha C_p} \alpha = \frac{1}{\omega^{\alpha-1} \omega C_p} \alpha = \frac{1}{\omega \left( \frac{C_p}{\alpha \omega^{1-\alpha}} \right)}$$

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

# 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

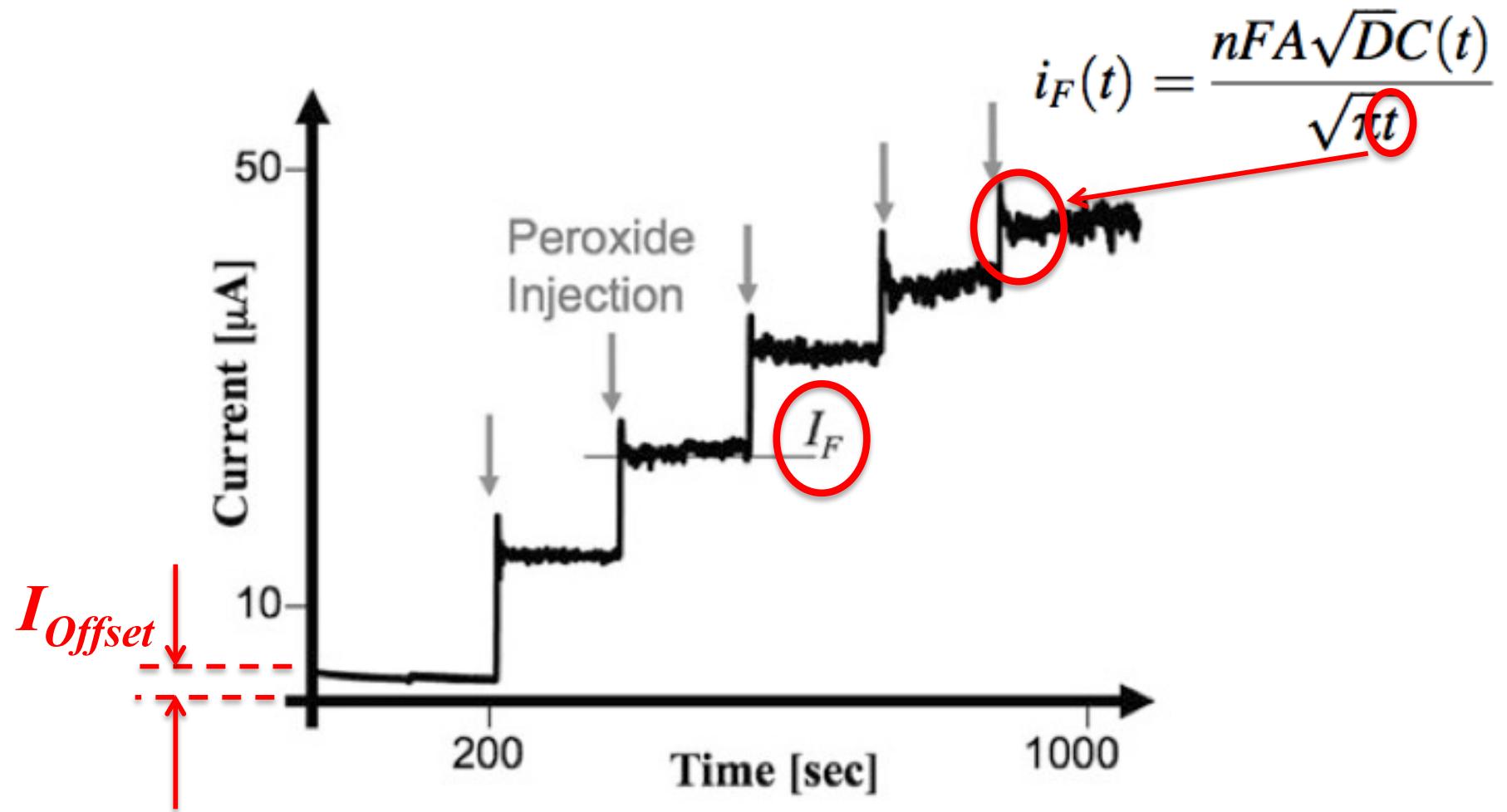


Q4

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

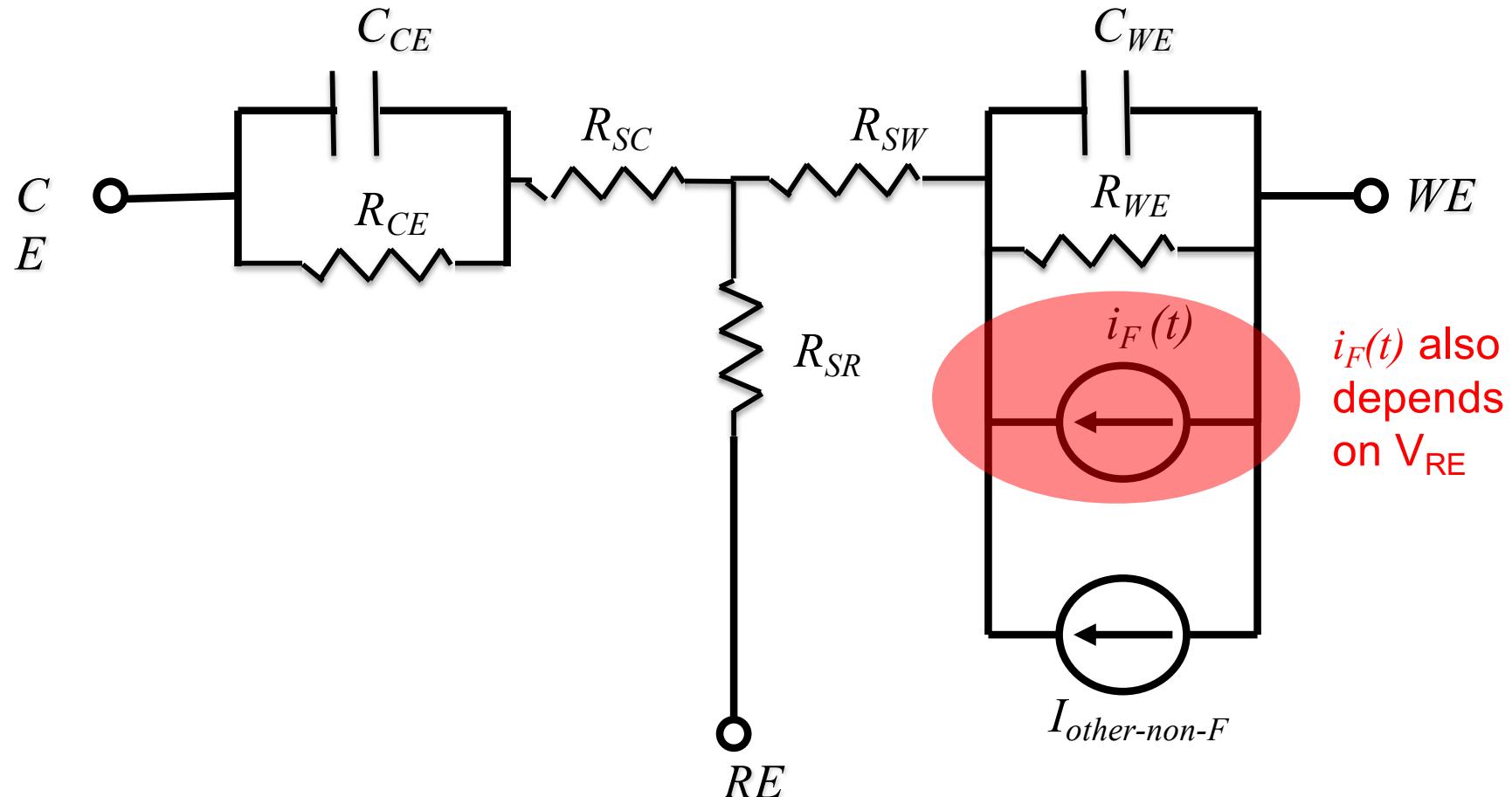
- A. Since Faradaic currents do not follow Ohm law
- B. Since Faradaic currents also depend on species' concentration
- C. Since it is not possible to correctly model the Faradaic currents
- D. Since it is very difficult to correctly model the Faradaic currents

# Faradaic Current

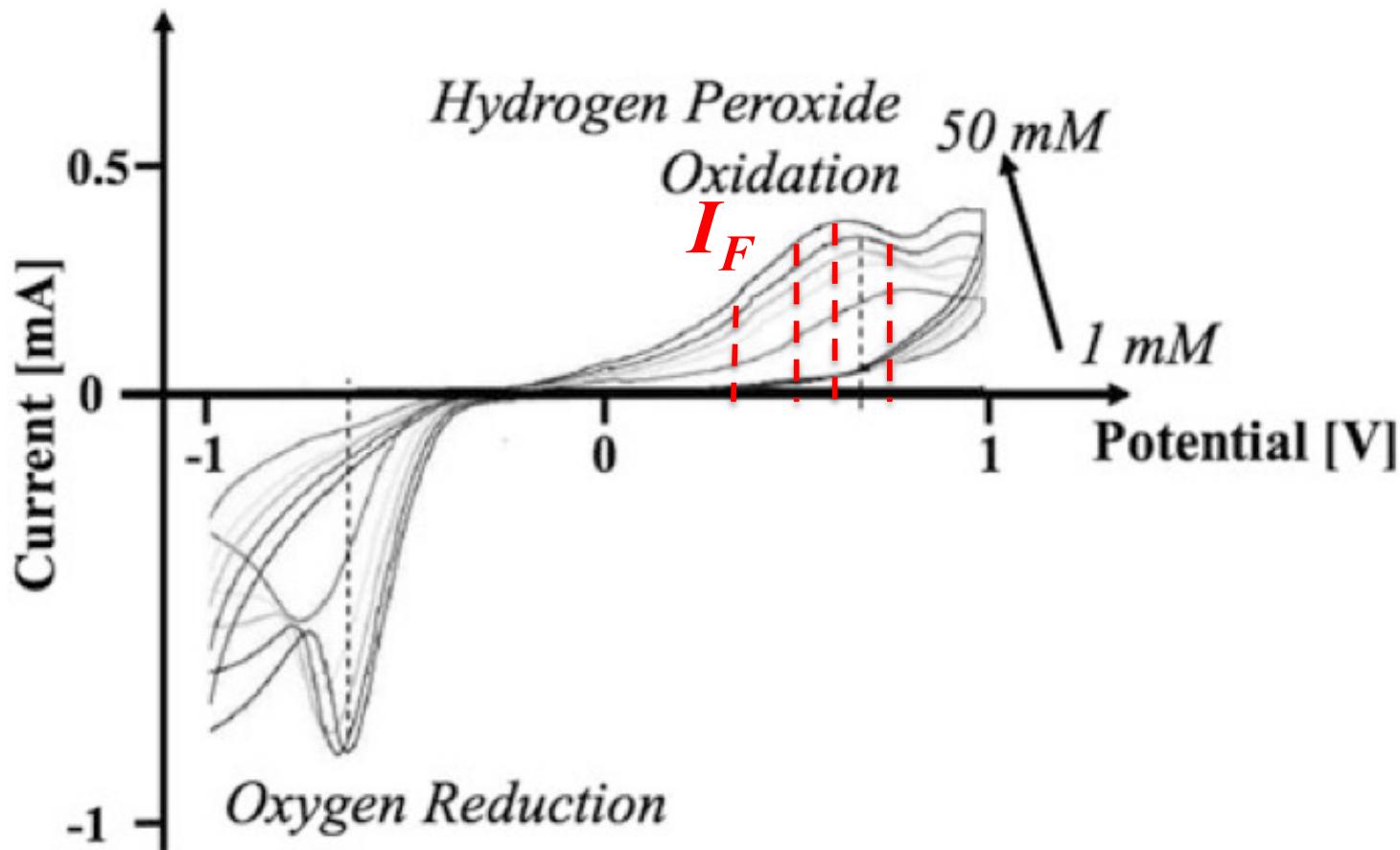


Typical curve in chronoamperometry

# Equivalent circuit: active model

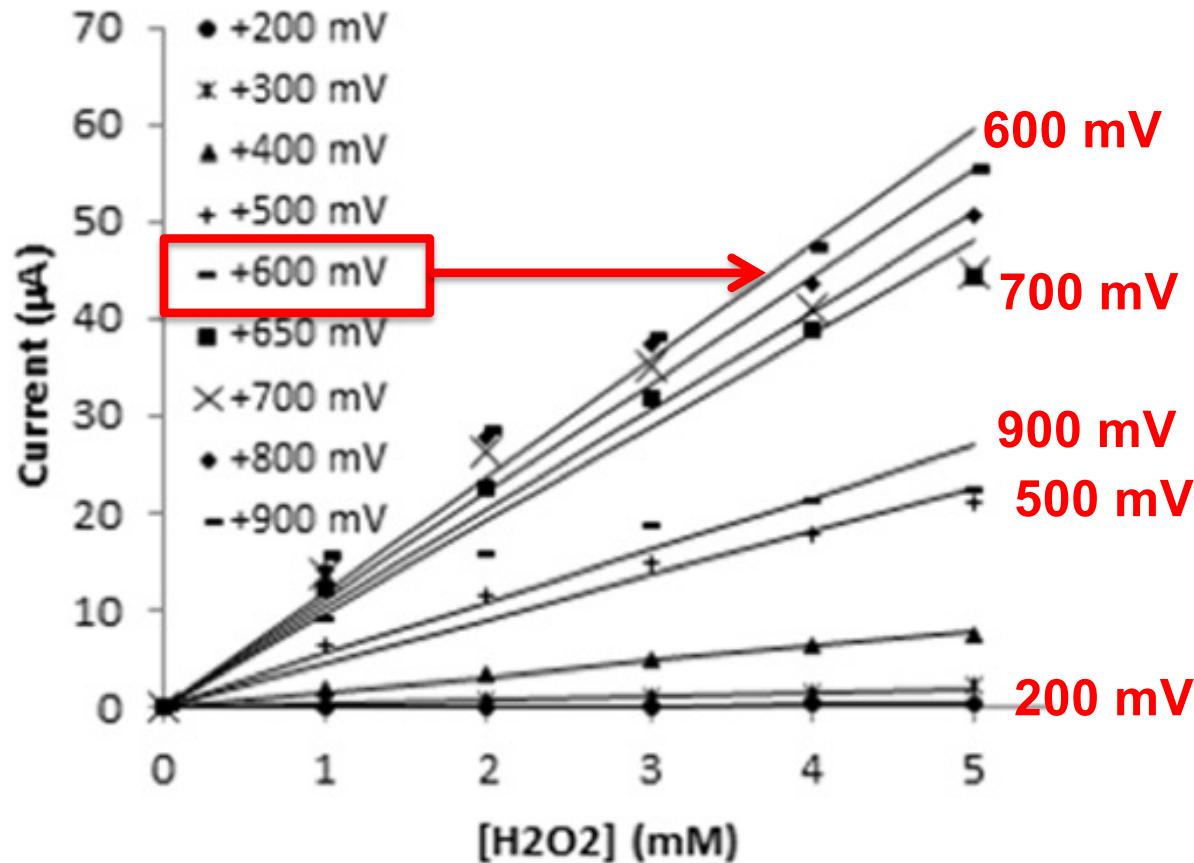


# Redox with hydrogen peroxide



$O_2$  reduction and  $H_2O_2$  oxidation observed by potential sweeping

# Faradaic Current Generator



The sensitivity depends on the Reference Potential

# Faradaic Current Generator

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



$$I_{Offset} = 0$$



$$I = SC$$

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

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

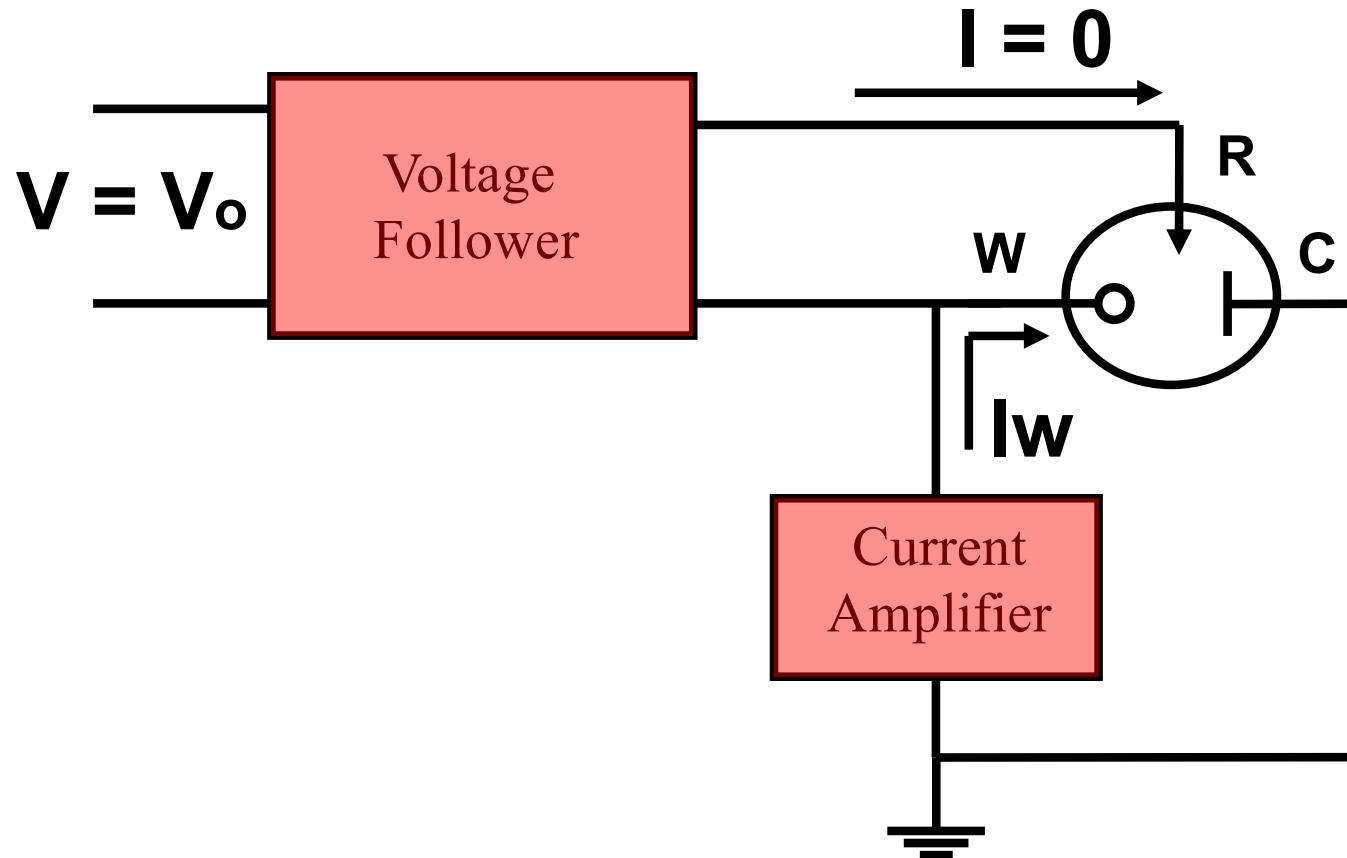


Q6

# 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

Voltage  
Follower

Analog  
Adder

Analog  
Shifter

Current  
Amplifier

Analog  
MUX

Analog  
Integrator

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



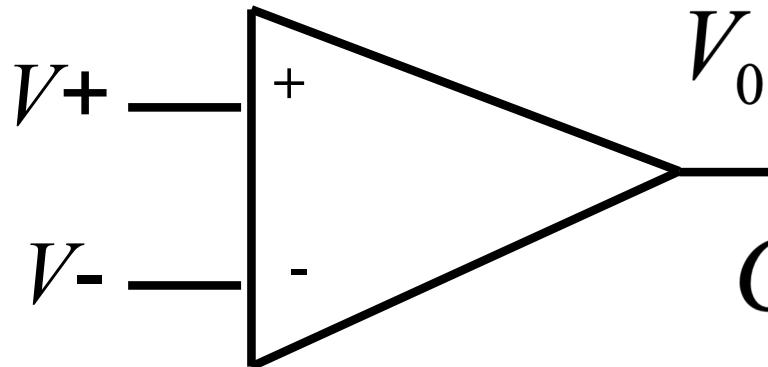
Q8

# 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



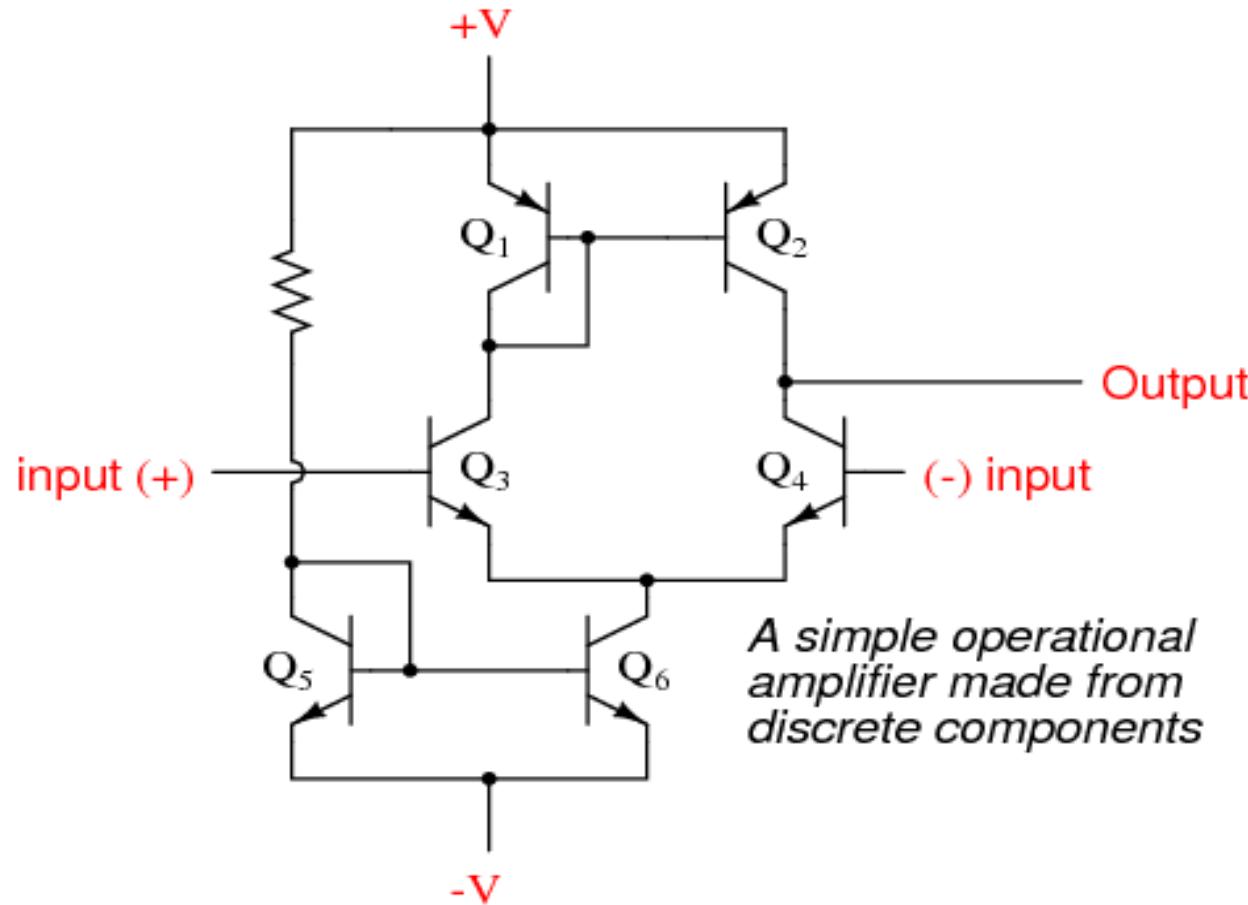
$$V_0 = G_0(V_+ - V_-)$$

$$G_0 \rightarrow \infty$$

$$R_i \rightarrow \infty \rightarrow I_i \approx 0$$

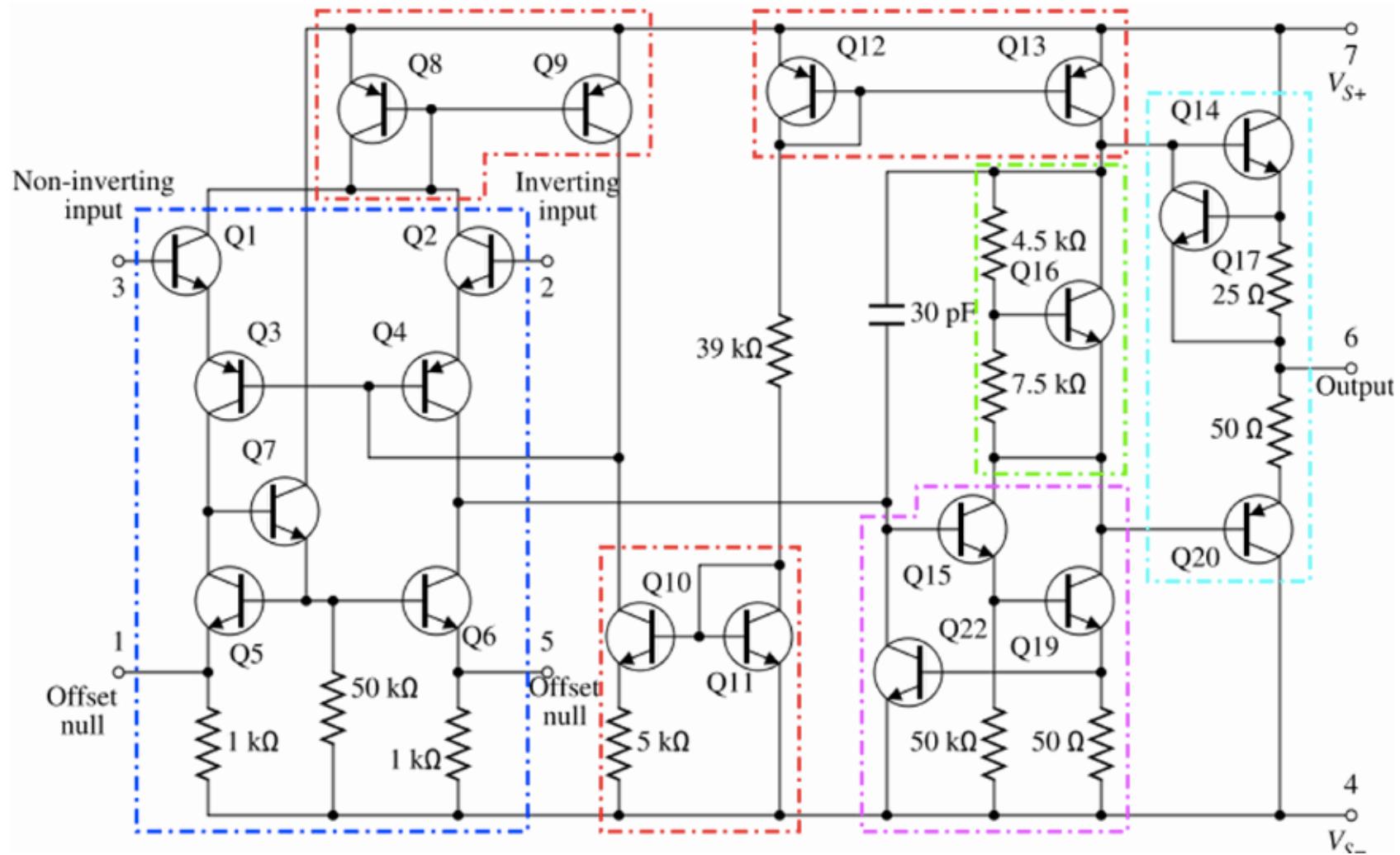
$$R_o \approx 0 \rightarrow V_o \neq f(R_L)$$

# What's an Op. Amp.?



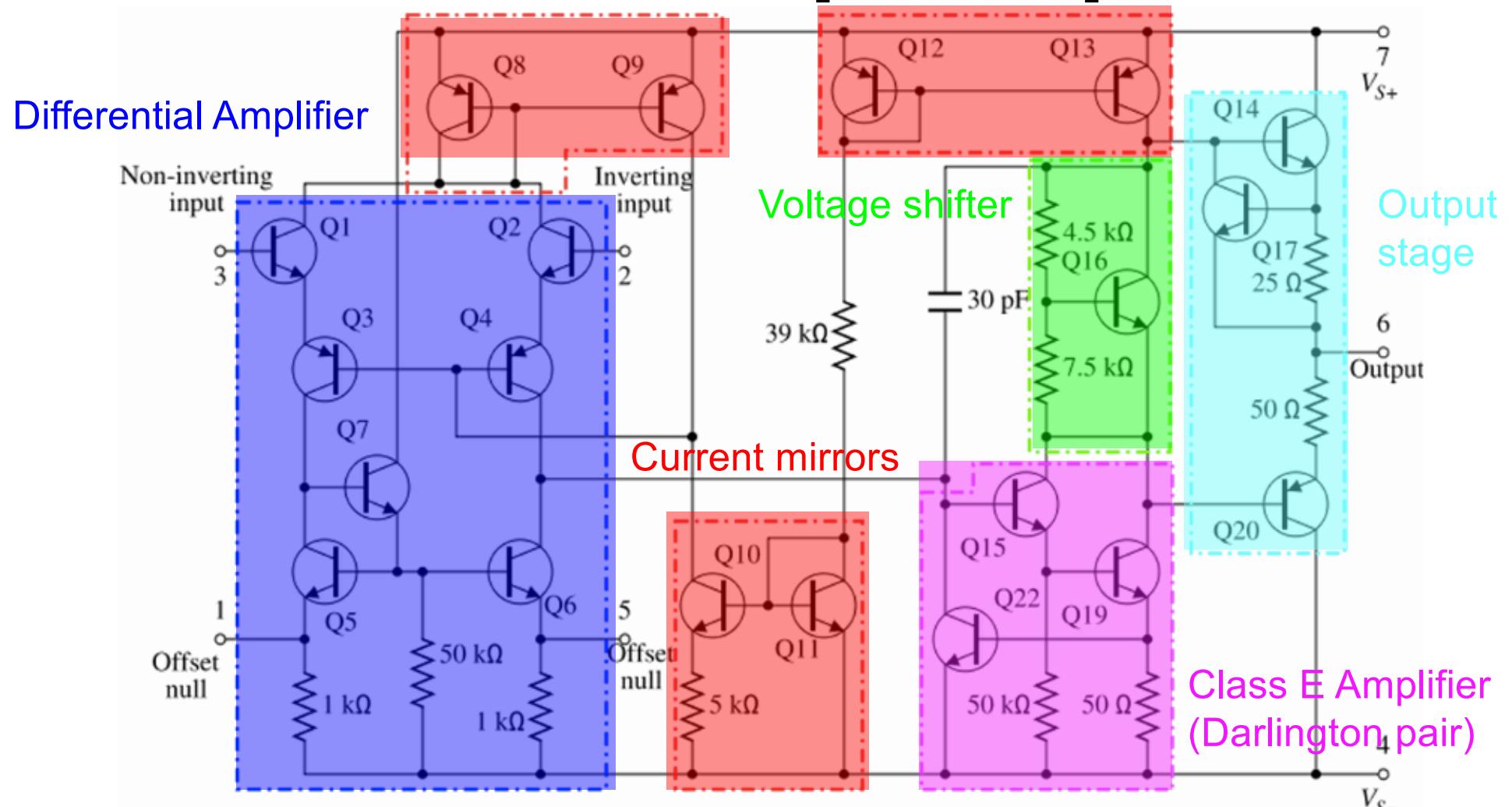
A simple scheme of a differential amplifier at transistors level

# What's an Op. Amp.?



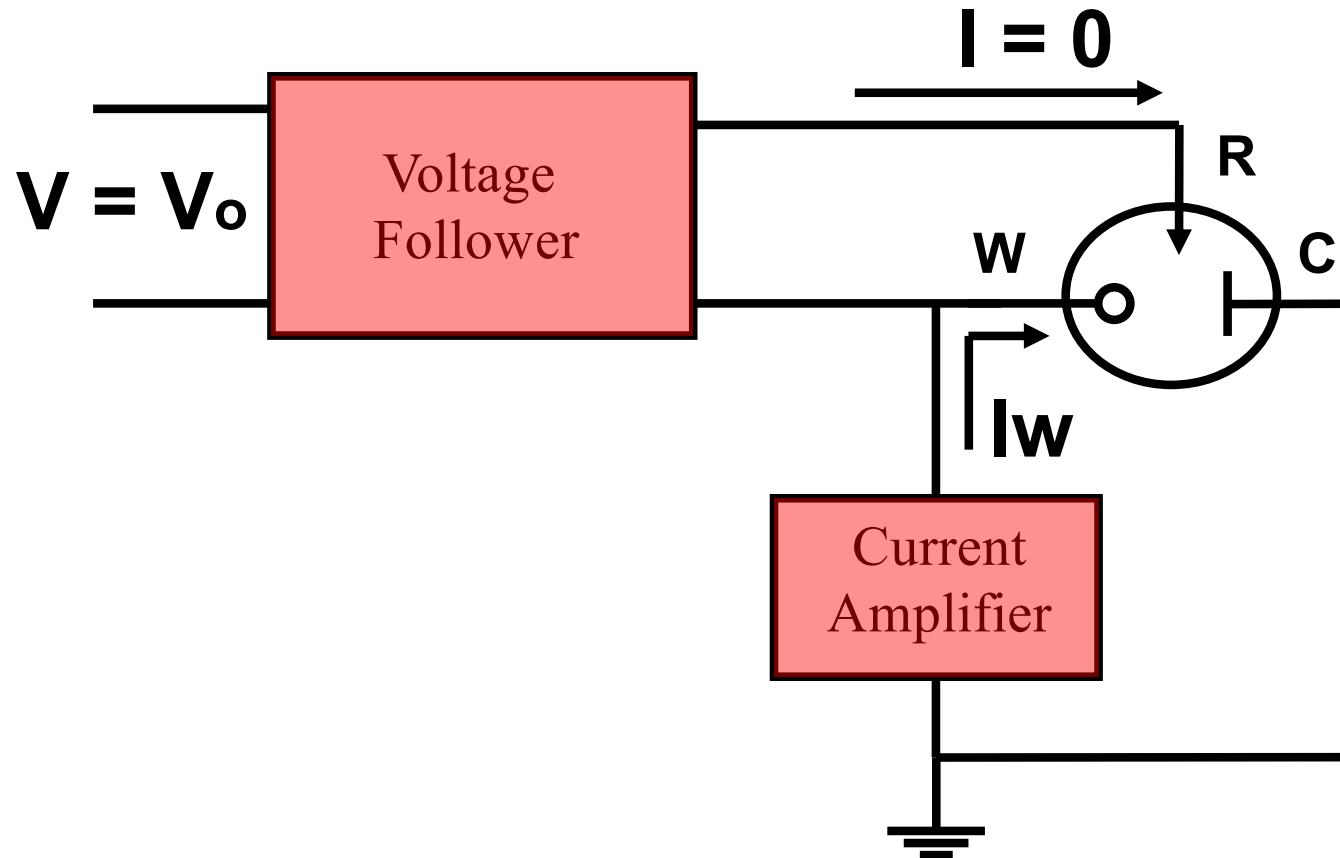
A more complex architecture of an Operational Amplifier (the common 741)

# What's an Op. Amp.?

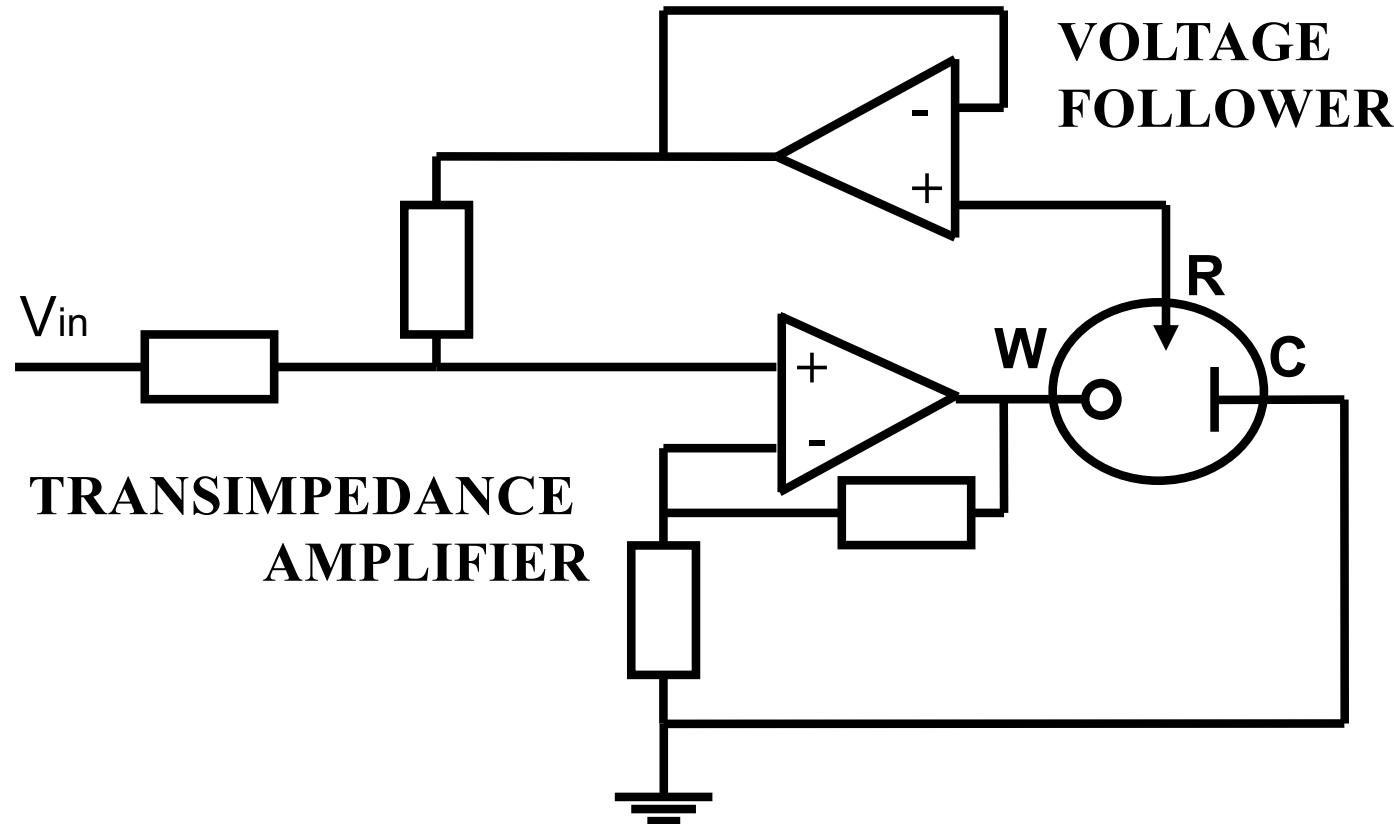


A more complex architecture of an Operational Amplifier (the common 741)

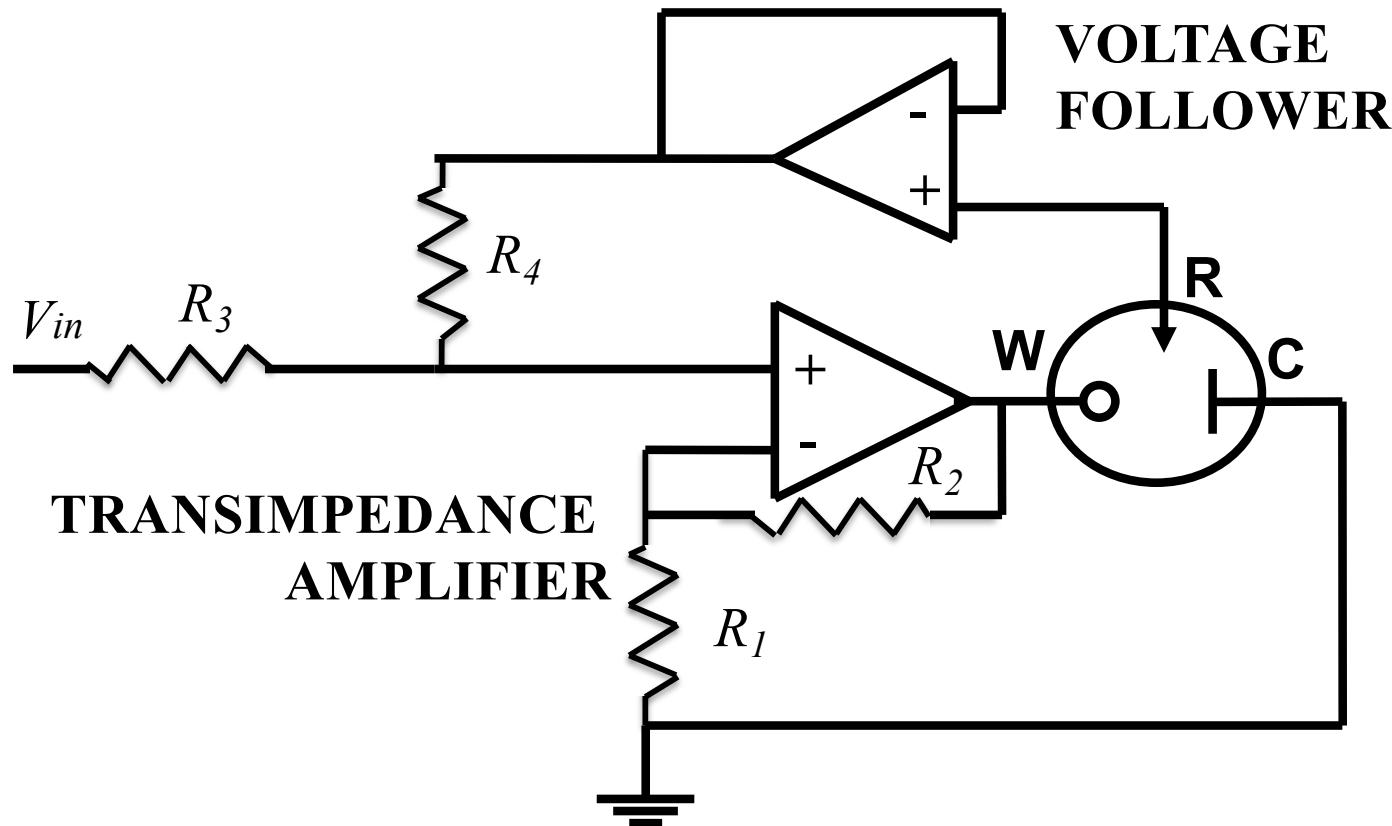
# CMOS for Redox



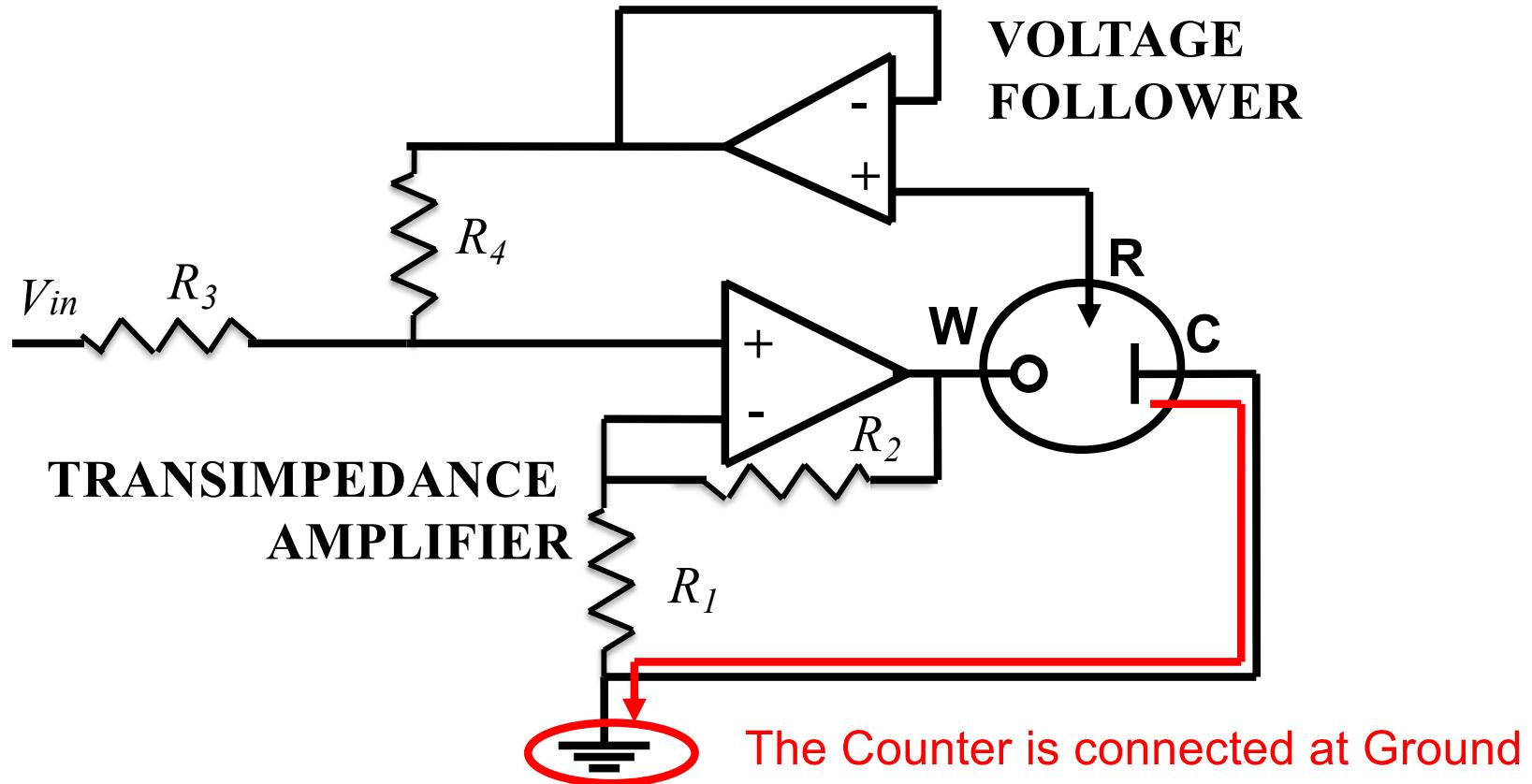
# The basic CMOS for Redox



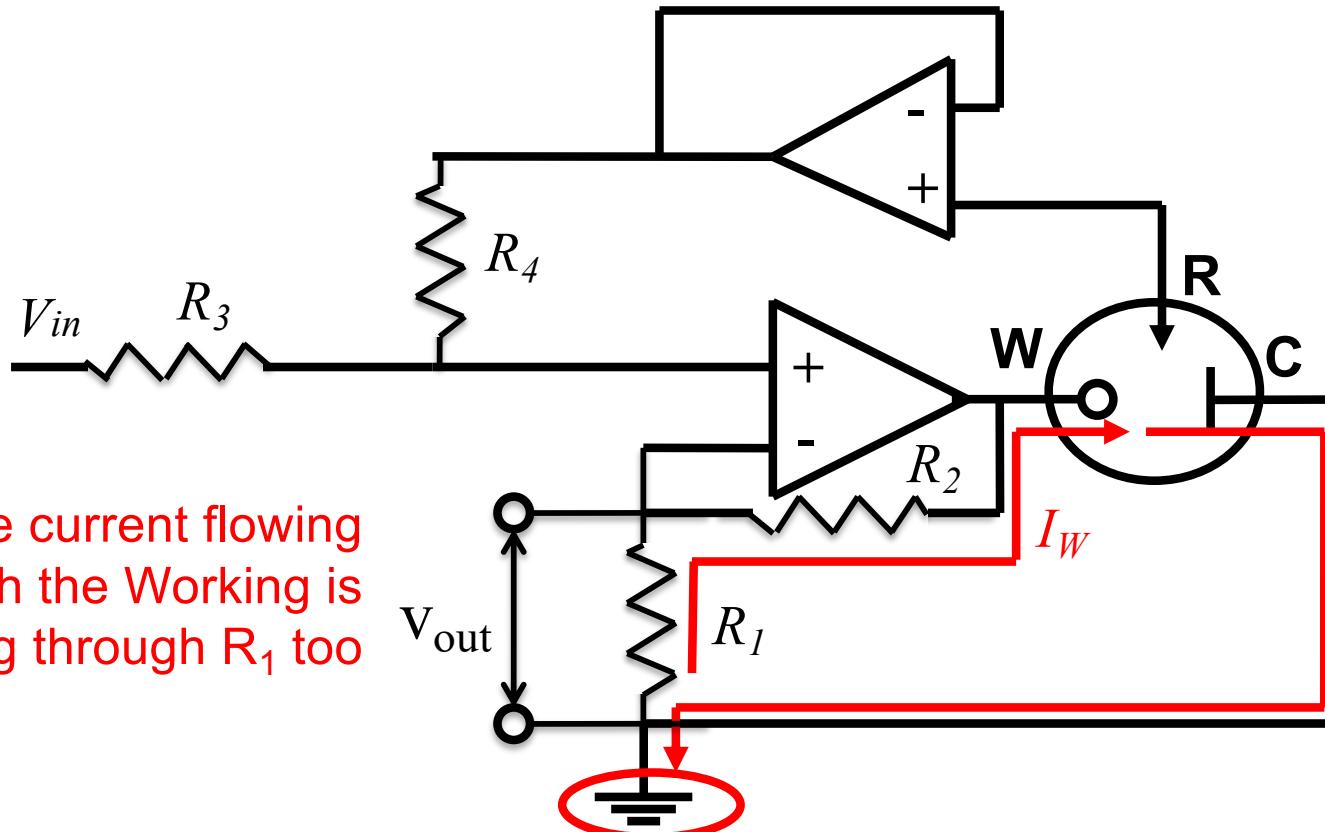
# The basic CMOS for Redox



# Grounded Counter

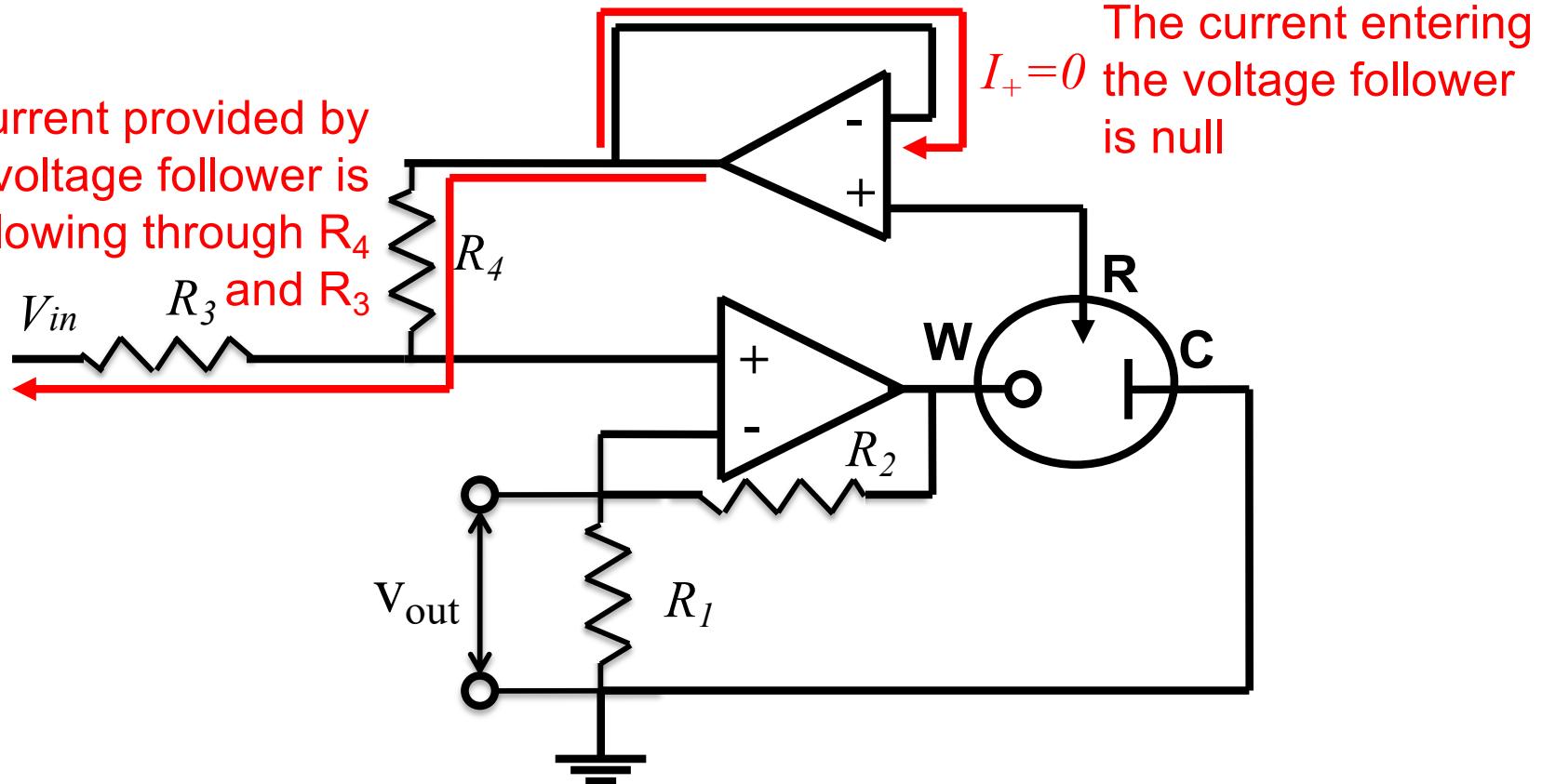


# Grounded Counter

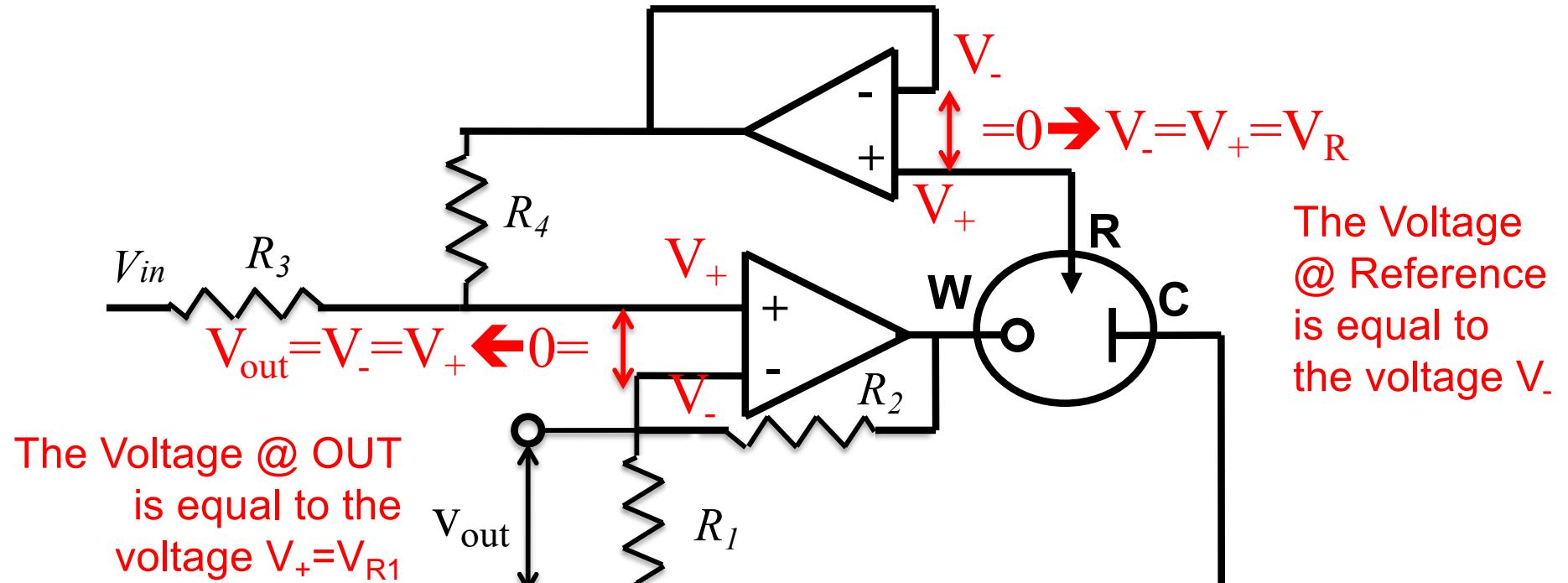


# Grounded Counter

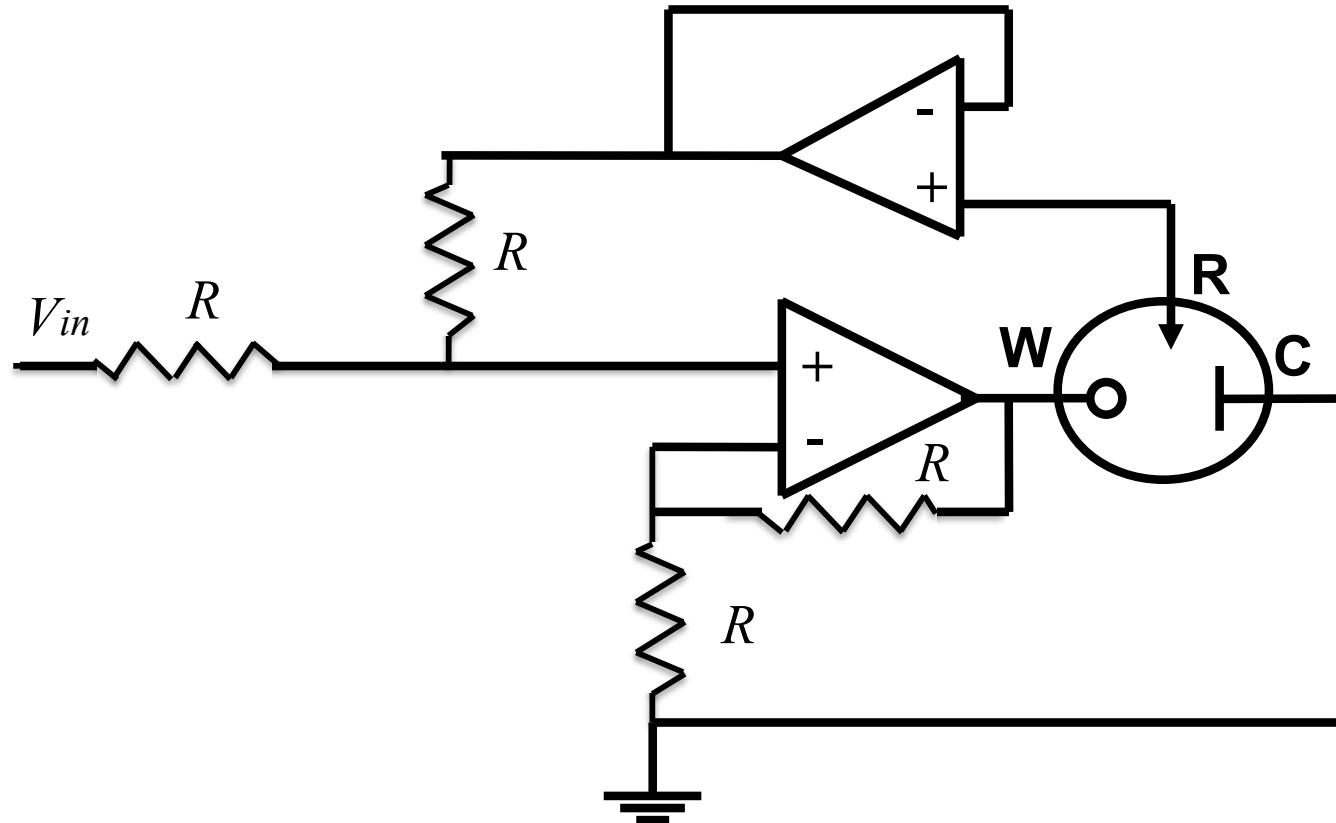
The current provided by the voltage follower is only flowing through  $R_4$



# Grounded Counter

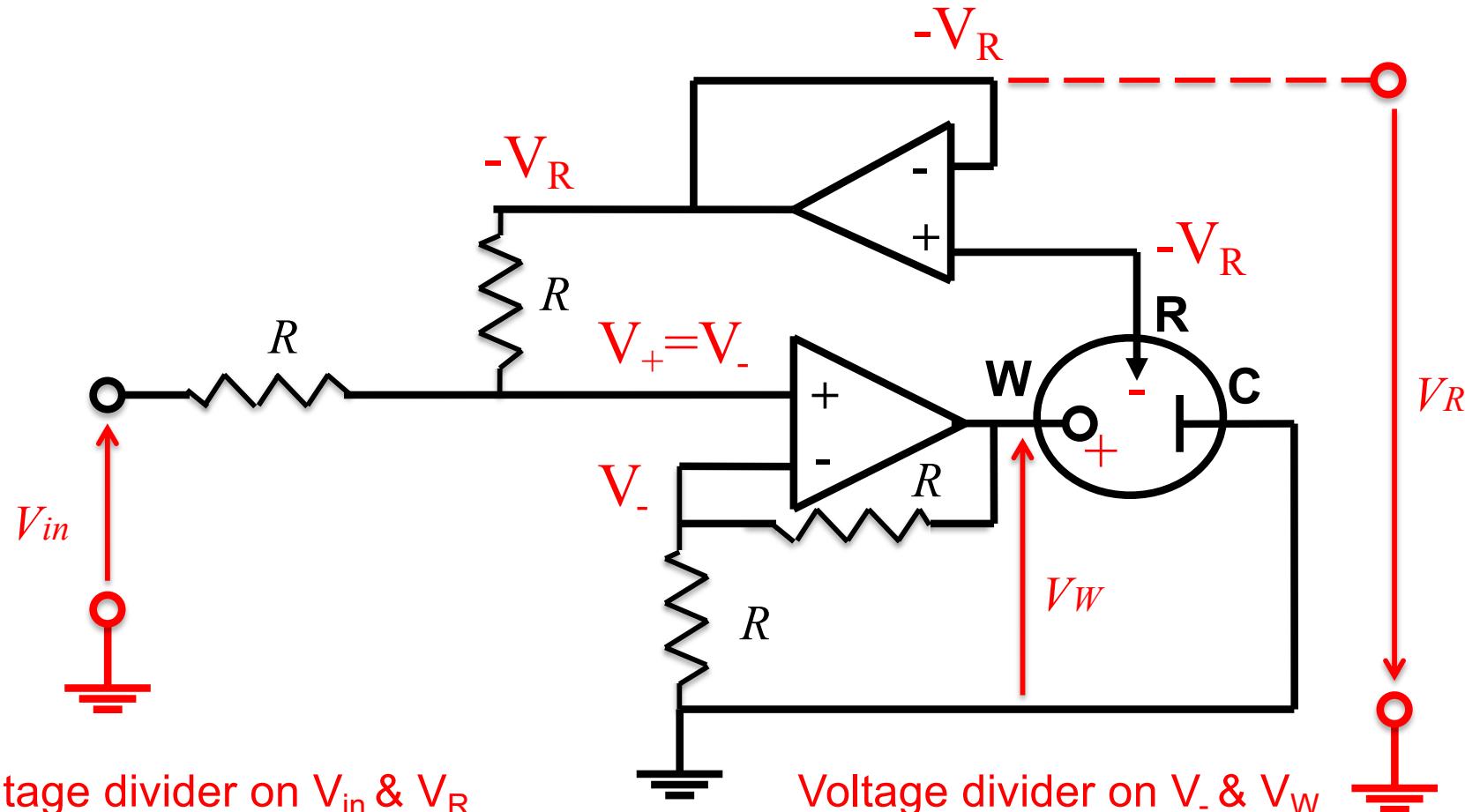


# Grounded Counter



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

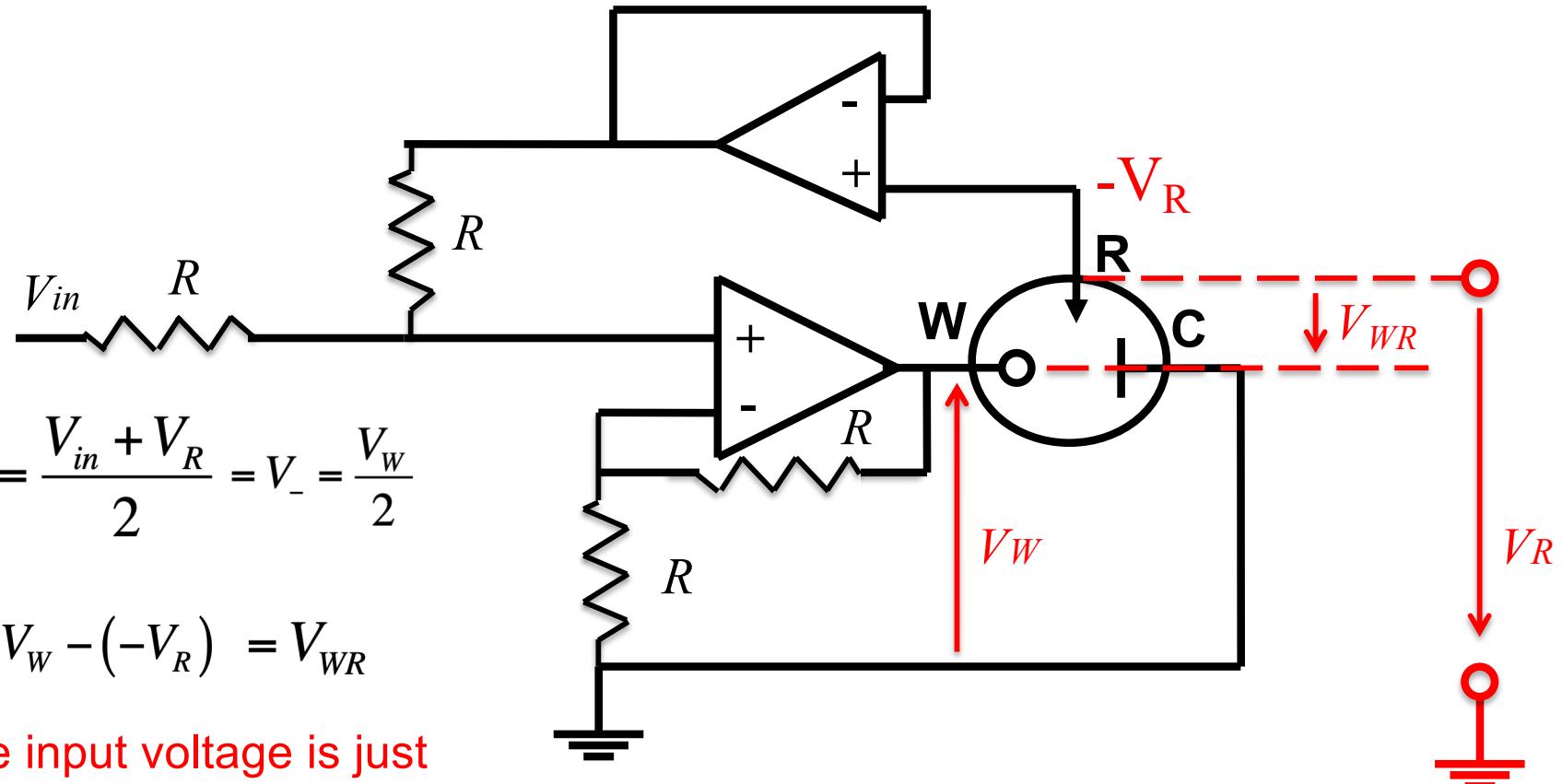
# Grounded Counter



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

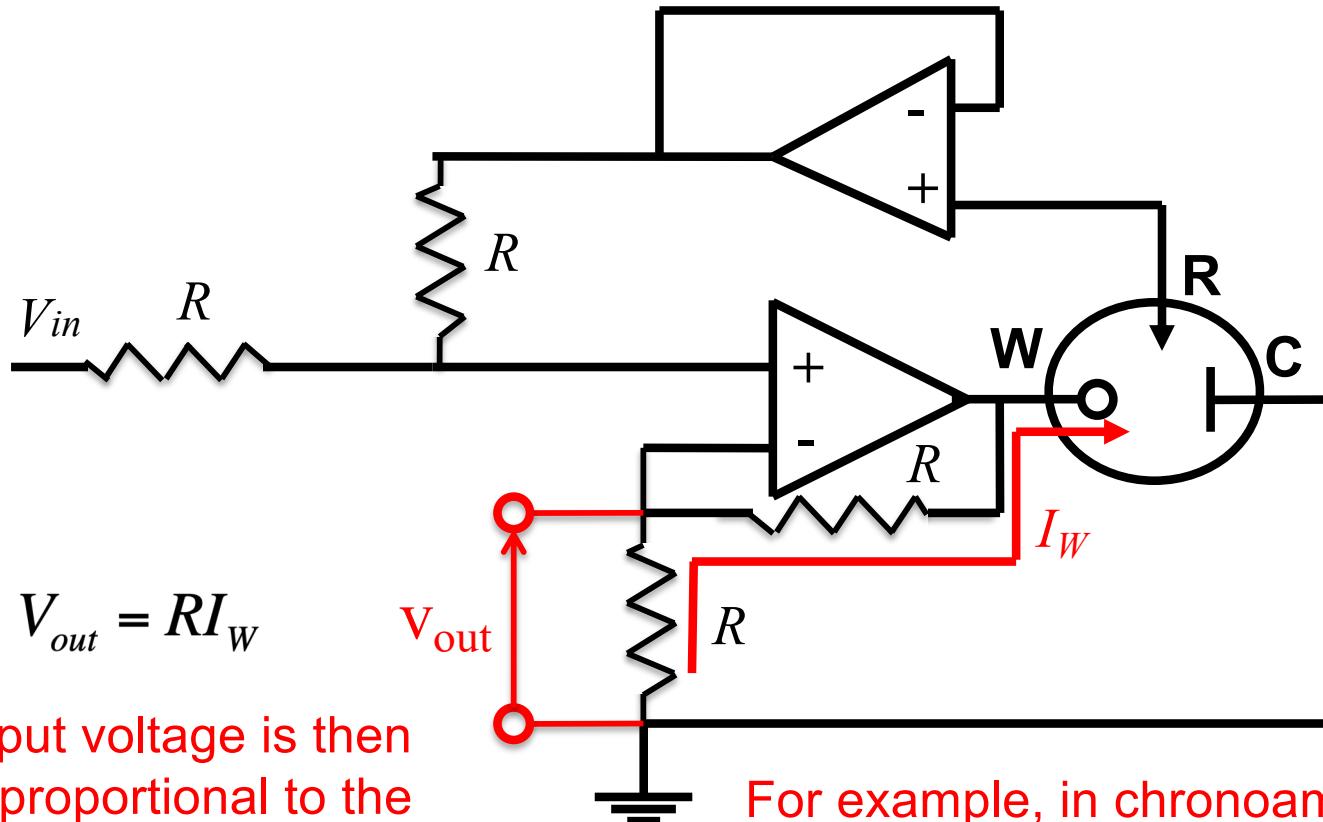
$$V_- = V_W \frac{R}{R+R} = \frac{V_W}{2}$$

# 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

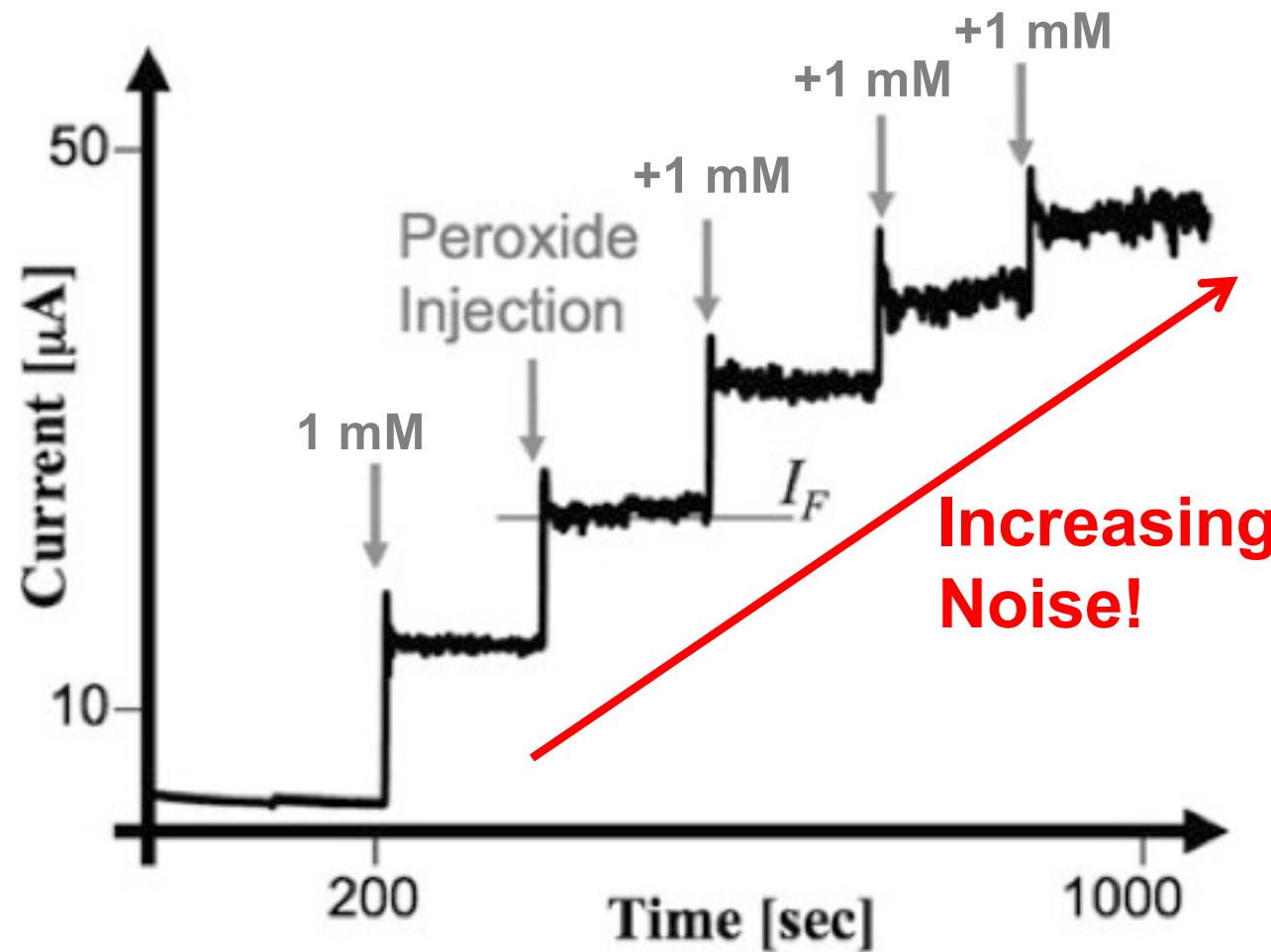


Q9

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

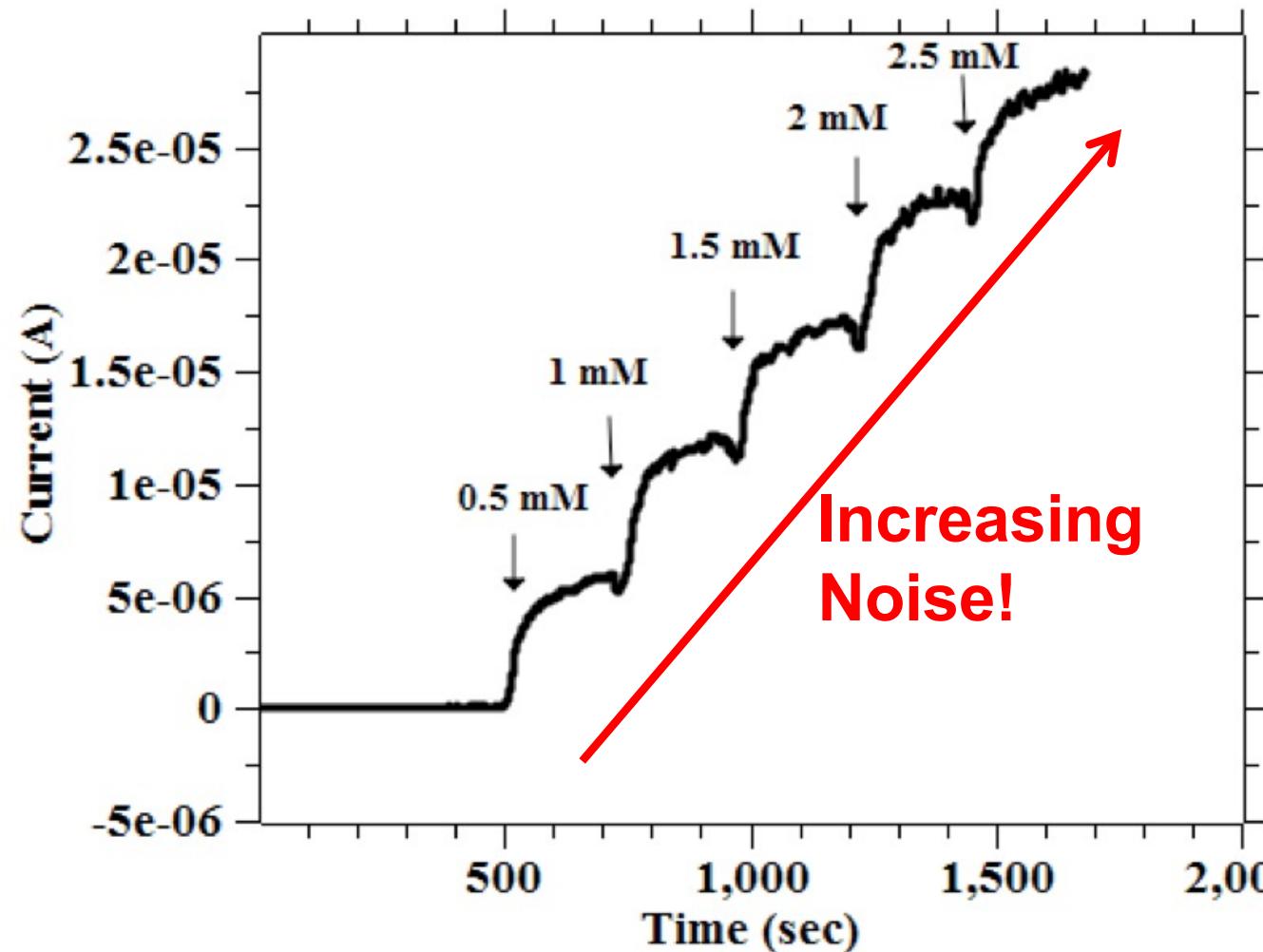
- A. Yes, of course!
- B. Almost, since it is the dominant one
- C.** No, since it is not the dominant one
- D. Not Really

# Noise @ the Bio-interface



Typical chronoamperometry (650 mV) on hydrogen peroxide

# Noise @ the Bio-interface



Typical chronoamperometry (300 mV) on Ferrocyanide

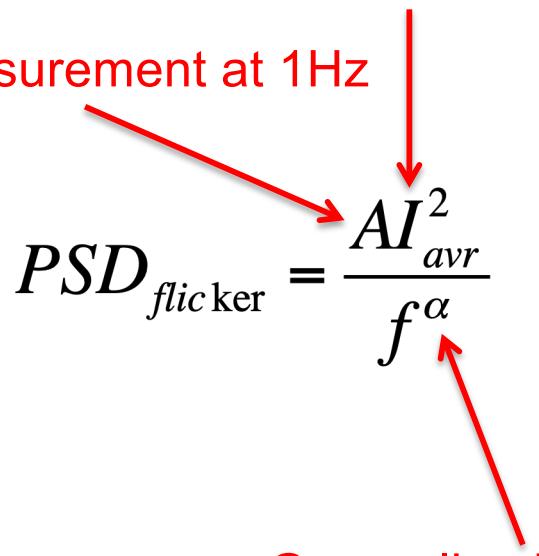
# Noise Power Spectra Density

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

Average current of the biosensor

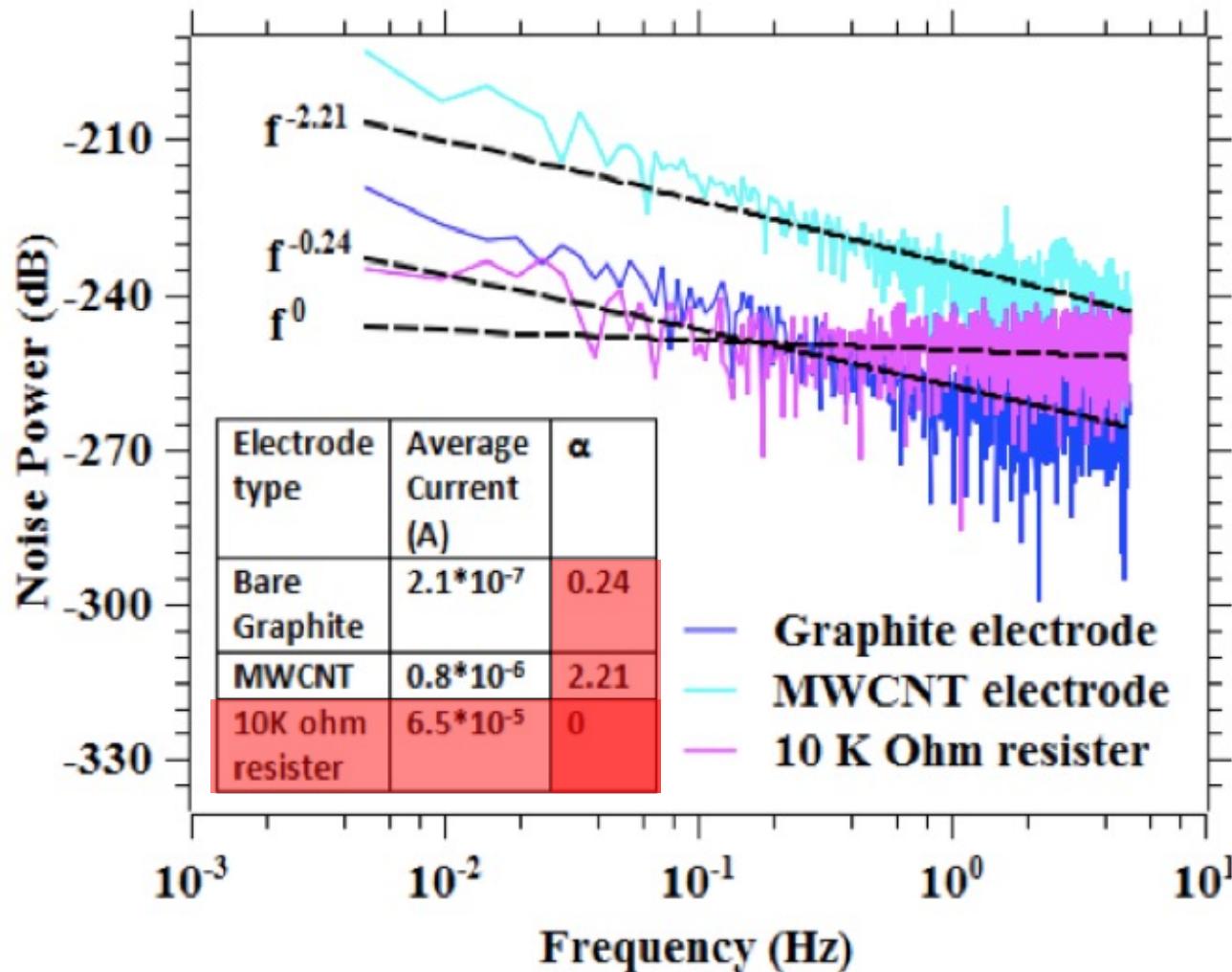
The inverse SNR of the measurement at 1Hz

Generalized frequency dependence



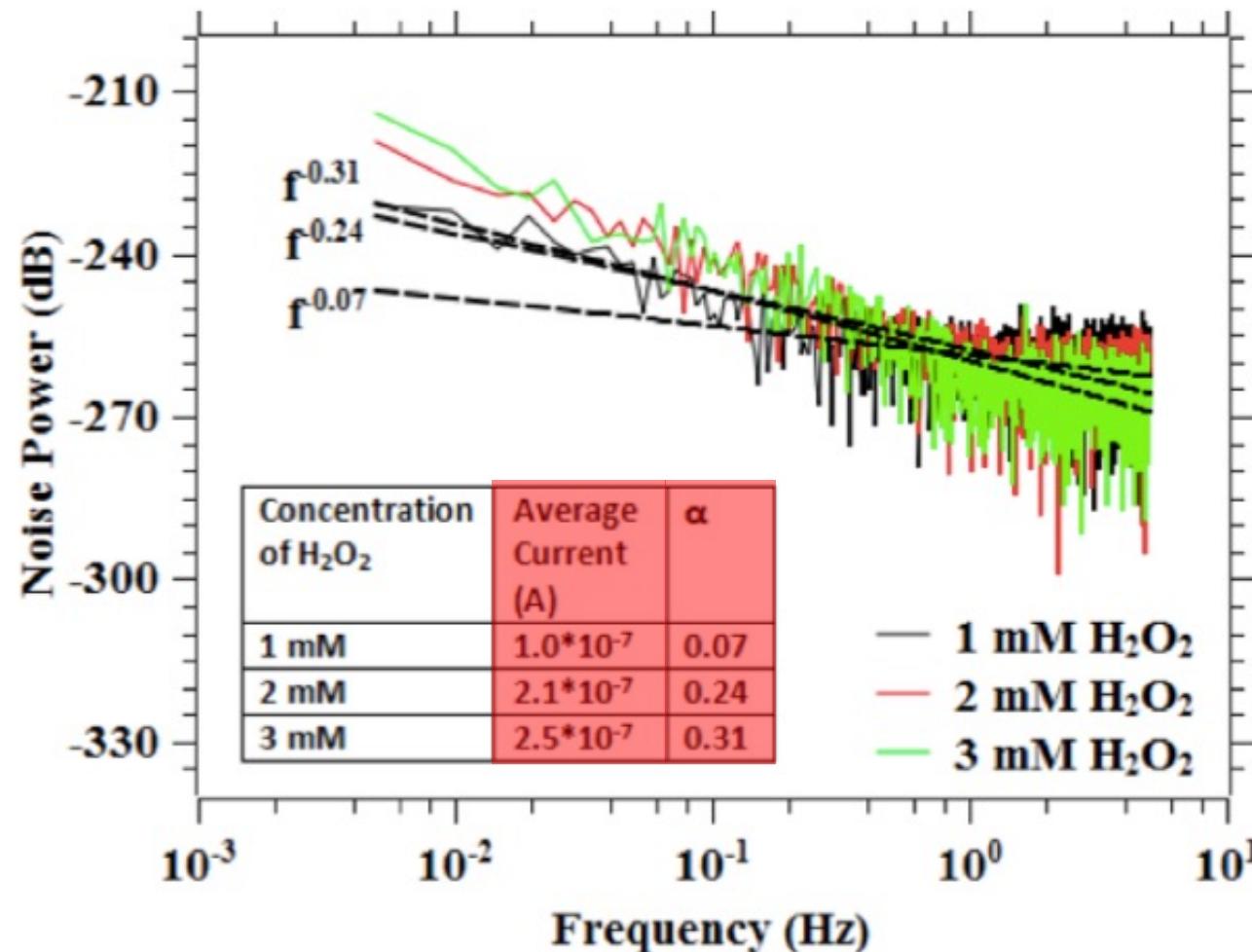
Generalized flicker formula to extract the values of noise coefficients by fittings on the electrochemical interface

# Power Spectra Density



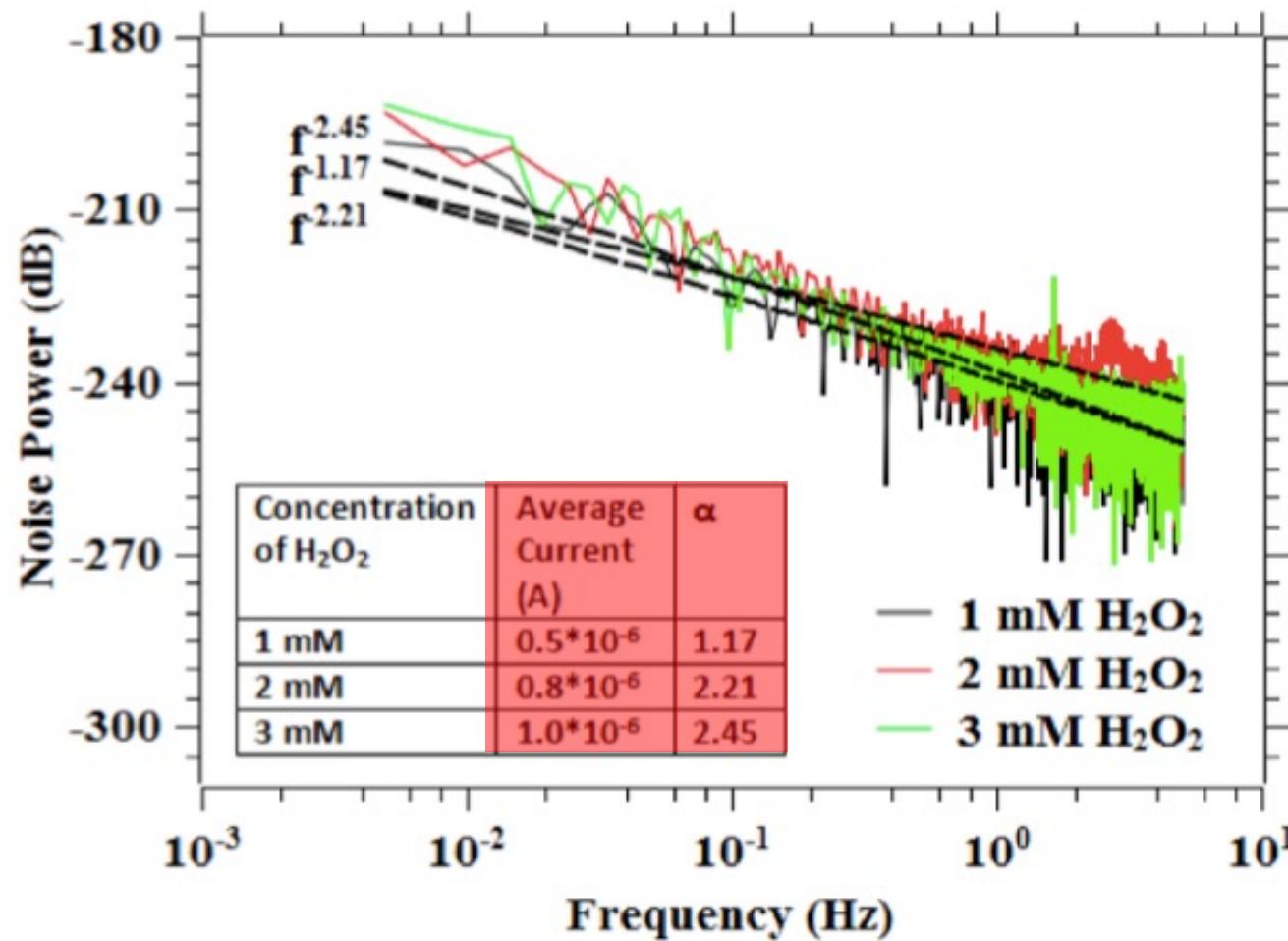
Noise PSD in chronoamperometry measurements with bare and MWCNT electrodes and a  $10 \text{ k}\Omega$  resistor

# Noise PSD on Bare



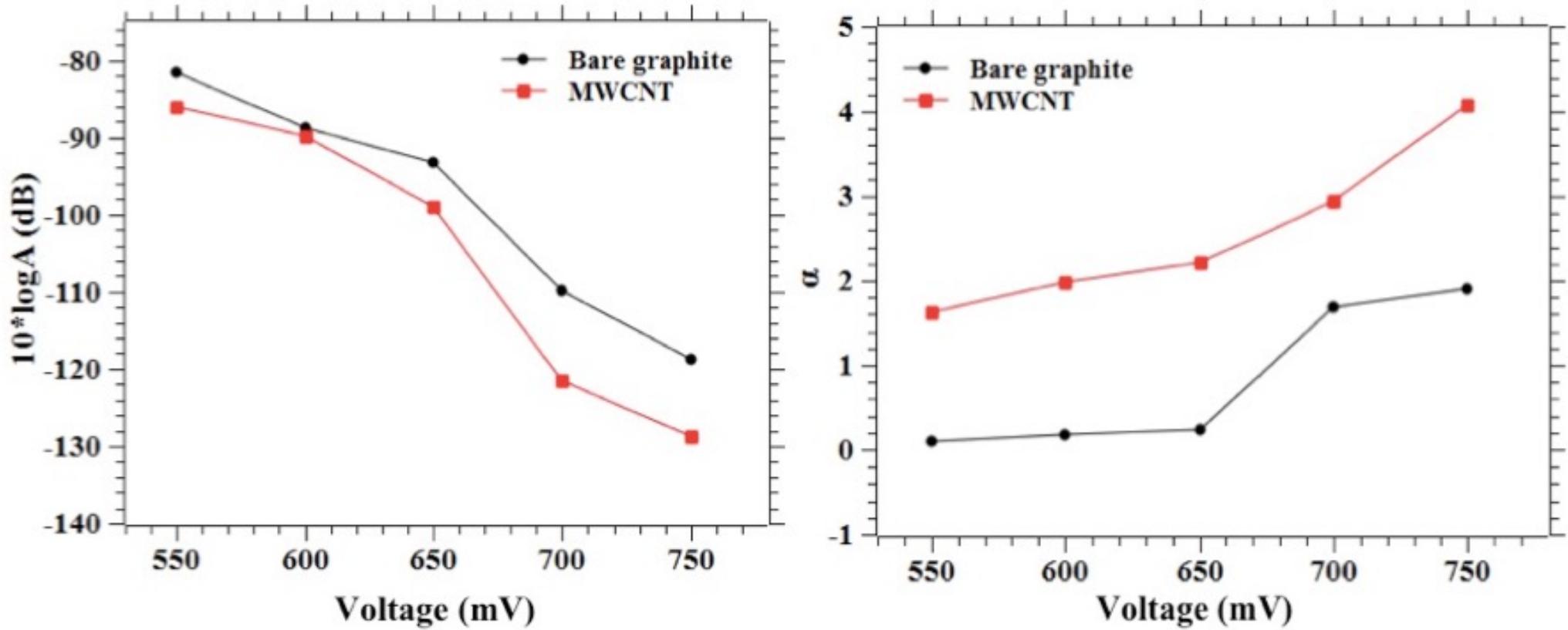
Noise PSD in chronoamperometry measurements (650 mV) of  $\text{H}_2\text{O}_2$  with bare screen-printed electrode

# Noise PSD on MWCNT



Noise PSD in chronoamperometry measurement (650 mV) of  $\text{H}_2\text{O}_2$  with MWCNT structured electrode

# Dependence by the Voltage



Values of parameters A (left) and  $\alpha$  (right) versus the applied voltage, estimated on 2mM of  $\text{H}_2\text{O}_2$

# Equivalent circuit with all the current sources

