Electrical and Electronics Engineering

EE-518

Analog Circuits for Biochip

Master in Electrical and Electronics Engineering

EE-518: Analog Circuits for Biochip

	Subject of the week	Chapter' paragraphs
Week 1	Biochips & Related Applications (Sandro)	§1.1-1.4*
Week 2	Equivalent Circuits for Bio/CMOS interfaces (Sandro)	§2.2-3,8-9; §4.4.2-3; §5.5.4; §10.2*
Week 3	Brain/Machine interfaces: Circuit for Electrical Stimulation/Sensing (Sandro)	Course slides (**)
Week 4	Circuits for Amperometric Potentiometric Chemical Sensing (Sandro)	§5.2-3; §10.1-6, and §12.1*
Week 5	Circuits for Capacitive & Impedimetric Chemical Sensing (Sandro)	§5.5 & Chap. 13*
Week 6	Architecture of wireless implantable systems (Alexandre, 3 hours lecture)	Course slides (**)
Week 7	Inductive links TX (power, data) (Alexandre, 2 hours lecture, 1 hour exercise)	Course slides (**)
Week 8	Inductive links RX (Alexandre, 2 hours lecture, 1 hour exercise)	Course slides (**)
18-23/04	EASTER HOLIDAY	
Week 9	RF telemetry TX, RX (power, data) (Alexandre, 2 hours lecture, 1 hour exercise)	Course slides (**)
Week 10	RF telemetry (Alexandre, 1 hour lecture, 2 hours exercises)	Course slides (**)
Week 11	Introduction to antennas and radiation regulations (Anja)	Course slides
Week 12	WBAN Antennas (Anja)	Course slides
Week 13	WBAN Antennas (Anja)	Course slides
Week 14	Review for final exam	-

S. Carrara

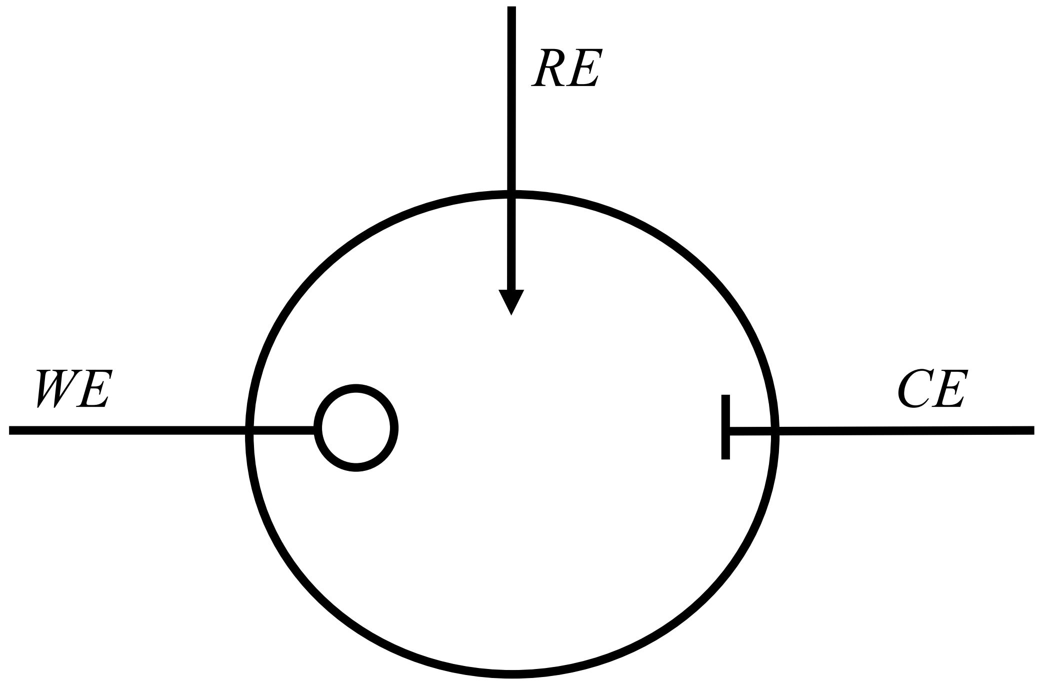
A. Schmid

A. Skrivervik

* S. Carrara, Bio/CMOS interfaces and Co-Design, 2nd edition, Springer, 2024 – ** Supporting reading references announced in the slide set

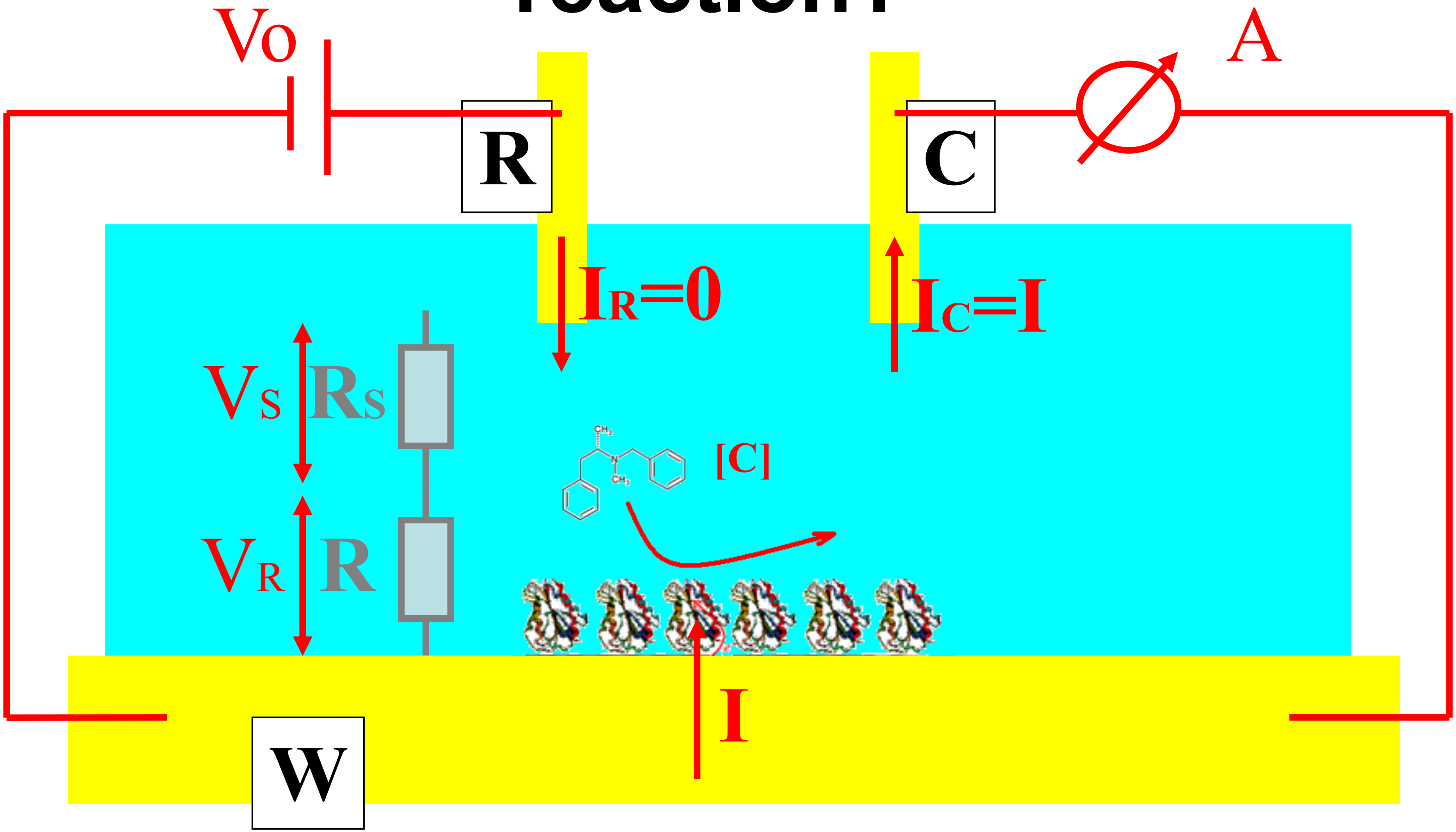
Glucometer on iPhone

The electrochemical Cell

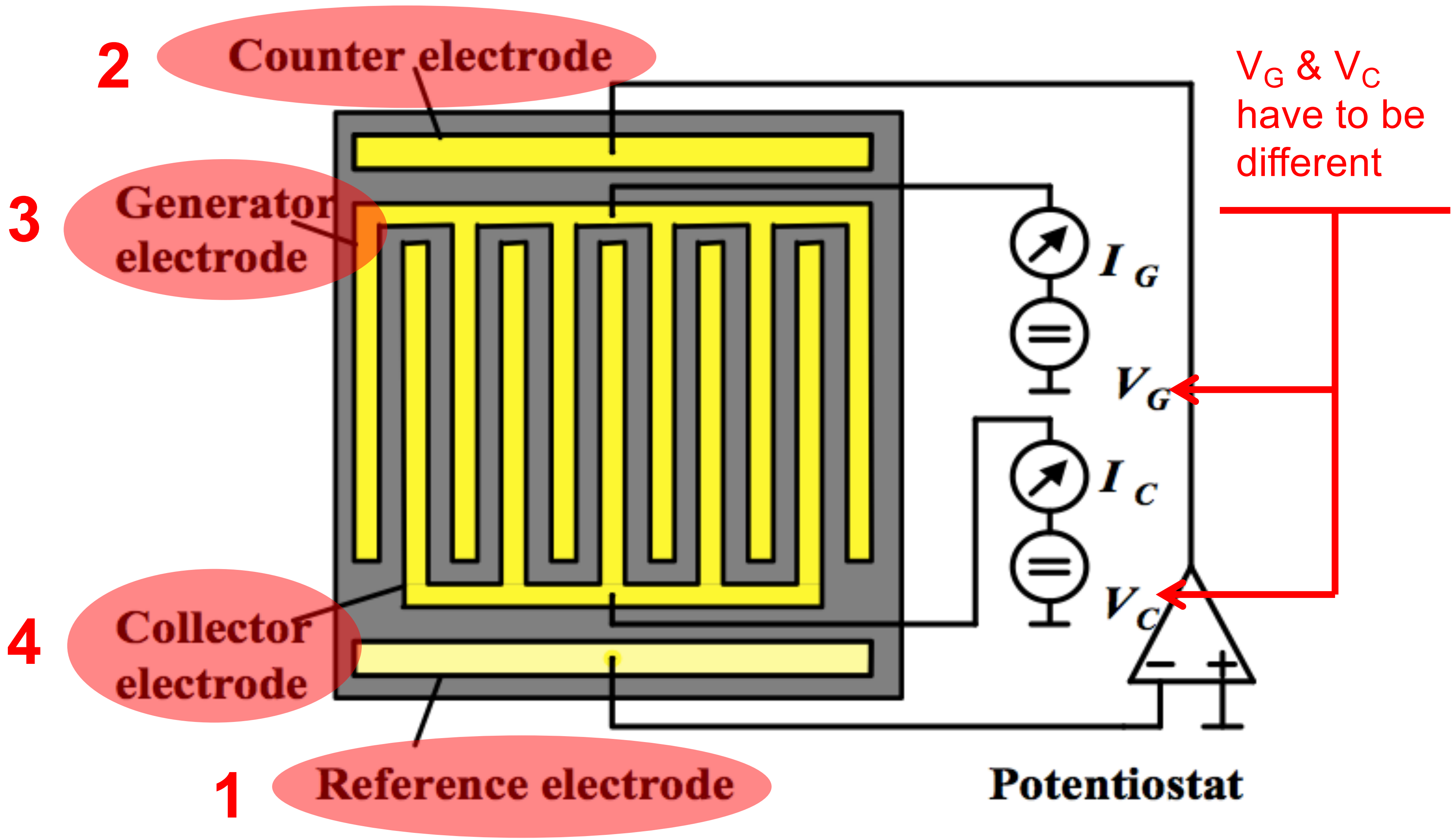


The typical electrochemical cell needs 3 electrodes: the working, the counter, and the reference

How to measure a redox reaction?

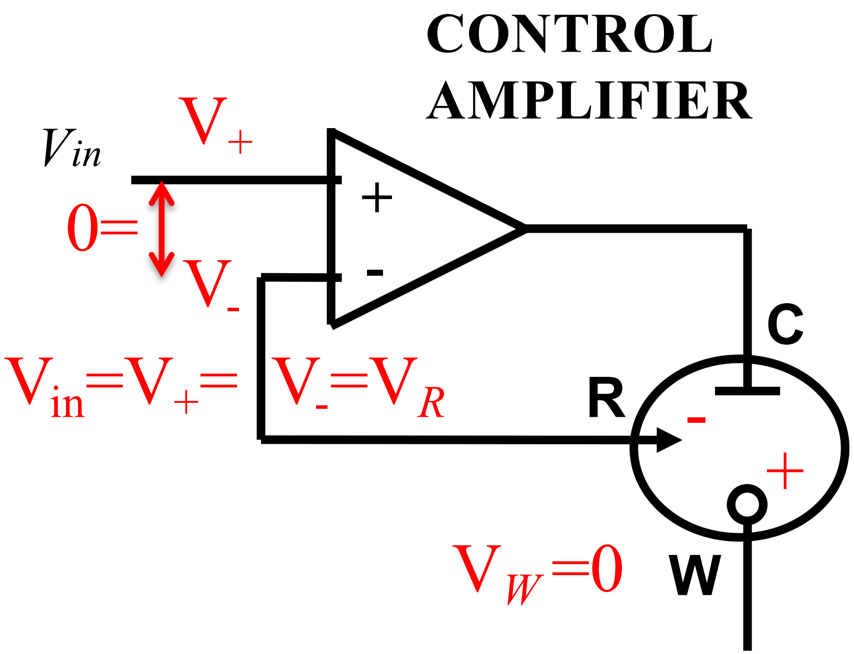


The 4e Electrochemical Cell



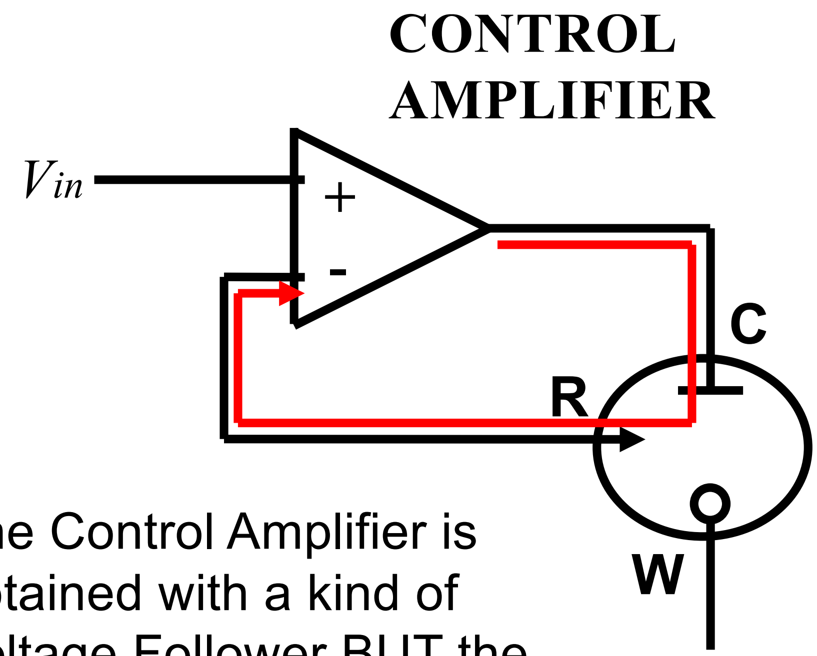
A 4-electrode Electrochemical Cell is here required

Control Amplifier @ RE



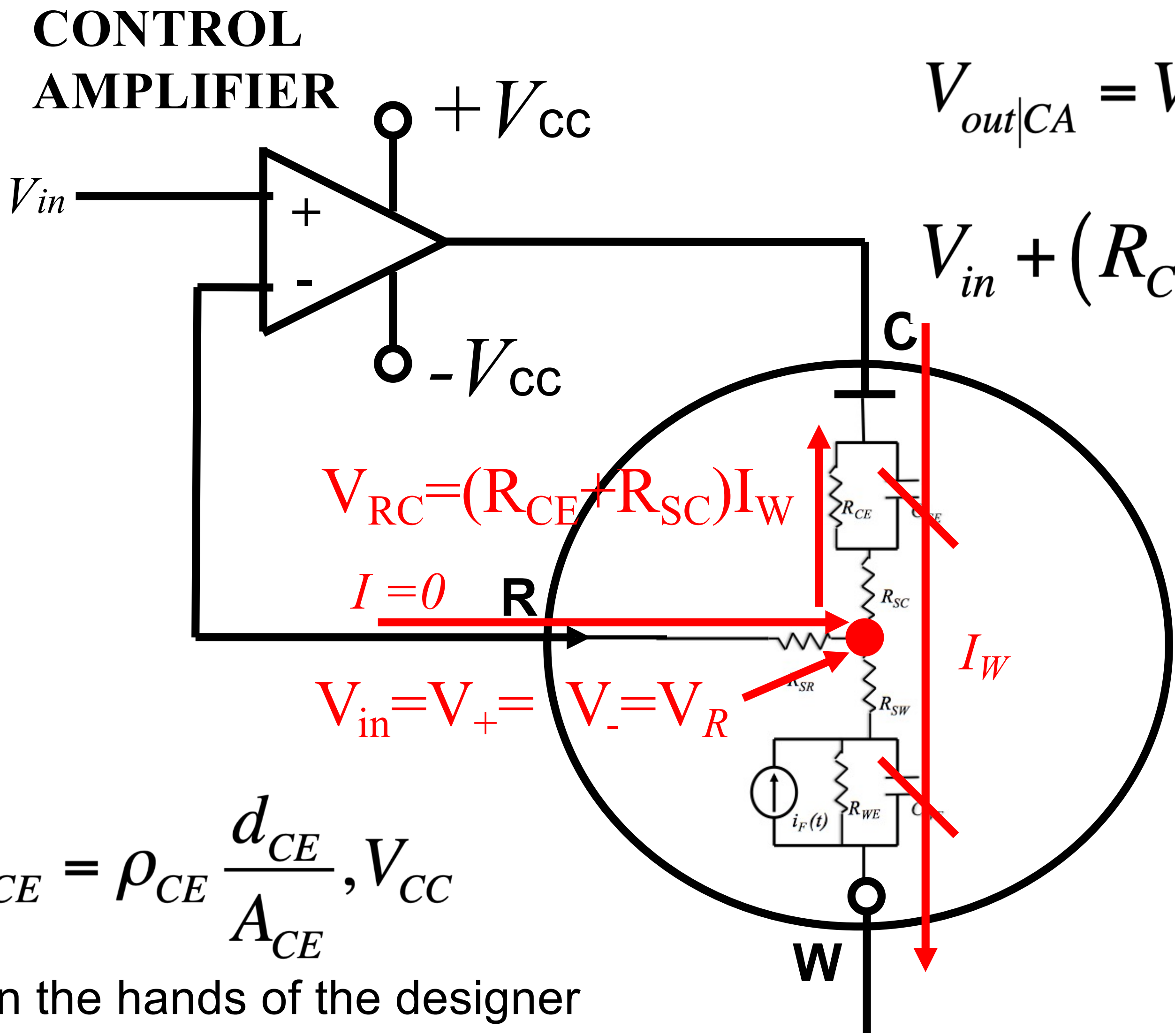
$$V_{in} = V_R = - V_{WR}$$

Risk of Saturation



1. The Control Amplifier is obtained with a kind of Voltage Follower BUT the Cell is inserted in its feedback loop
2. Thus, the Voltage Follower might saturate if the design (both Cell & Follower) are not co-designed properly

Risk of Saturation



$$V_{out|CA} = V_{in} + (R_{CE} + R_{SC}) I_W$$

$$V_{in} + (R_{CE} + R_{SC}) I_W > V_{CC}$$

The Control Amplifier is then in SATURATION!

$$V_{in}, R_{SC}, I_W$$

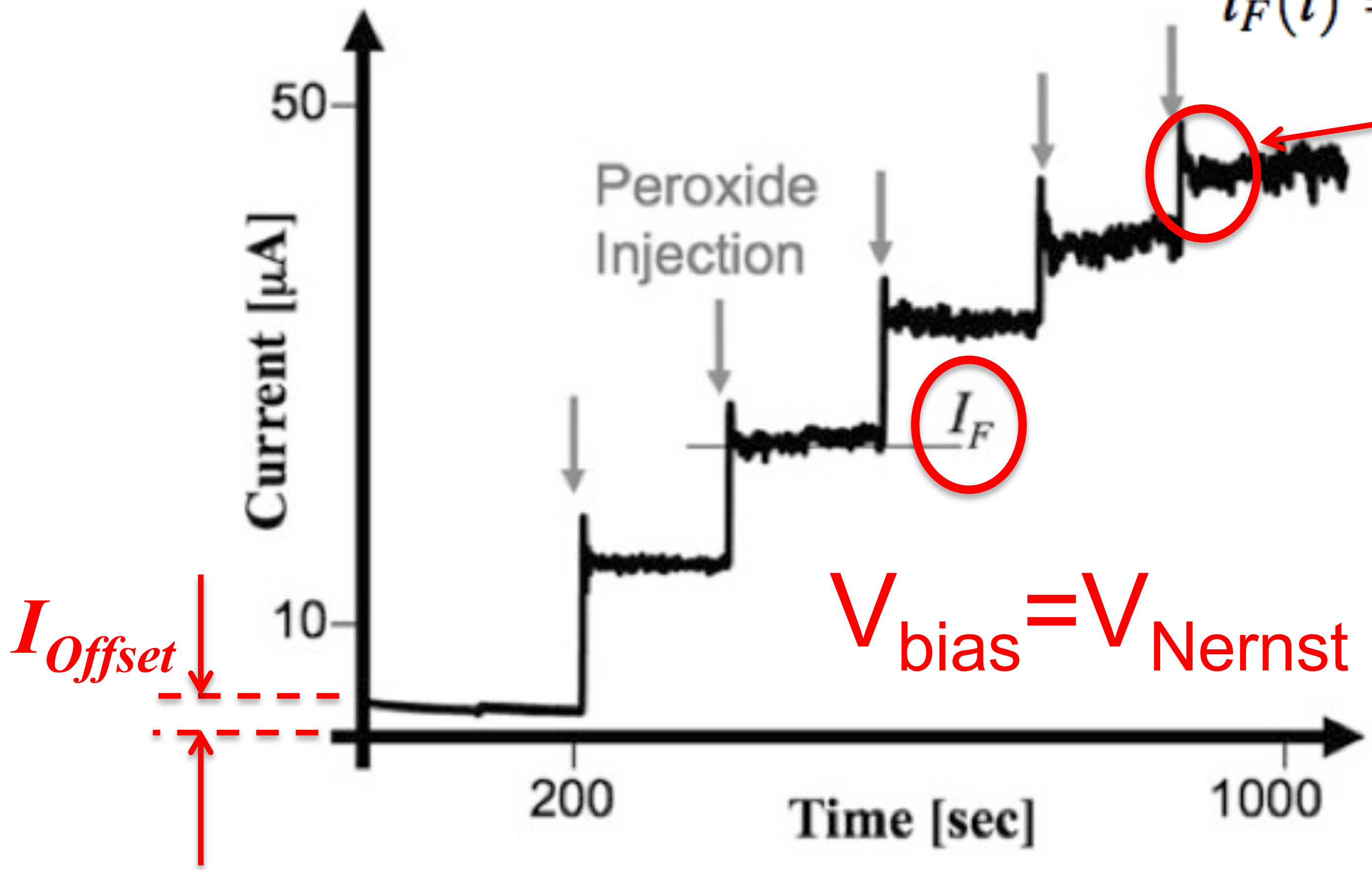
Typically depend on the application (kind of redox we are monitoring)

$$R_{CE} = \rho_{CE} \frac{d_{CE}}{A_{CE}}, V_{CC}$$

Are on the hands of the designer (the size of the counter electrode and/or the circuit powering)

Faradaic Current @ Fixed Bias

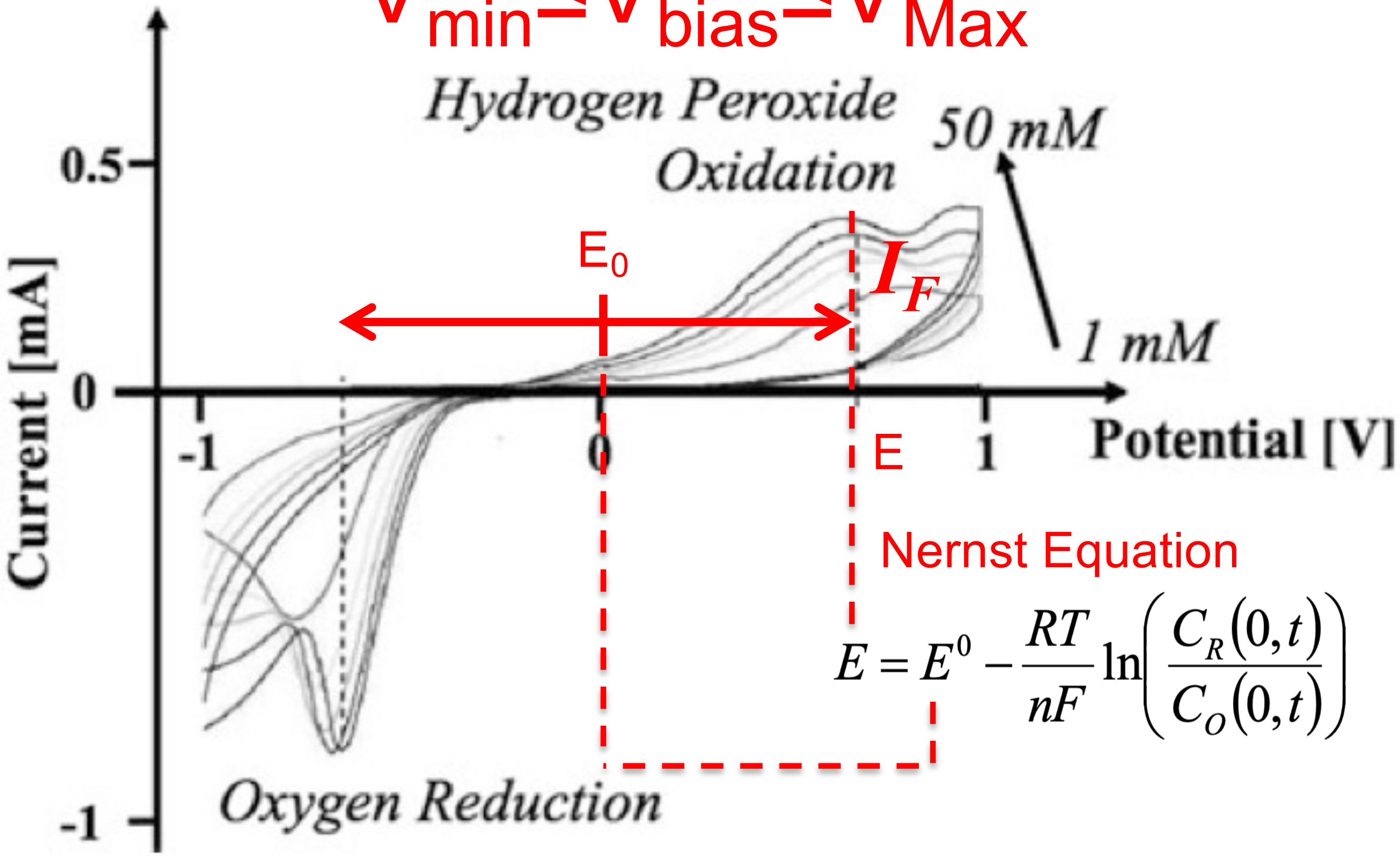
$$i_F(t) = \frac{nFA\sqrt{D}C(t)}{\sqrt{\pi t}}$$



Typical curve in chronoamperometry

Faradaic Current in Voltage Scan

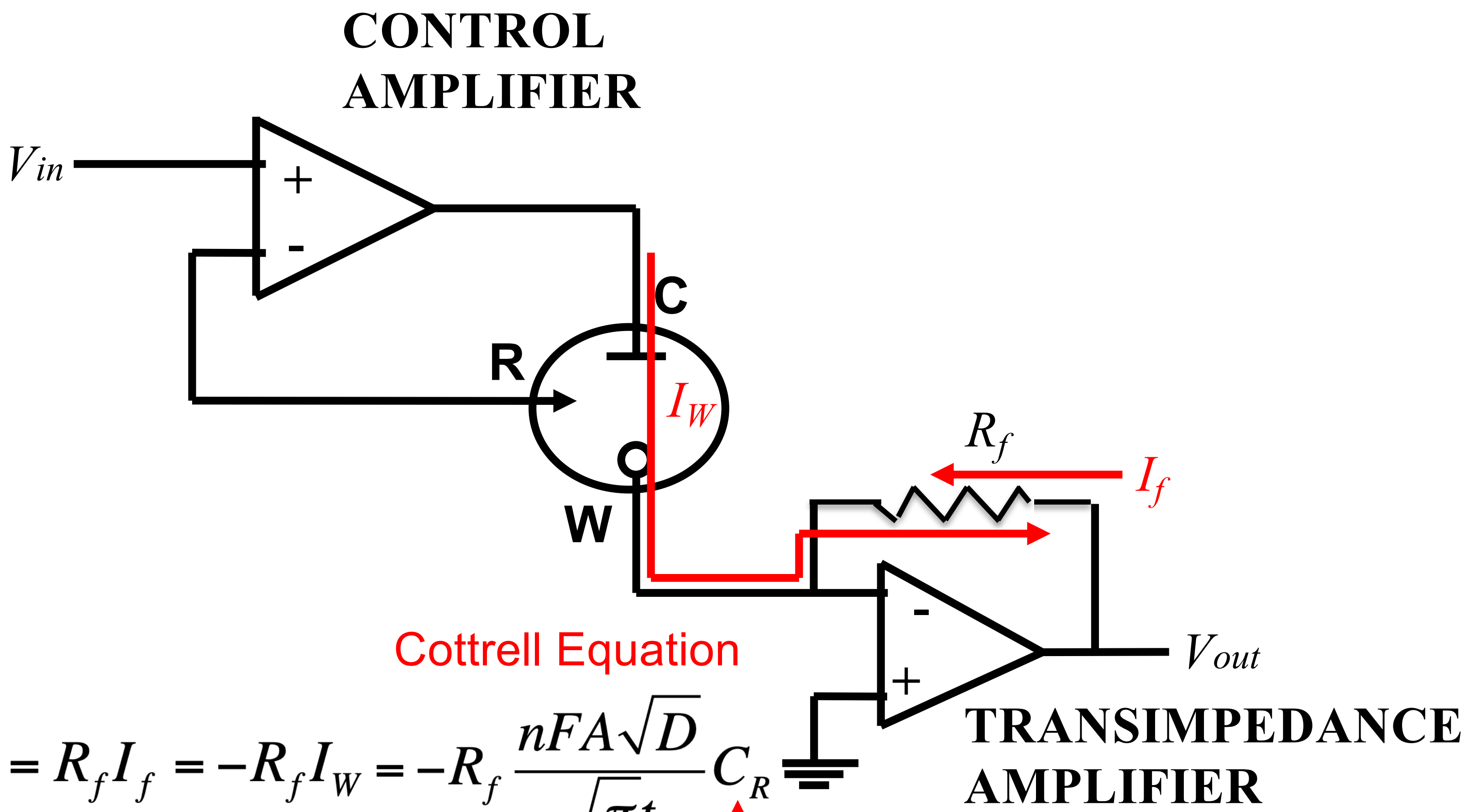
$V_{min} \leq V_{bias} \leq V_{Max}$



$$E = E^0 - \frac{RT}{nF} \ln\left(\frac{C_R(0,t)}{C_O(0,t)}\right)$$

O+ reduction and H_2O_2 oxidation observed in Cyclic Voltammetry (CV)

Transimpedance Amplifier @ WE

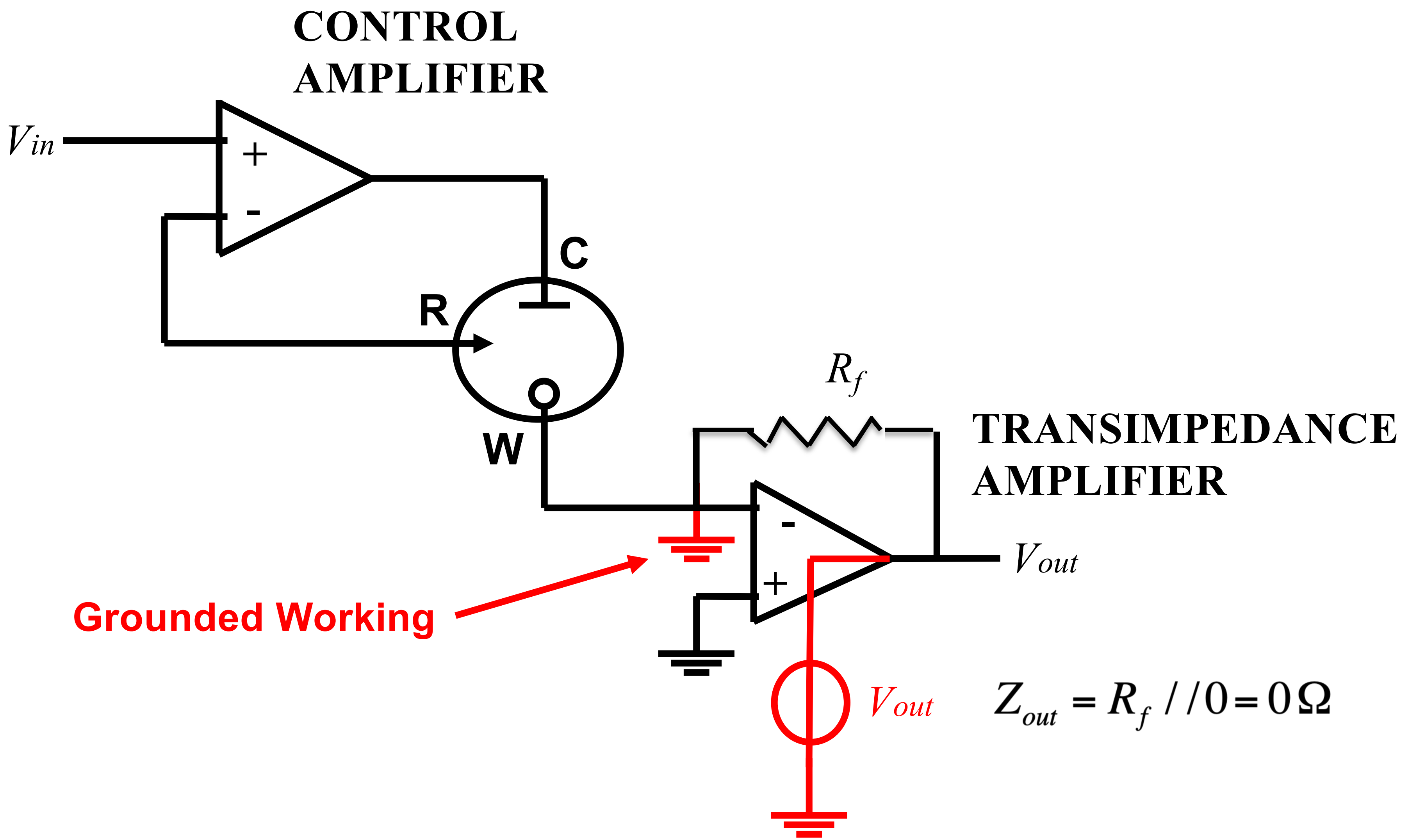


Cottrell Equation

$$V_{out} = R_f I_f = -R_f I_W = -R_f \frac{nFA\sqrt{D}}{\sqrt{\pi t}} C_R$$

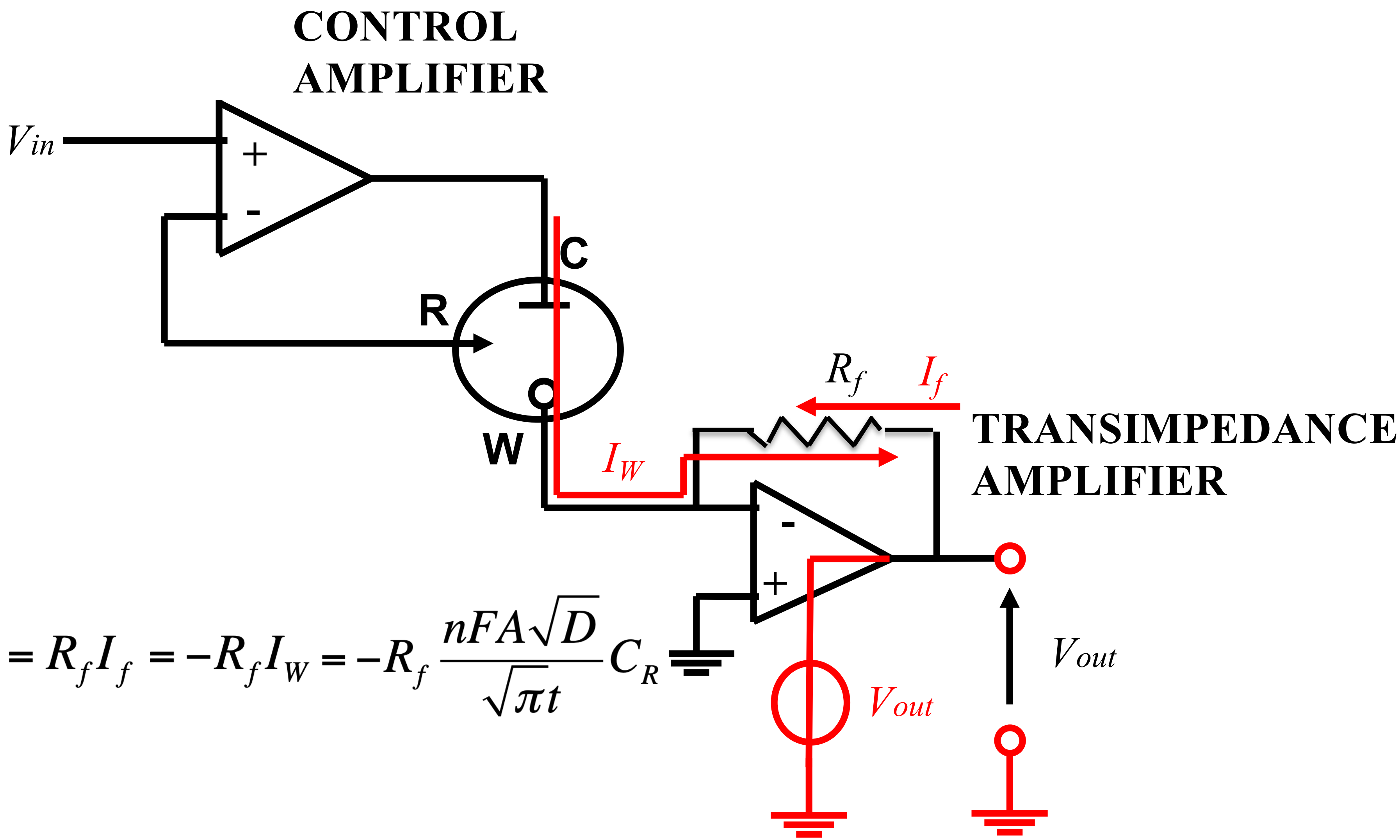
Concentration of Redox specie

Grounded Working



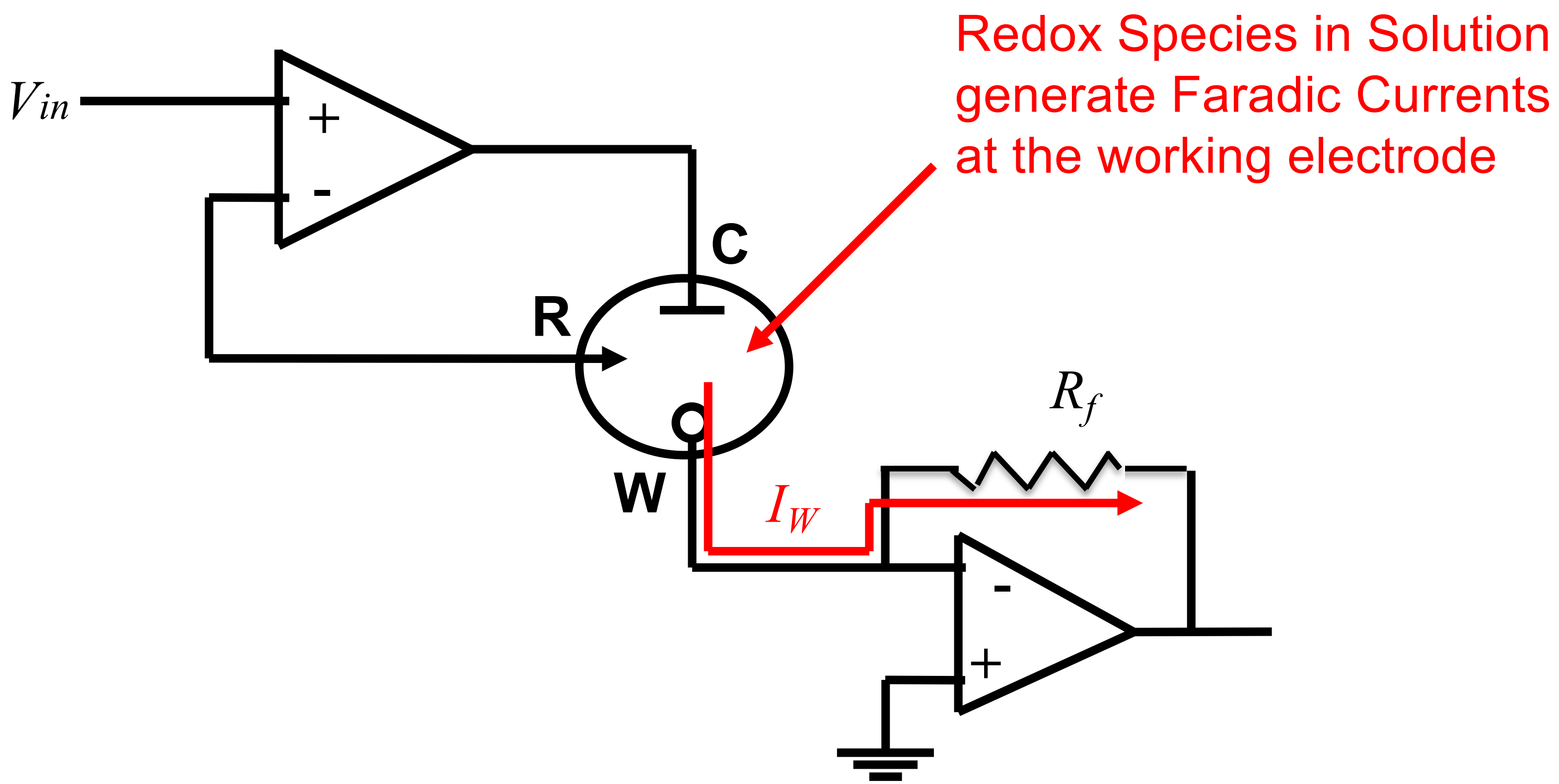
$$Z_{out} = R_f // 0 = 0\Omega$$

Current-to-Voltage Conversion

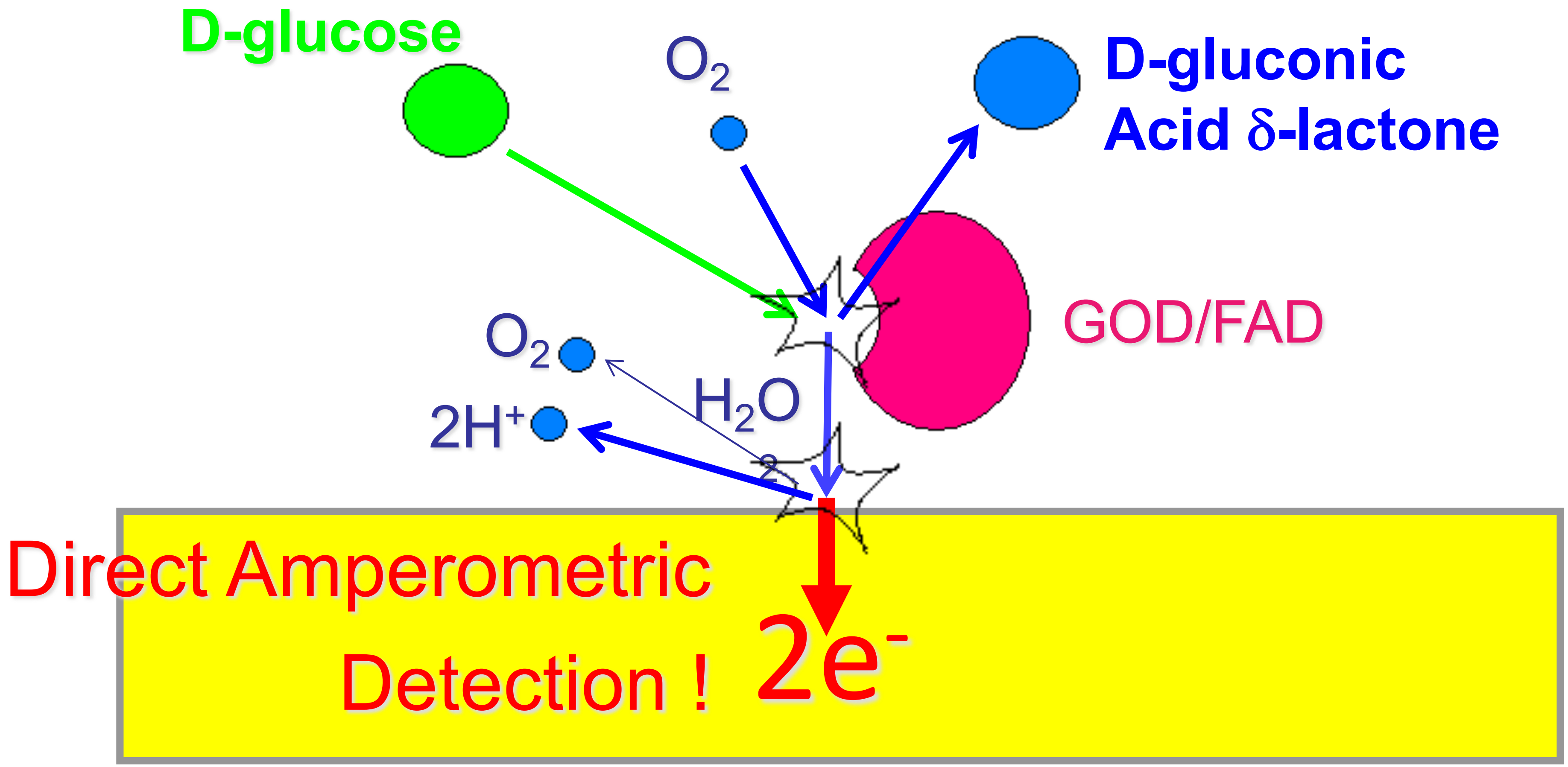


$$V_{out} = R_f I_f = -R_f I_W = -R_f \frac{nFA\sqrt{D}}{\sqrt{\pi t}} C_R$$

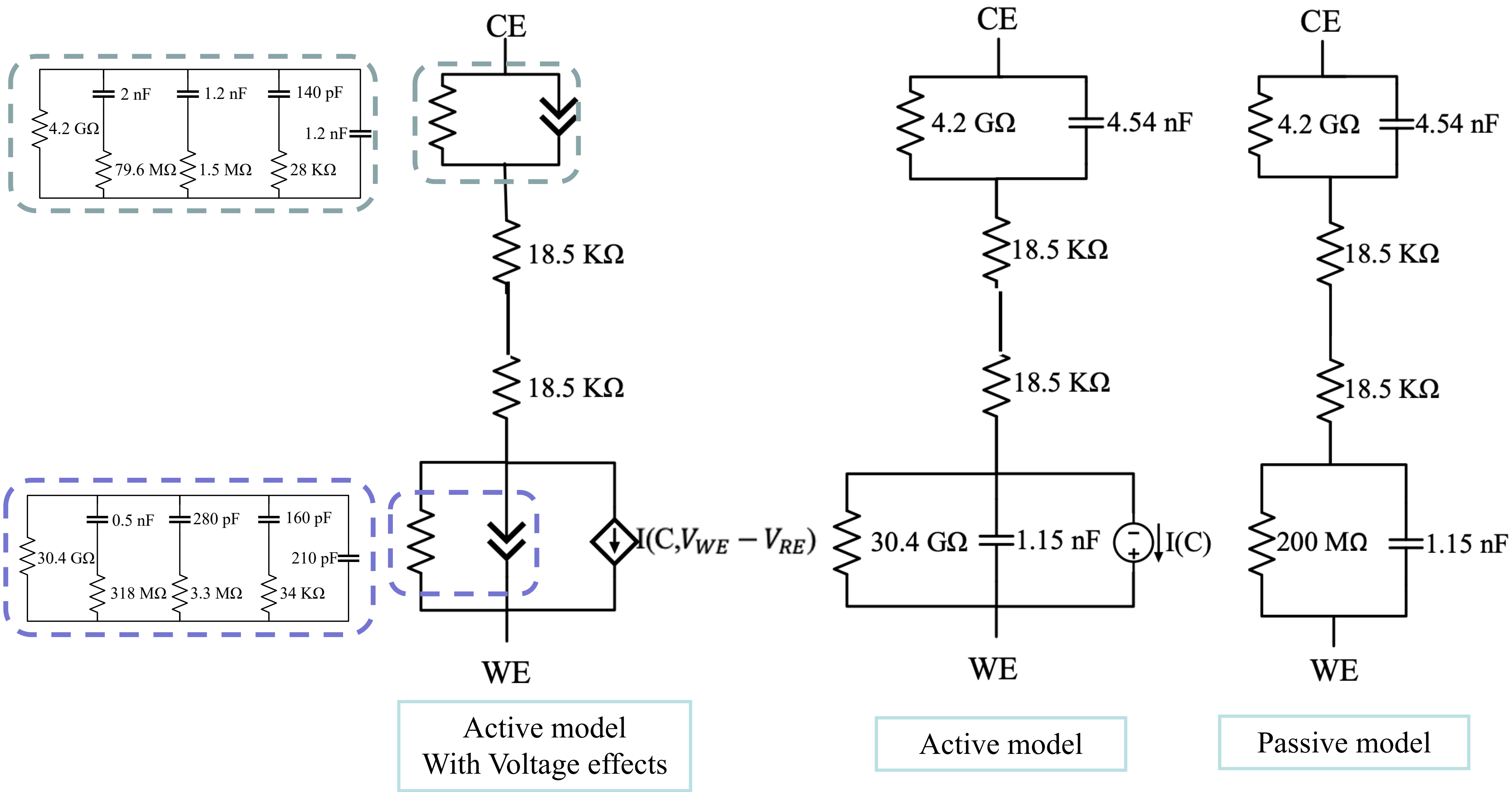
Inside the Cell: Faradaic Currents



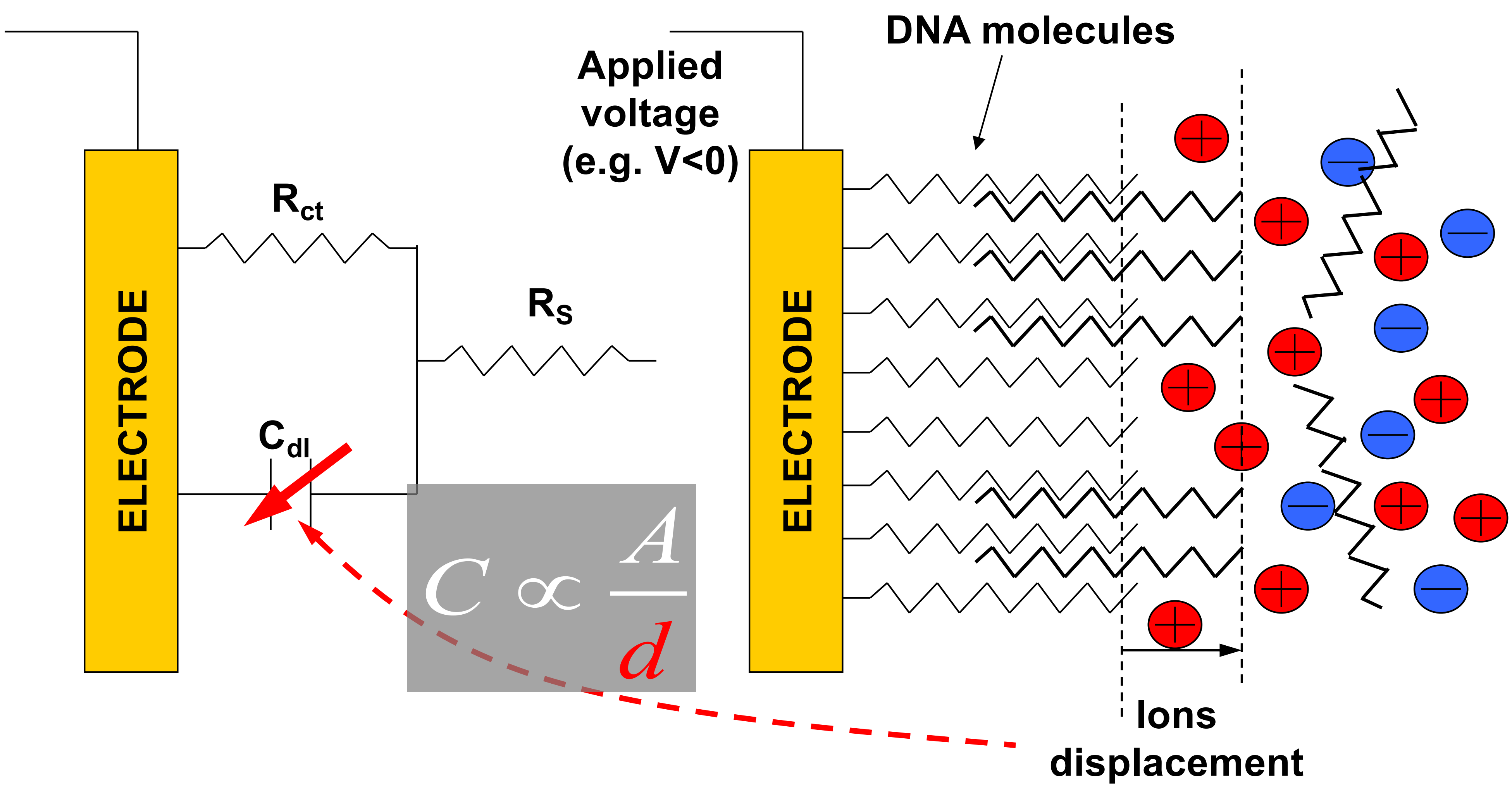
Oxidases based detection



Equivalent Circuit for Bio/CMOS interfaces

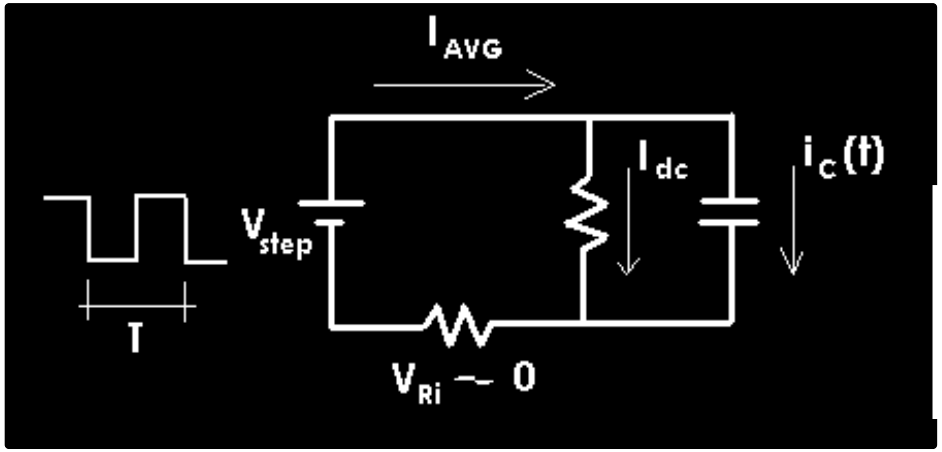


The Capacitance DNA Detection



Unlabeled ssDNA may be detected with capacitance measurements as due to charge displacement

Charge-Based Capacitance Measurement (CBCM)



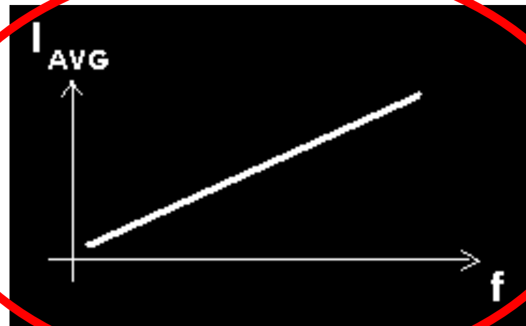
$$i(t) = I_{dc} + i_C(t)$$

Frequency!

$$I_{AVG} = \frac{I_{dc}}{2} + \frac{1}{T}\int_0^{T/2} i_C(t)\,dt$$

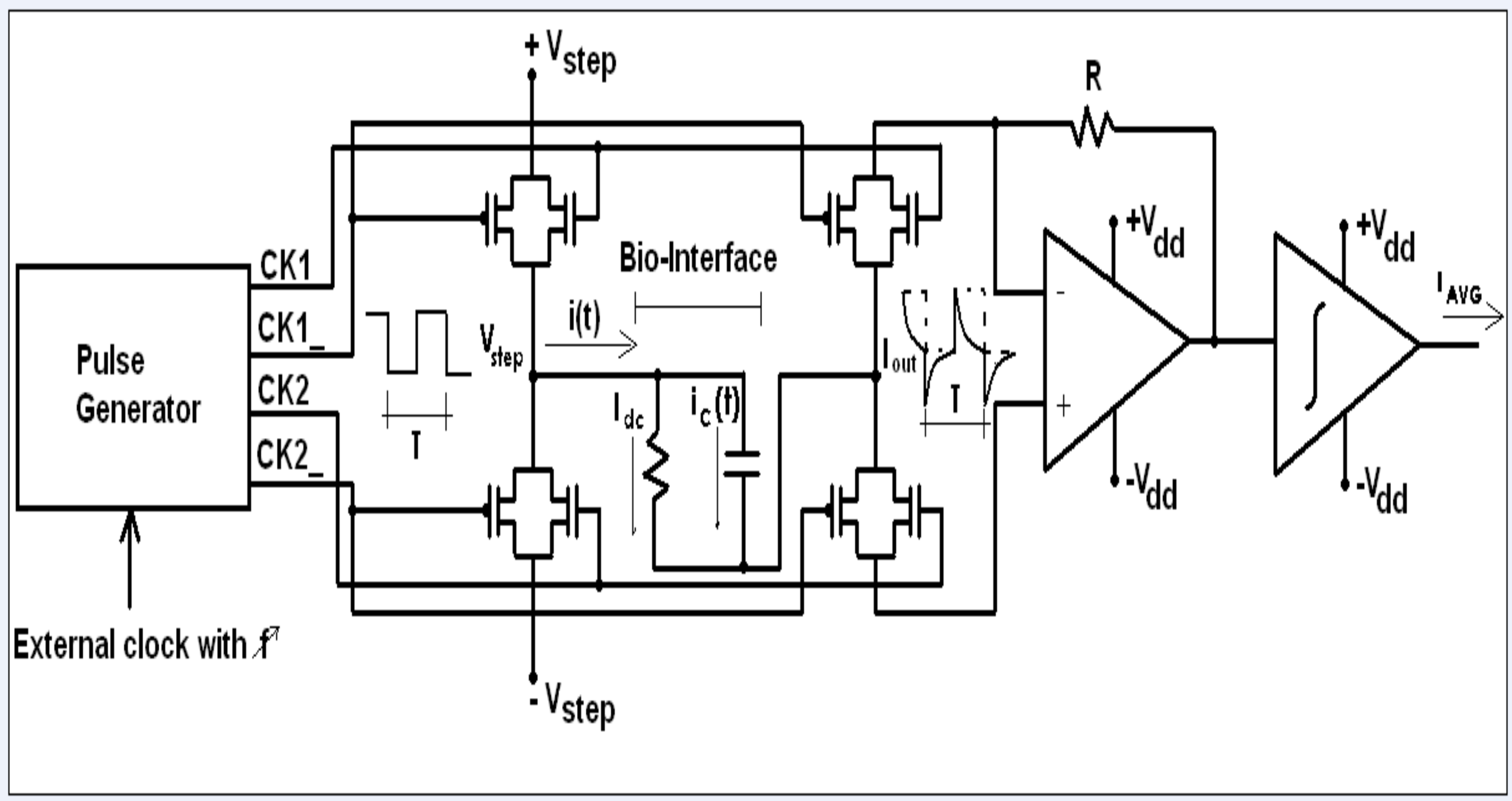
$$I_{AVG} = \frac{I_{dc}}{2} + C V_{step} f$$

THE CAPACITANCE !



Method for a precise Capacitance measurement

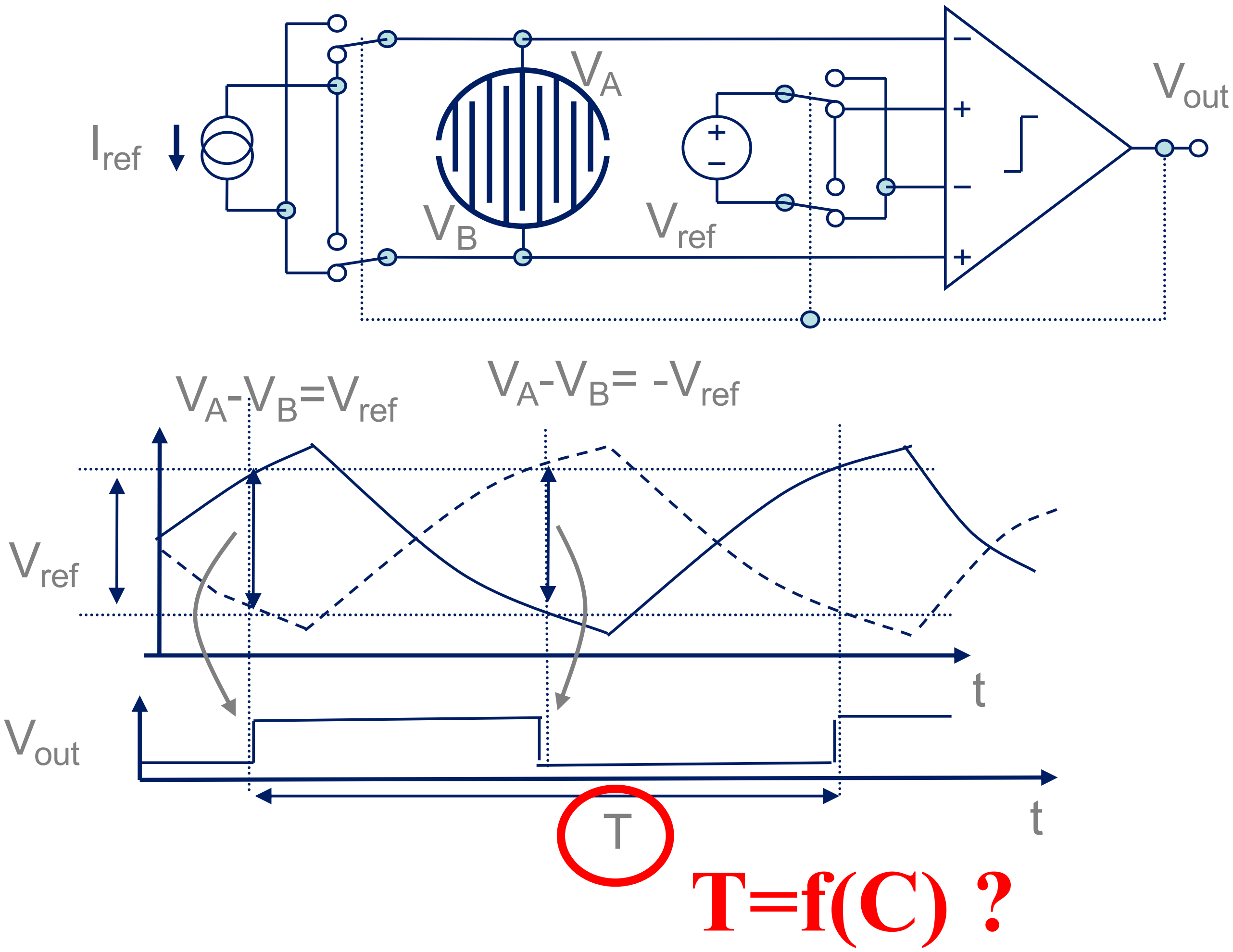
CMOS for CBCM detection



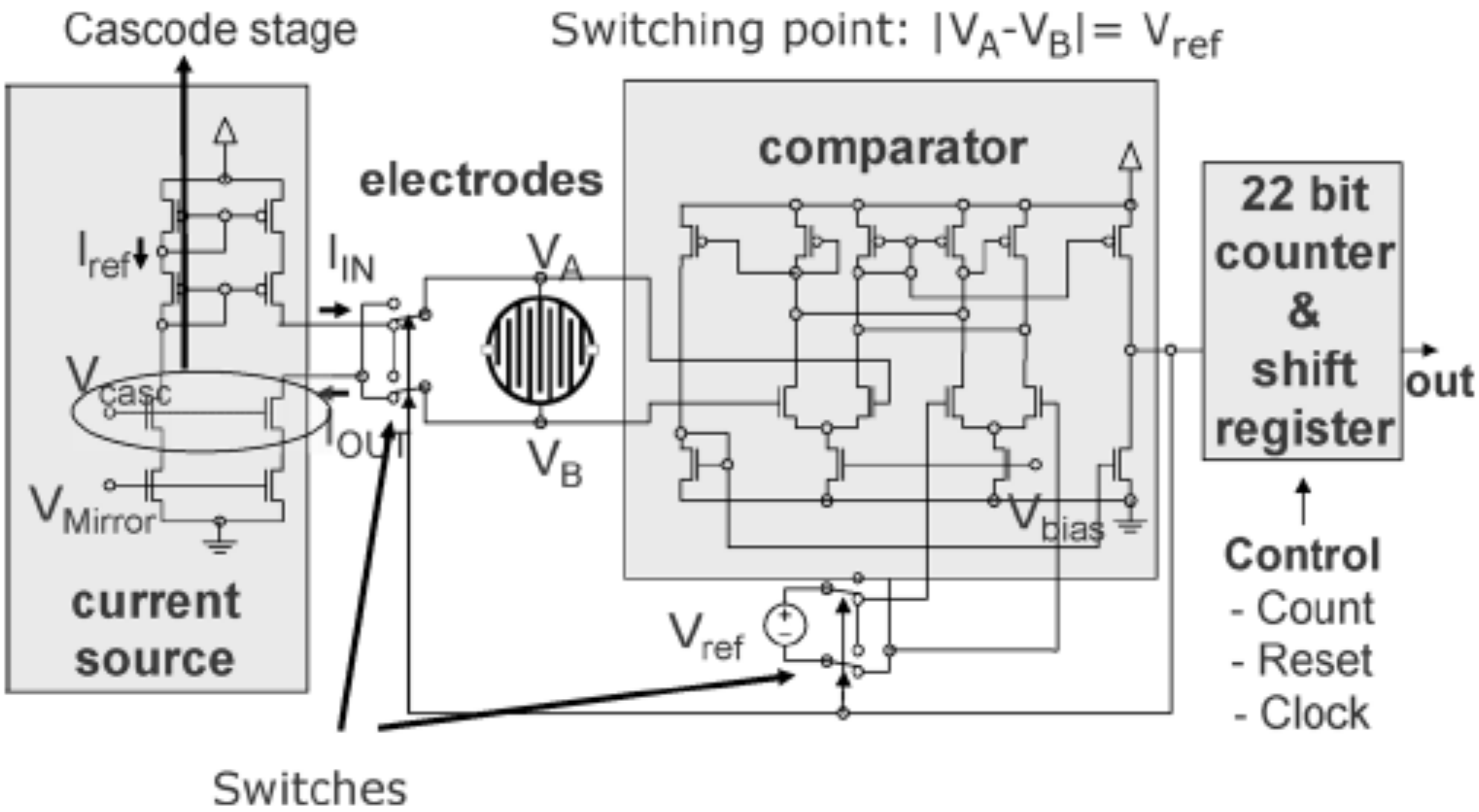
The circuit assures the square signal generator, an inverters, and an integrator to calculate the average current

Frequency to Capacitance Measurement (FTCM)

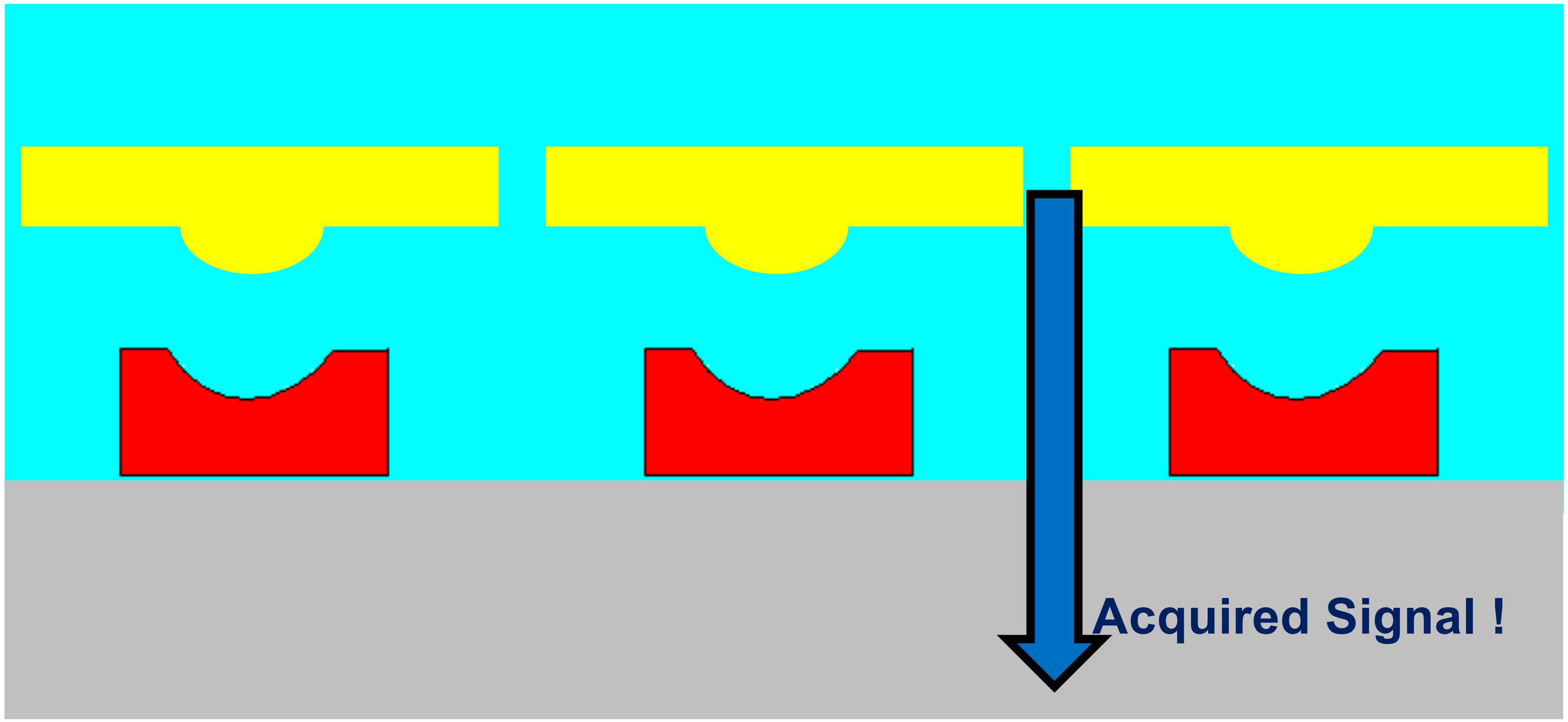
Principle: Frequency To Capacitance Mode



Chip Architecture (FTCM)

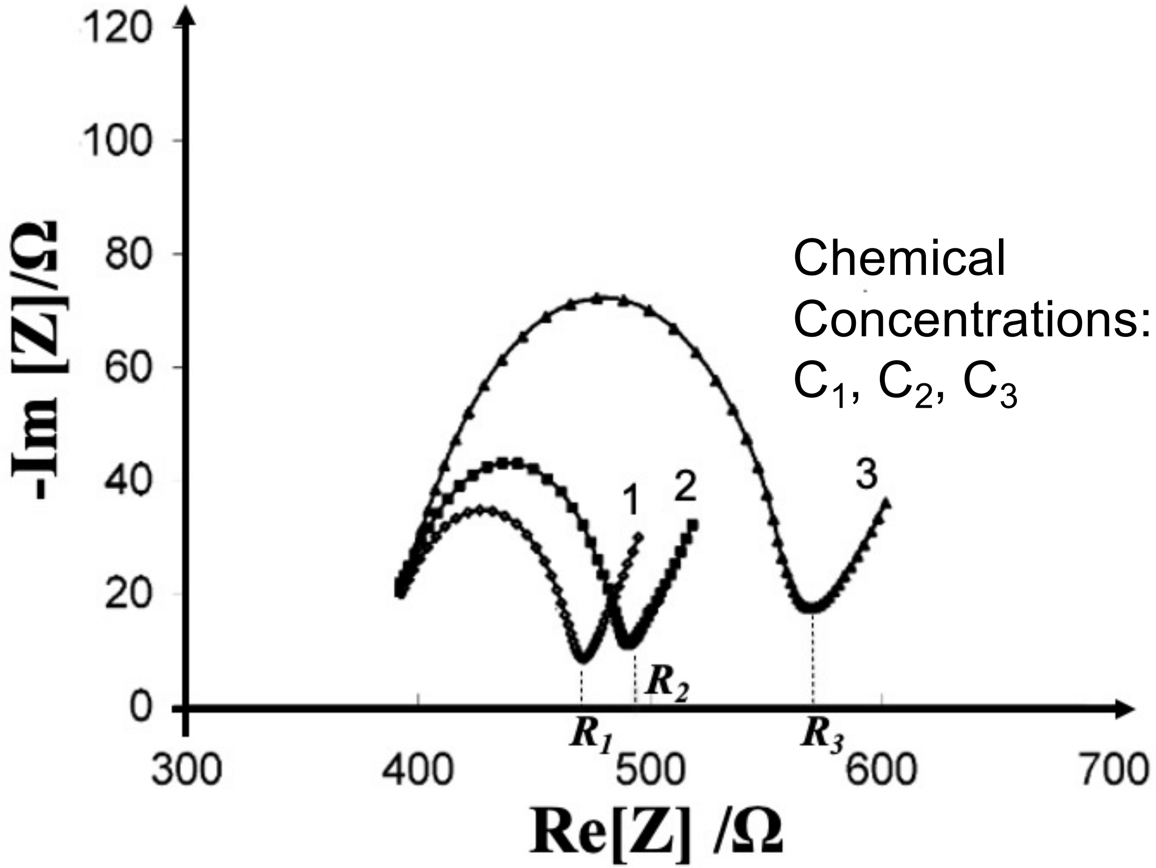


Impedimetric Sensing



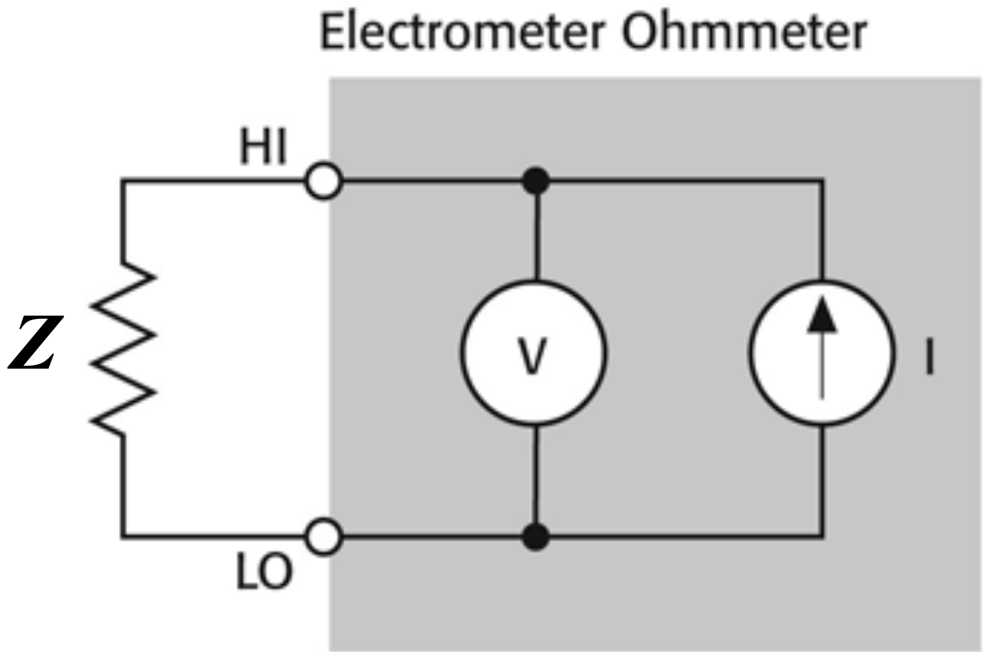
Clearly, the impedance of the Bio/CMOS interface changes accordingly to molecular steric hindrance

Impedimetric Sensing



Nyquist Plots may be used for Molecular Detection by following changes in Z

Impedimetric Sensing

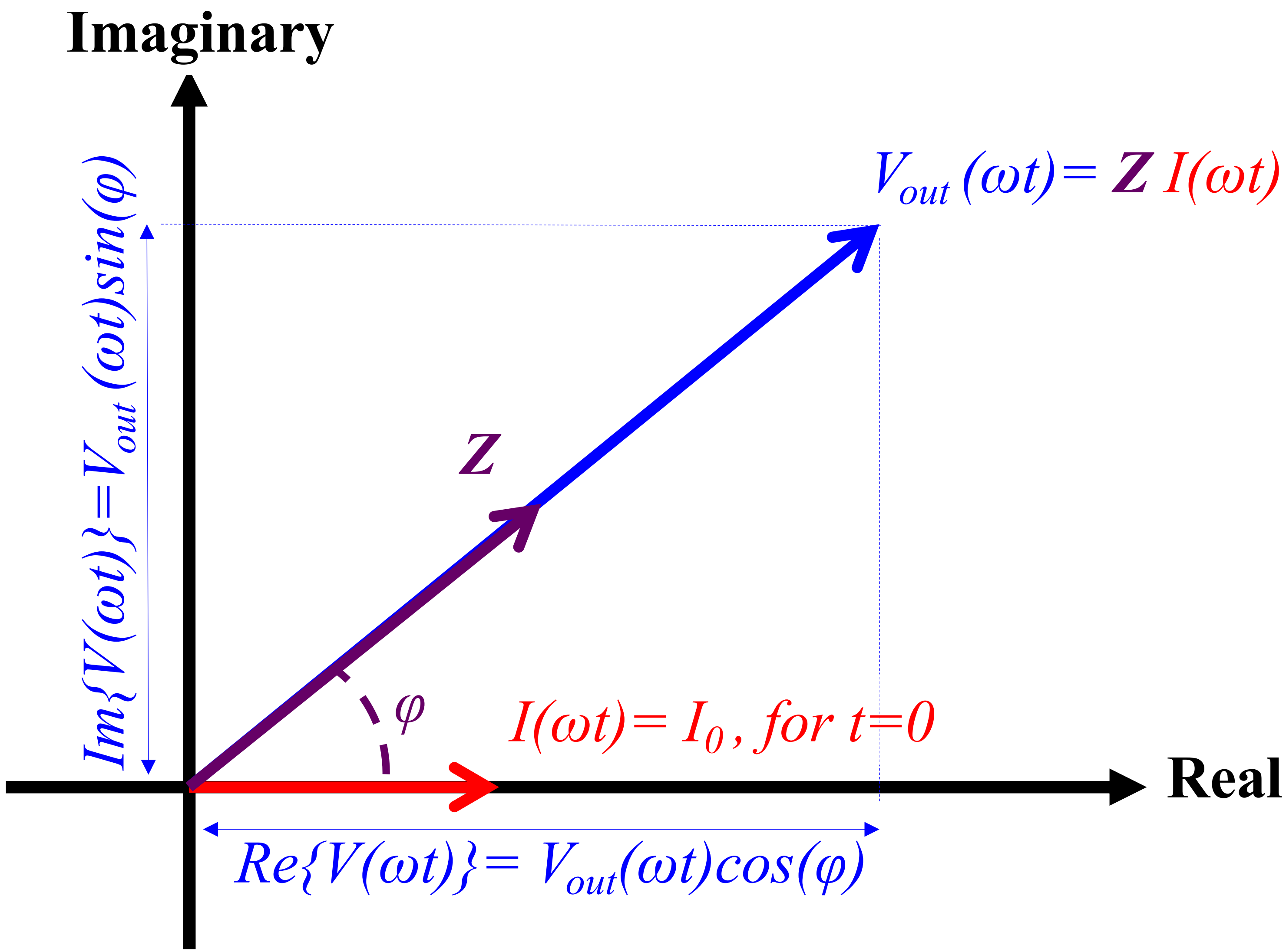


$$\underline{Z} = |\underline{Z}|e^{j\varphi} = Z[\cos(\varphi) + j\sin(\varphi)]$$

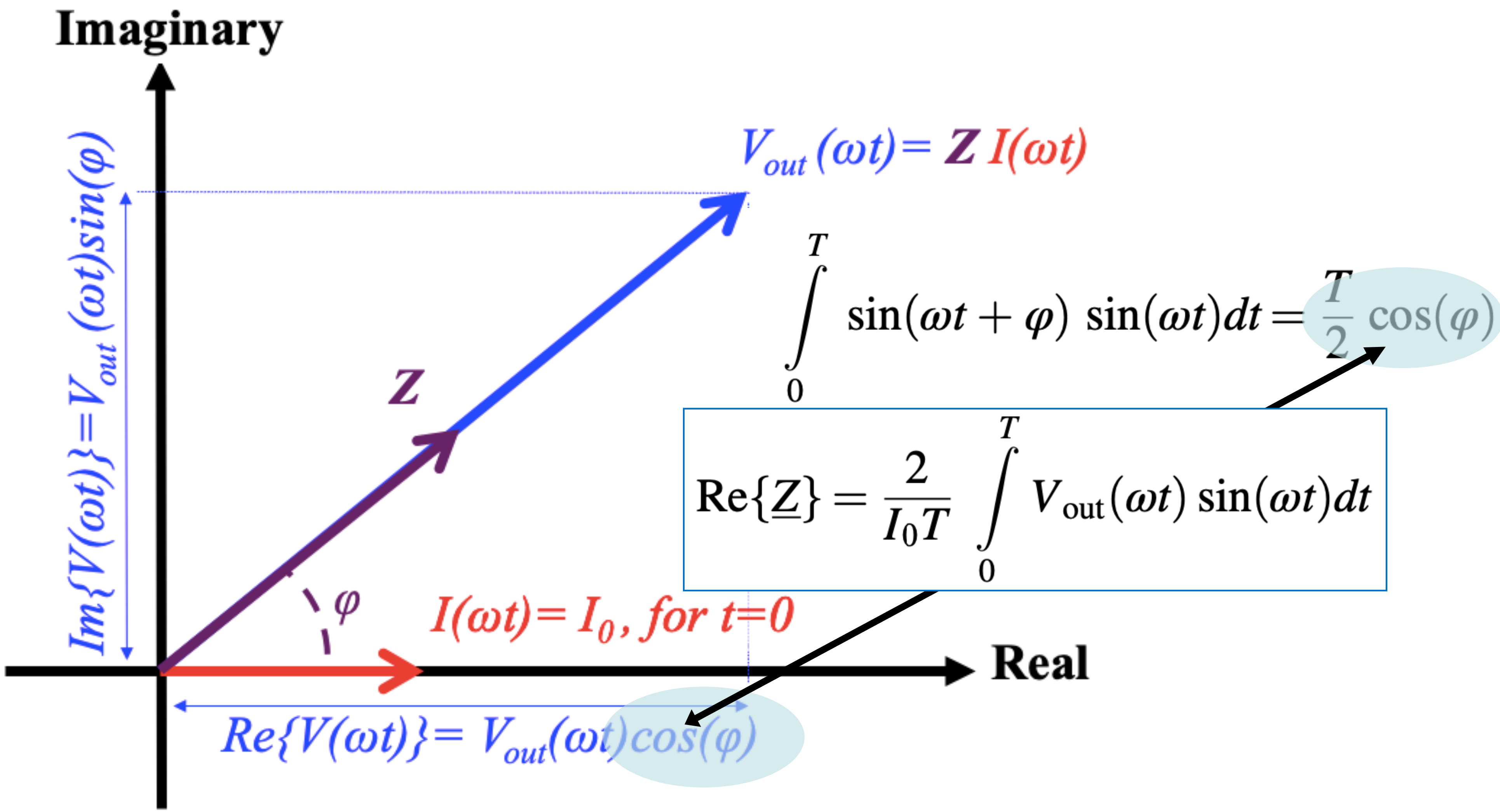
$$\underline{I}(t) = I_0 \sin(\omega t)$$

$$V_{\text{out}} = \underline{ZI}(t) = ZI_0 \sin(\omega t + \varphi)$$

Impedimetric Sensing

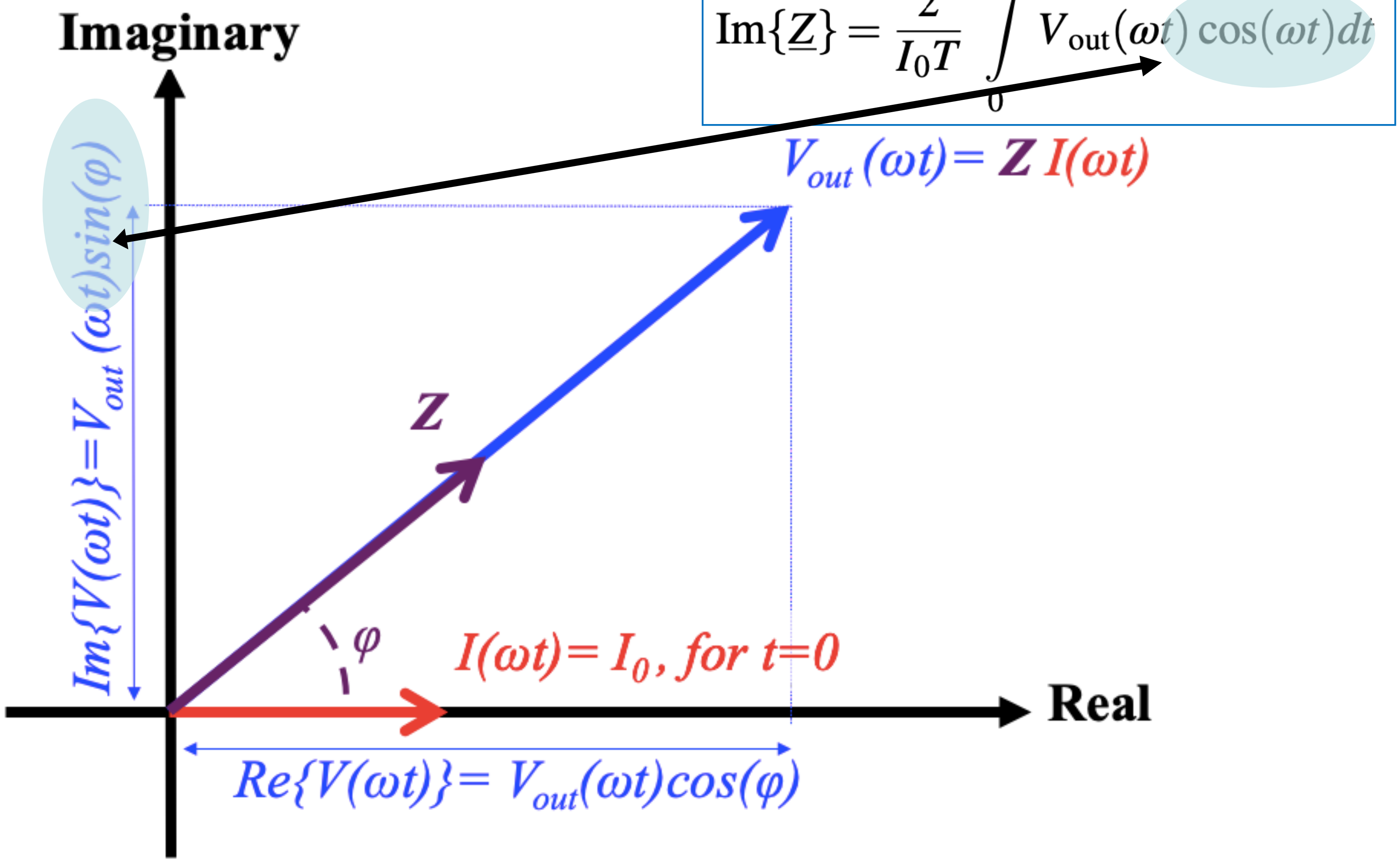


Impedimetric Sensing



Impedimetric Sensing

$$\mathrm{Im}\{\underline{Z}\} = \frac{2}{I_0 T} \int_0^T V_{\mathrm{out}}(\omega t)\cos(\omega t)\,dt$$

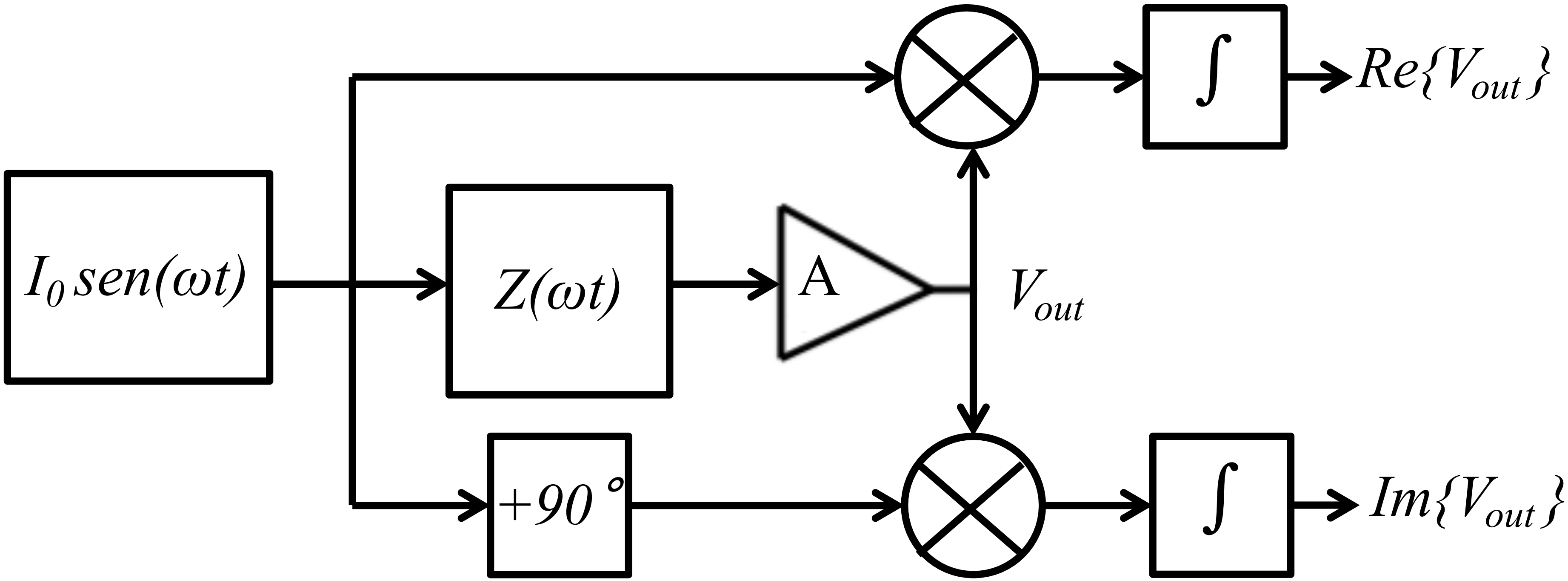


Impedimetric Sensing

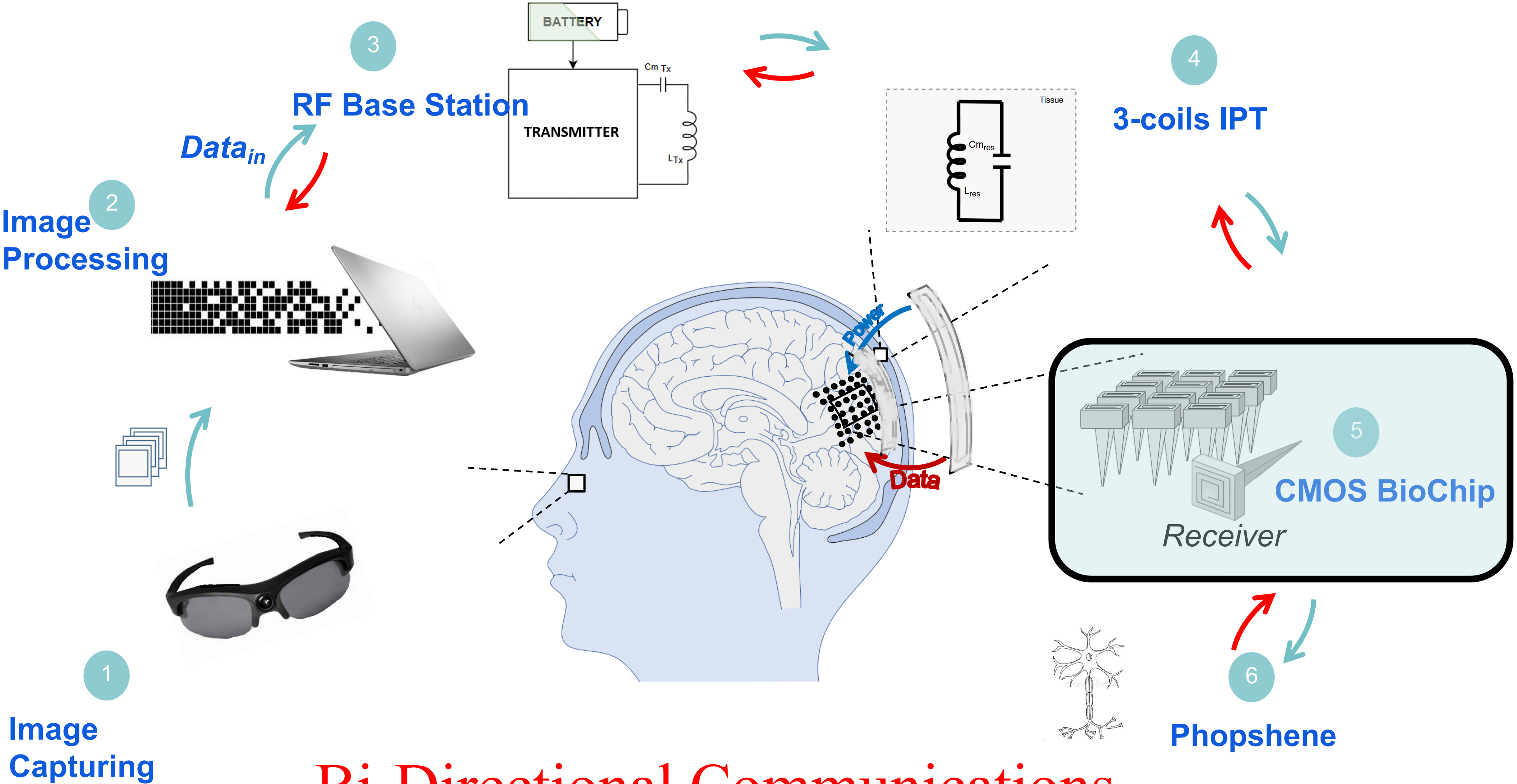
$$
\begin{cases}
\mathrm{Re}\{\underline{Z}\} = \dfrac{2}{I_0 T} \displaystyle\int_0^T V_{\mathrm{out}}(\omega t)\,\sin(\omega t)\,dt \\[2ex]
\mathrm{Im}\{\underline{Z}\} = \dfrac{2}{I_0 T} \displaystyle\int_0^T V_{\mathrm{out}}(\omega t)\,\cos(\omega t)\,dt
\end{cases}
$$

$+90°$

Impedimetric Sensing

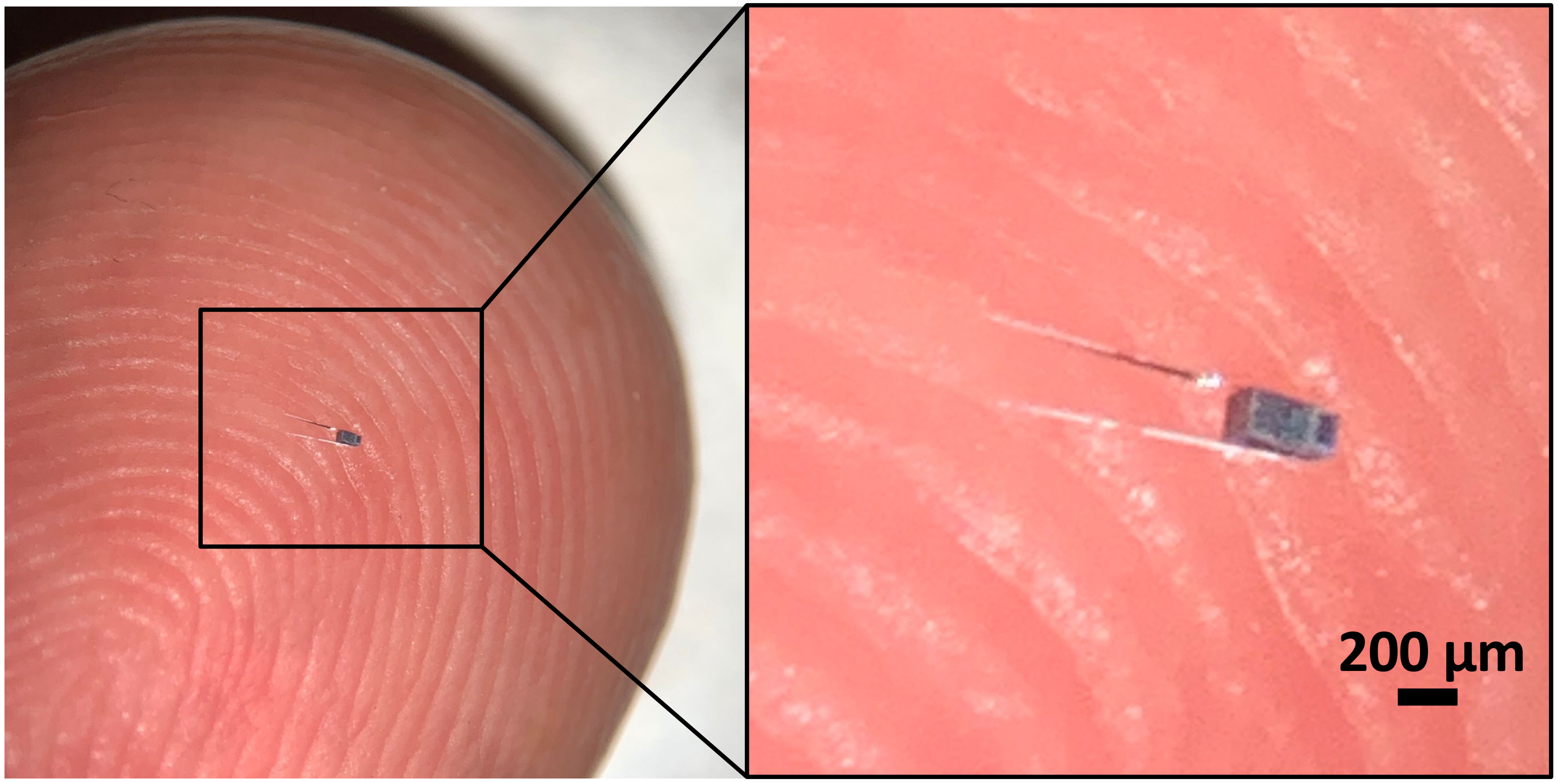


Brain/Machine interfaces



Bi-Directional Communications

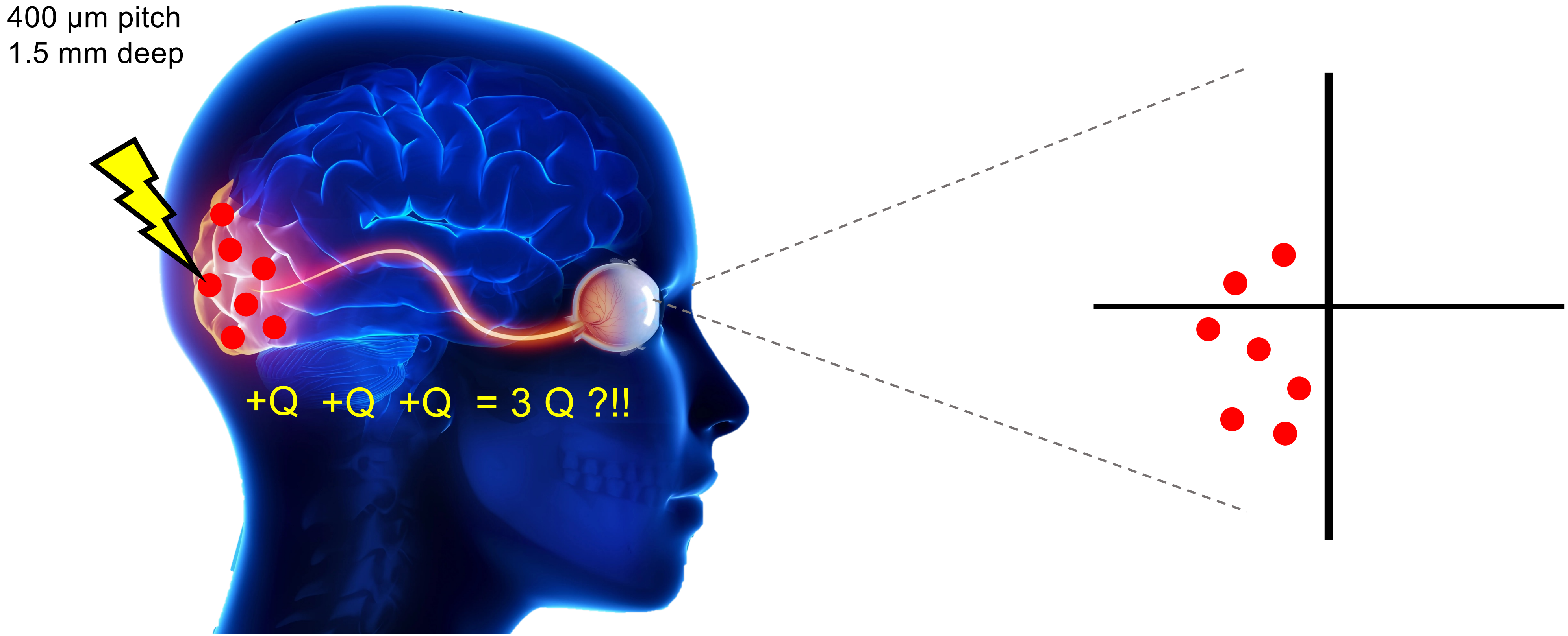
CMOS BioChip
for Intracortical Visual Stimulation



Barbruni et al., *PCT/IB2022/059944*, 2022

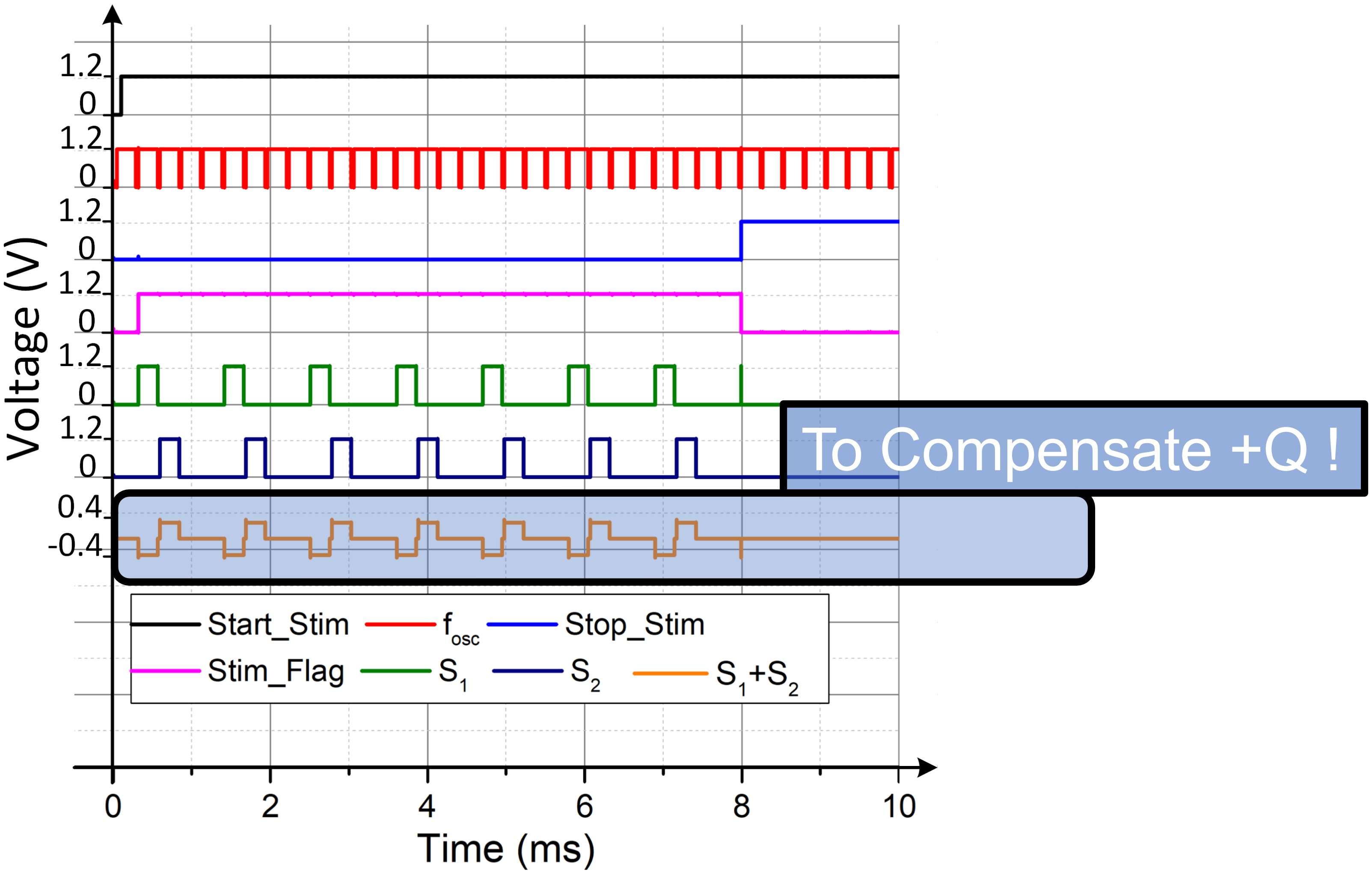
Intracortical BioChip to Vision Restoring in Blind Patients

Cortical Stimulation for Vision



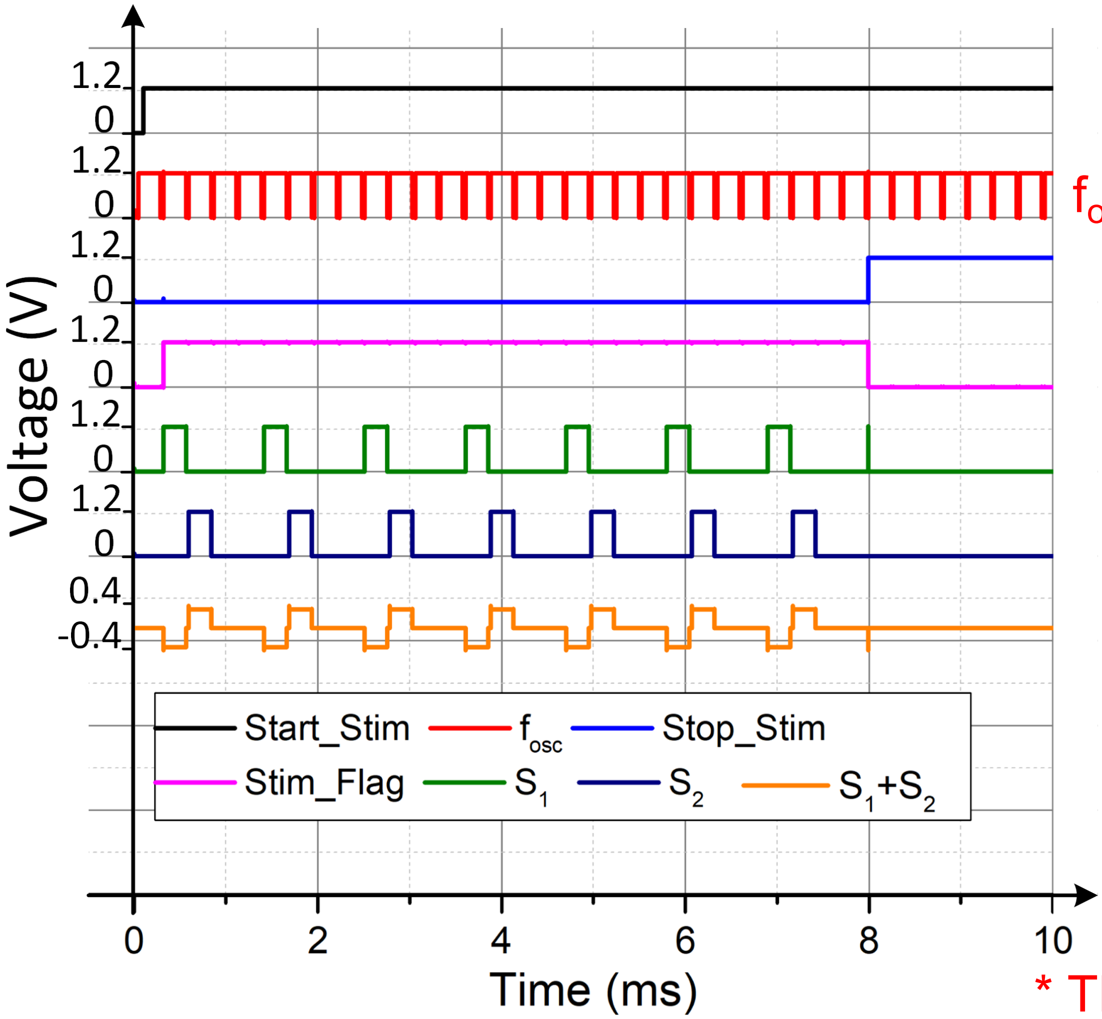
Charges sent to the Cortex need to be Compensated, not Accumulated!

BioChip Stimulator

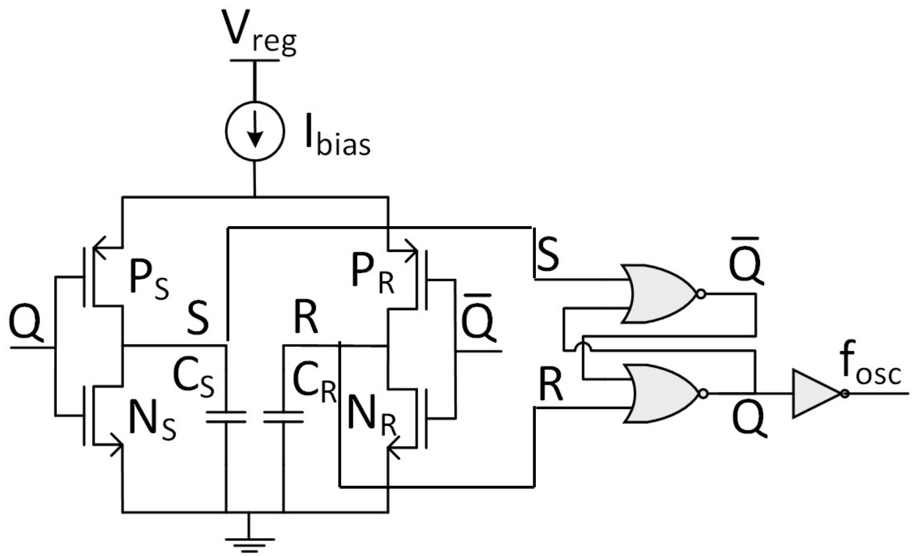


The Identified Logic Signal is now used to Stimulate

BioChip Stimulator

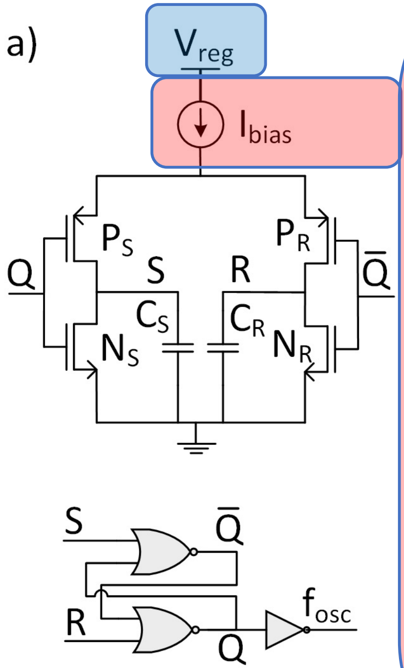


I_{bias} is used to charge C_S and C_R in a relaxation * oscillator, while couple of NOR logic gates return the desired pulses for f_{osc}



* The Relaxation Oscillator is a a nonlinear electronic oscillator circuit that produces a non-sinusoidal repetitive output signal

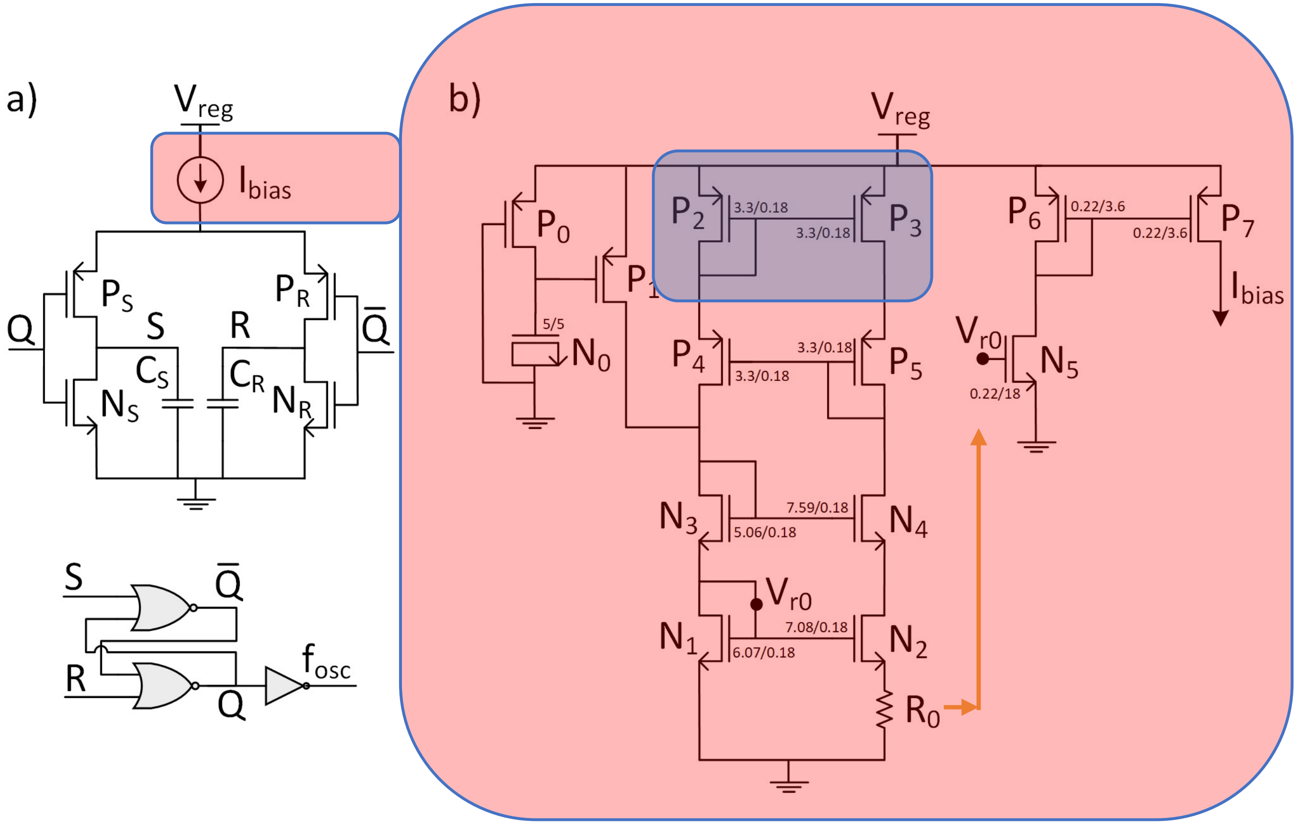
BioChip Stimulator



$$f_{osc} \propto \frac{I_{bias}}{(C_S + C_R) \cdot V_{reg}}$$

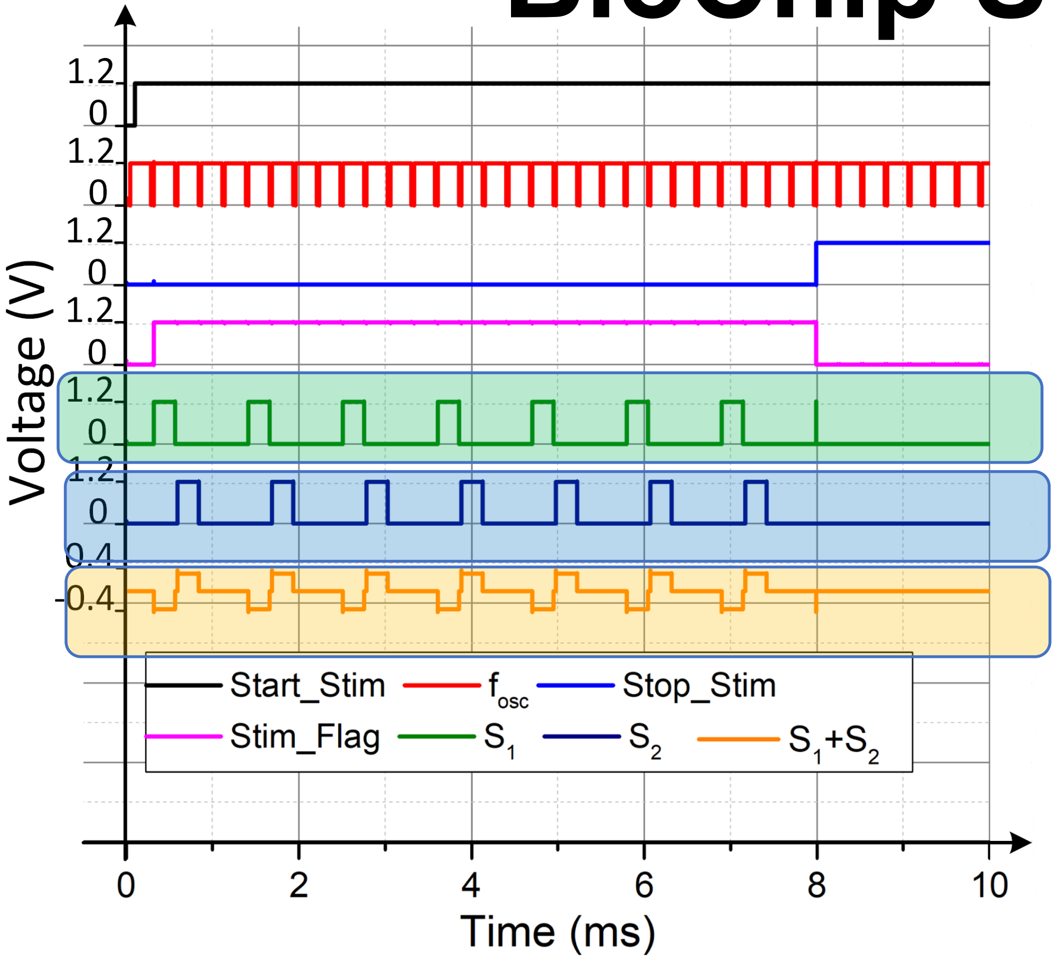
BioChip Stimulator

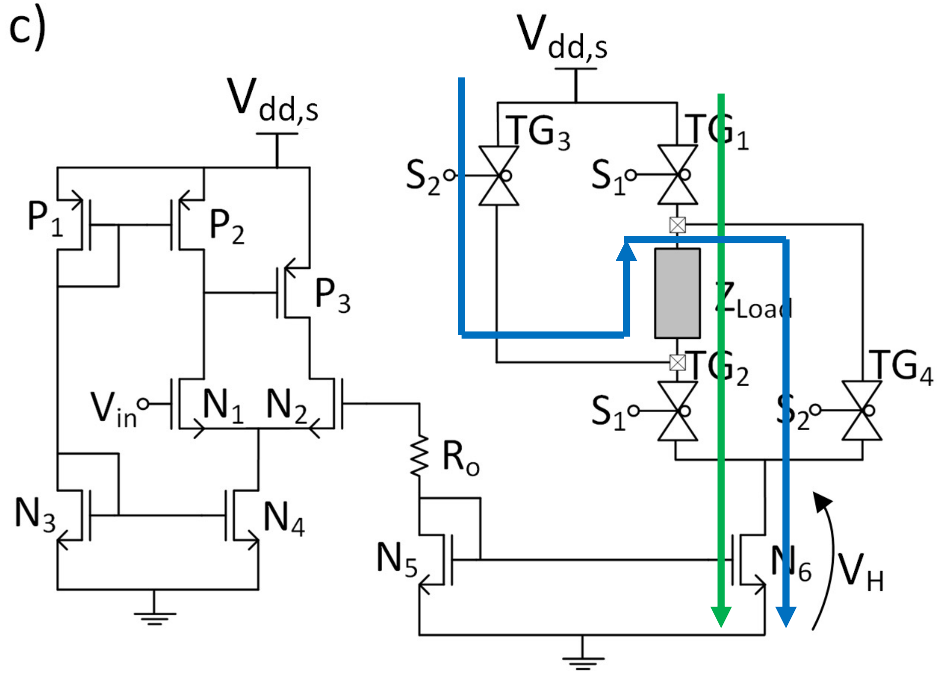
Current Mirror



$$f_{osc} \propto \frac{I_{bias}}{(C_S + C_R) \cdot V_{reg}}$$

BioChip Stimulator



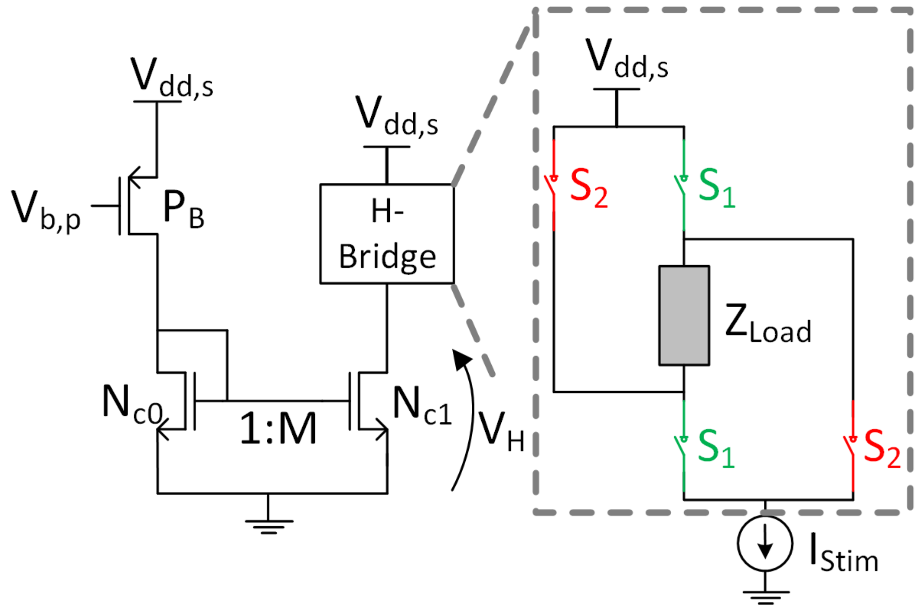


Barbruni et al., *IEEE MOCAST*, 2023

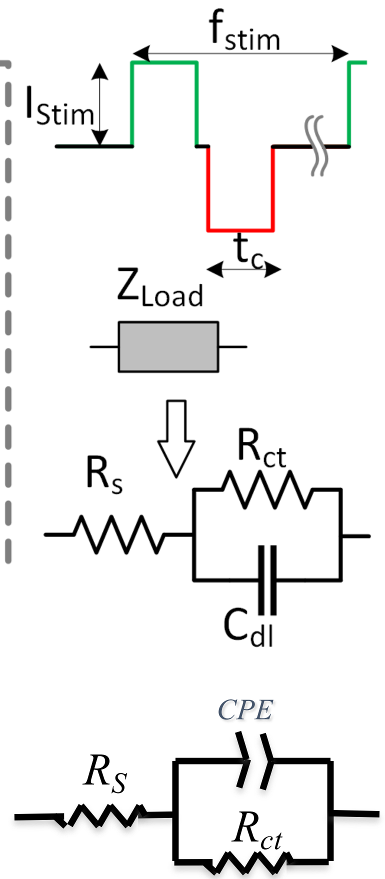
Finally, the H-Bridge provides

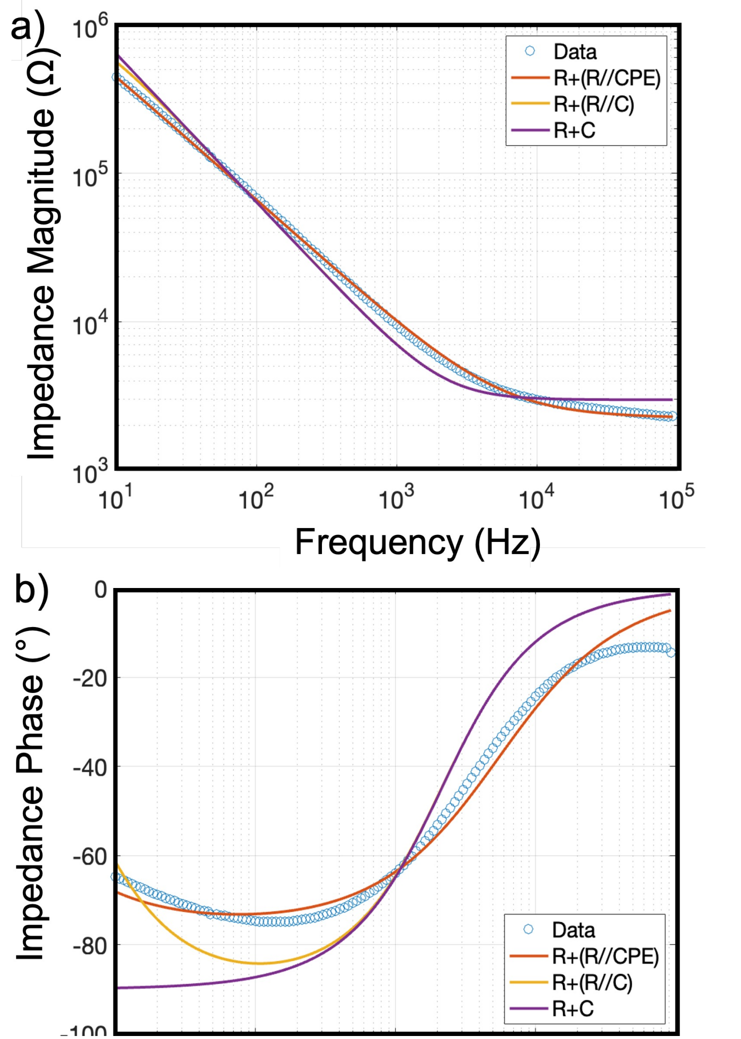
the Right Current with the mentioned Q-Compensation

BioChip Stimulator



Barbruni et al., *IEEE MOCAST*, 2023





The Simulated Performance changes
with Different Bio/CMOS interface models

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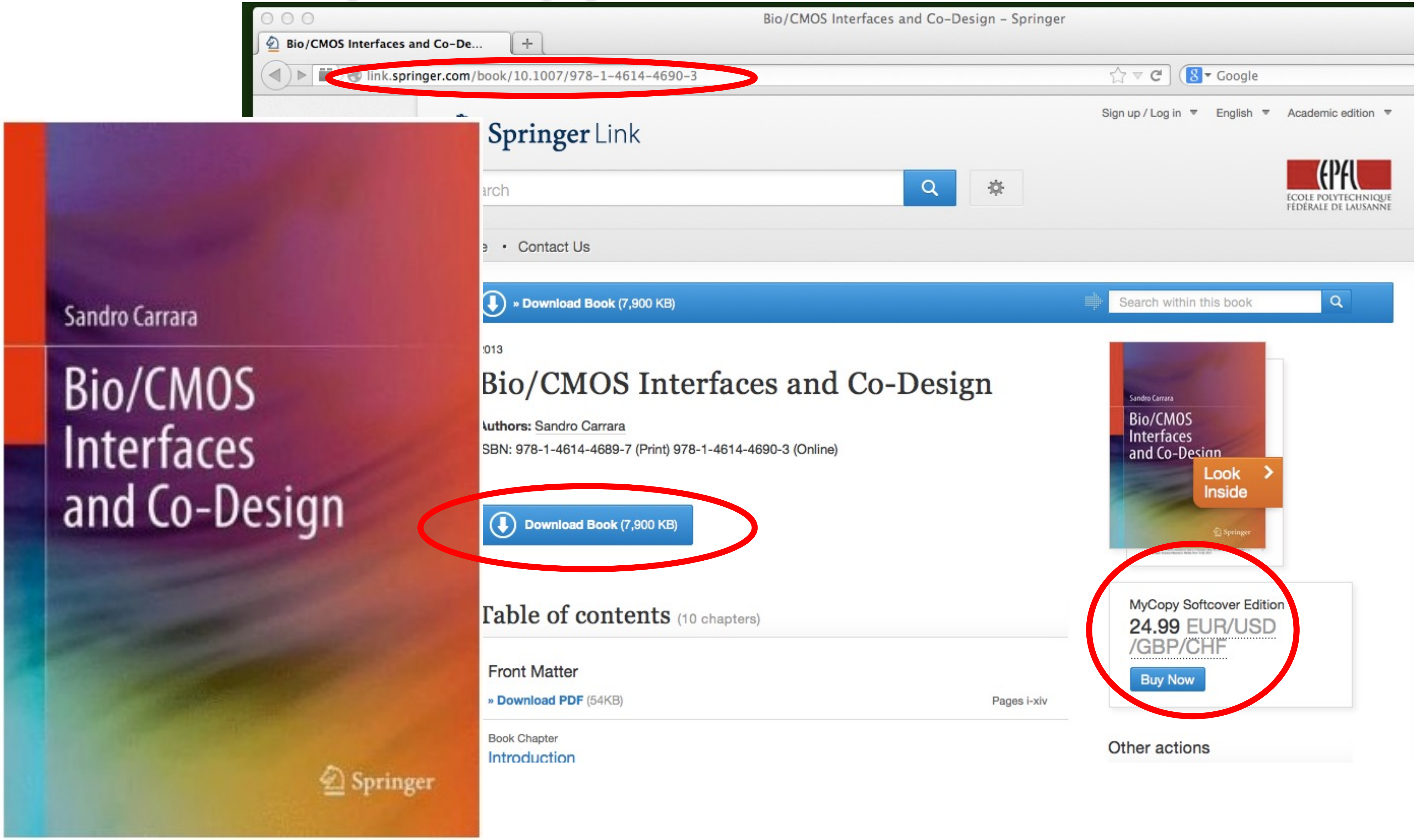


Master in Electrical and Electronics Engineering

EE-517: Bio-Nano-Chip Design

Subject of the week	Chapter' paragraphs*
Introduction to Bio-Nano-Chip design, and Conductive Solutions	§1.1-1.5, §2.1-2.7, §2.14-15
Biological molecules: Proteins and DNA building blocks	§3.5-9, §4.13 and §4.17-18
Biological molecules interactions (DNA, Antibodies, Oxidases and Cytochromes)	§4.4-17 and §4.19-23
Biosensors Principle with DNA, Antibodies, and Enzymes	§6.1-4 and §8.2
Biosensors Principle by Redox reactions and Faradaic processes **Bio**	§8.4-8
Nanotechnology for molecular assembly on chip' surfaces (absorption models)	§5.1
Nanotechnology for checking molecular assembly on chip' surfaces (SPR+ AFM)	§5.2
Nanotechnology to prevent electron transfer	§6.3-7
Nanotechnology to enhance electron transfer in redox reactions **Nano**	§8.4-8, and 8.3 and 8.9
Chip design for electrochemical sensing: basic configurations and equivalent circuits	§9.1-9.2
Amperometric biosensing in constant-bias (Current-to-Voltage & FTCC Methods)	§9.1.2 and 9.3-5
Amperometric biosensing in voltage-scan (VDCM & DDSM Methods)	§10.3-5
Label-free capacitance detection (CBCM & FTCM Methods)	§7.2-6
Review for final exam **CMOS**	

* textbook : Sandro Carrara, Bio/CMOS interfaces and Co-Design, Springer publisher, New York, 2013

Master Projects

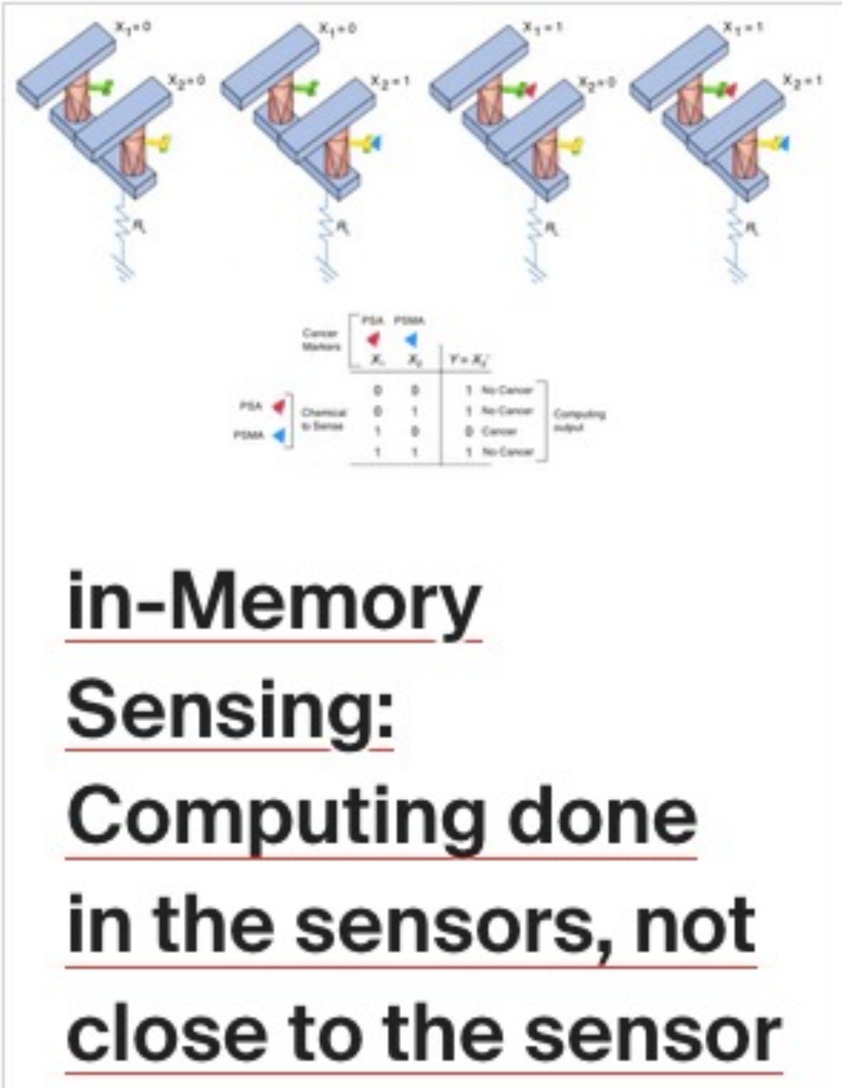
https://www.epfl.ch/labs/iclab/index-html/bci-group/

Body Dust: CMOS Design for Dopamine monitoring in the Brain

Collaboration with
Imperial Collage London

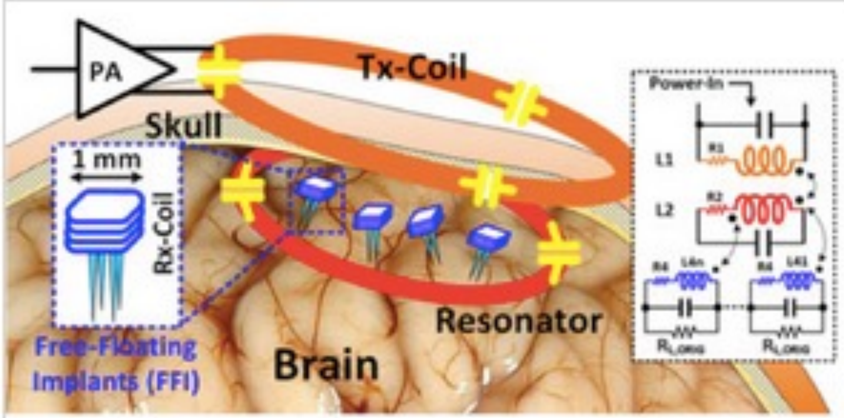
Master Projects

https://www.epfl.ch/labs/iclab/index-html/bci-group/



Master Projects

https://www.epfl.ch/labs/iclab/index-html/bci-group/

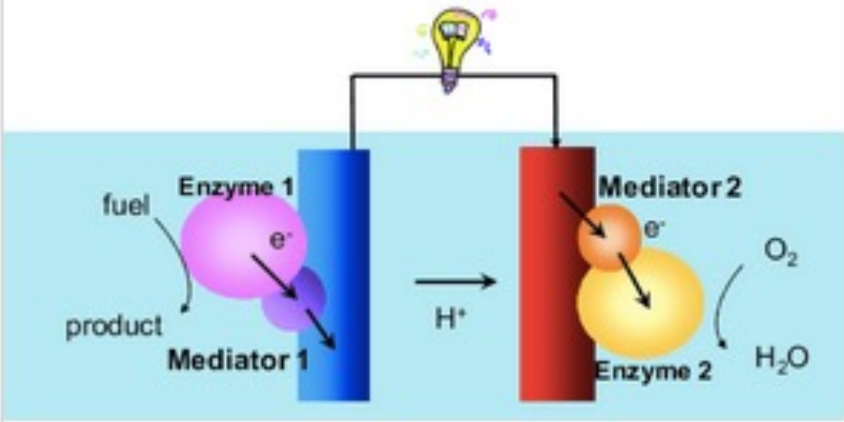


Challenges in sub-millimetric Neurostimulators Wirelessly Powered via highly efficient Inductive Links

Collaboration with
Politecnico di Torino

Master Projects

https://www.epfl.ch/labs/iclab/index-html/bci-group/



Self-Wake-Up Device for Therapeutic Compounds on Human Skin

Collaboration with
ST Microelectronics