



POLITECNICO DI MILANO

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Advanced Course on
**High Resolution Electronic Measurements in Nano-Bio
Science**

Electrochemical Instrumentation
Probing the Interface

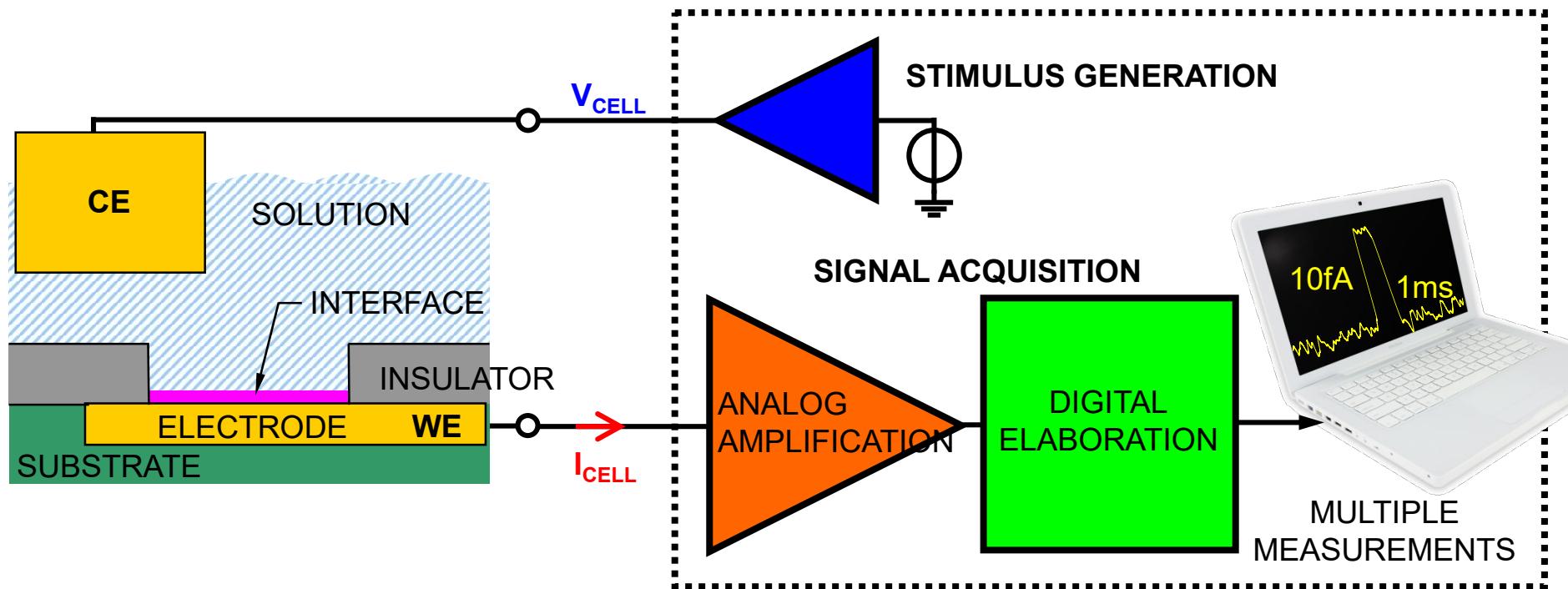
Marco Carminati

June 7th 2023

- Review of major **electrochemical techniques**:
 - Cyclic voltammetry / Square wave voltammetry
 - Amperometry
 - Potentiometry
 - Impedance spectroscopy
- **Instrumentation**:
 - Design criteria of a potentiostat
 - Low-noise potentiostat
 - Bipotentiostat and multichannel systems
 - Miniaturization and CMOS potentiostats

General Electrochemical Instrument

Potentiostatic configuration:

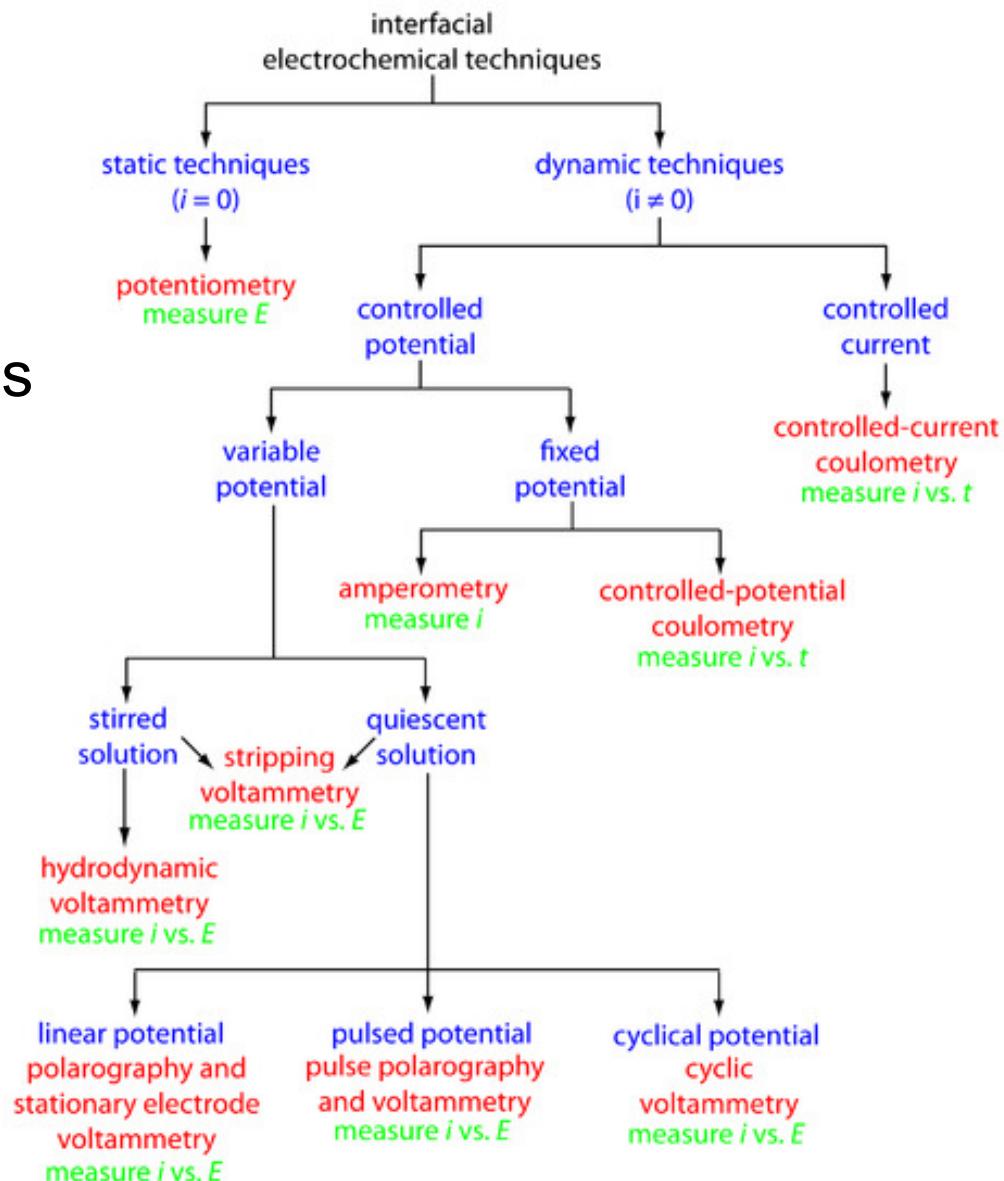


- Apply a voltage V_{CELL} and measure the current I_{CELL}
→ 2 sections: **generation** and **sensing**
- Multiple measurement types by changing stimulation waveform

Families of Analytical Techniques

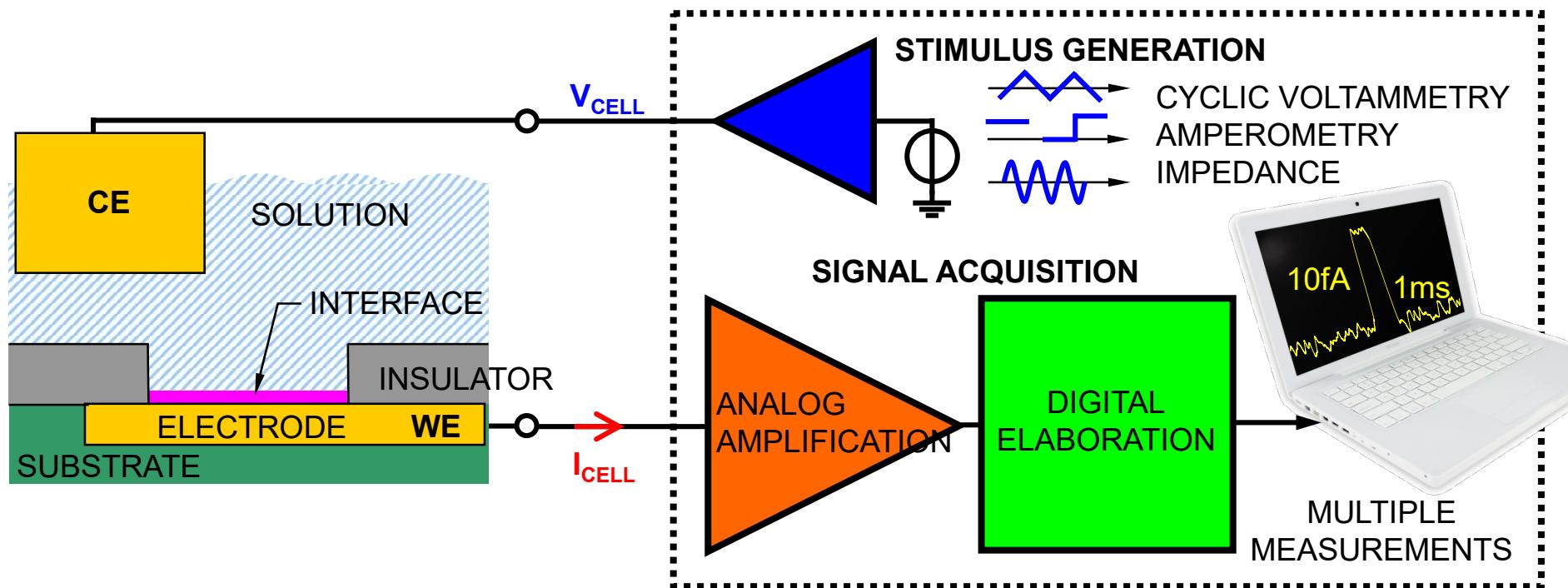
Detection techniques:

- Potential step/pulse methods
- Potential sweep methods
- Controlled-current techniques
- Methods based on impedance
- Scanning Electrochemical Microscopy





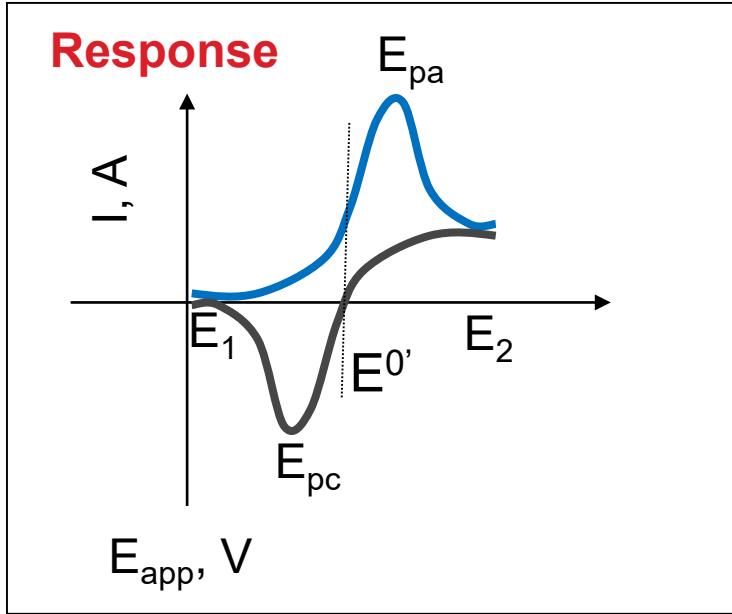
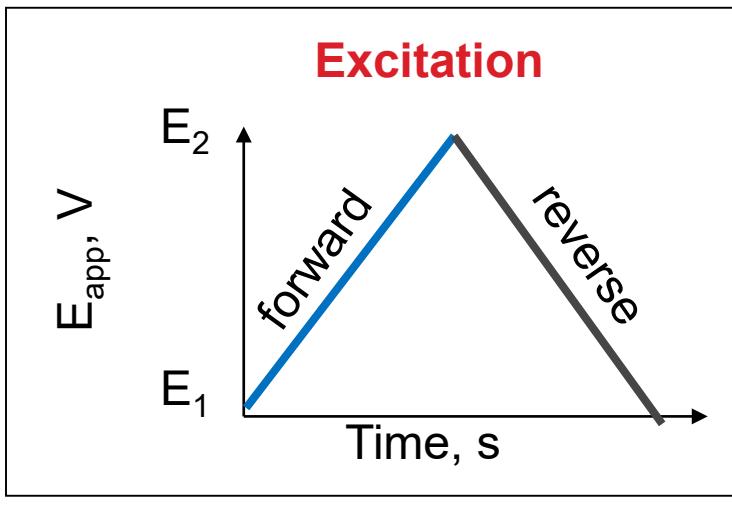
Families of Analytical Techniques



Major ones:

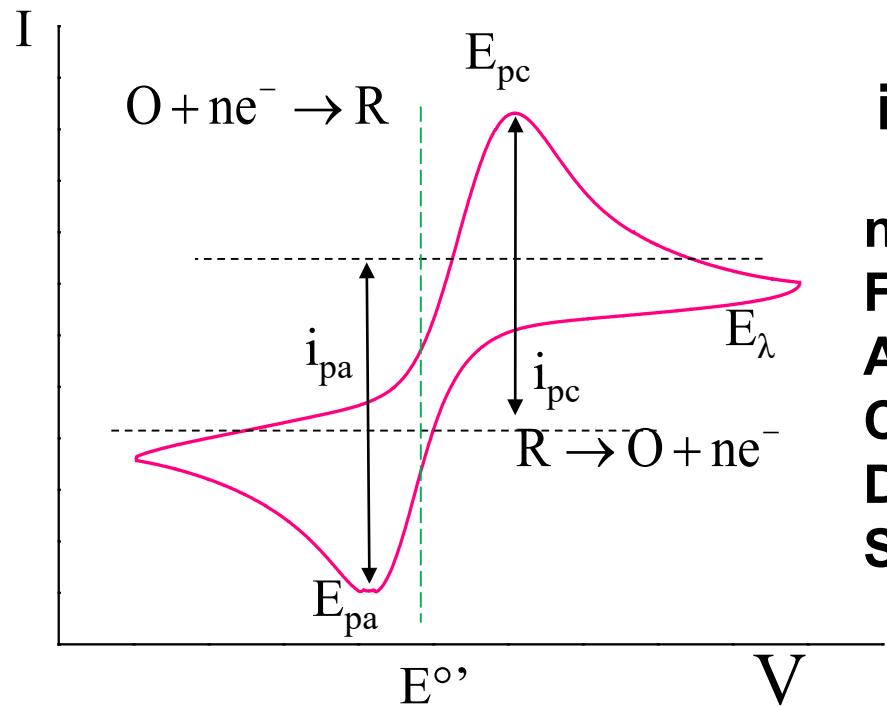
- *Cyclic Voltammetry*
- *Amperometry*
- *Impedance Spectroscopy and Tracking*

Cyclic Voltammetry



- Triangular wave: slope = **scan rate**
- **Important parameters:**
 - E_{pa} and E_{pc}
 - i_{pc} and i_{ac}
 - $E^0 = (E_{pa} + E_{pc})/2$
 - $\Delta E = |E_{pa} - E_{pc}|$
- E^0 formal redox potential
- detection of chemical reactions
- evaluation of electron transfer kinetics and diffusion rates

Peak Current (Reversible Systems)



$i_{pa} = i_{pc}$ for a reversible system

$$i_p = 0.4463 \cdot n \cdot F \cdot A \cdot C \cdot (D \cdot SR \cdot nq/kT)^{1/2}$$

n : n. of electrons

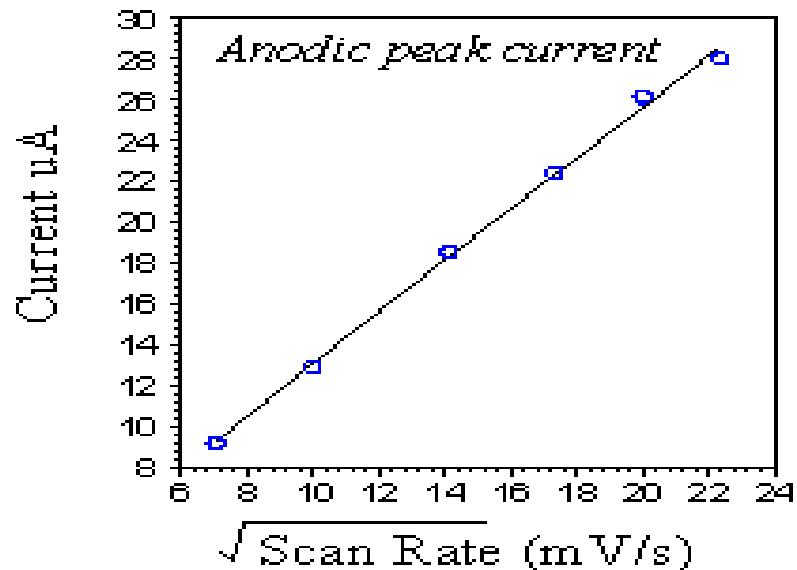
F : Faraday's constant (96485 C/mol)

A : electrode area;

C: concentration (mol/litre)

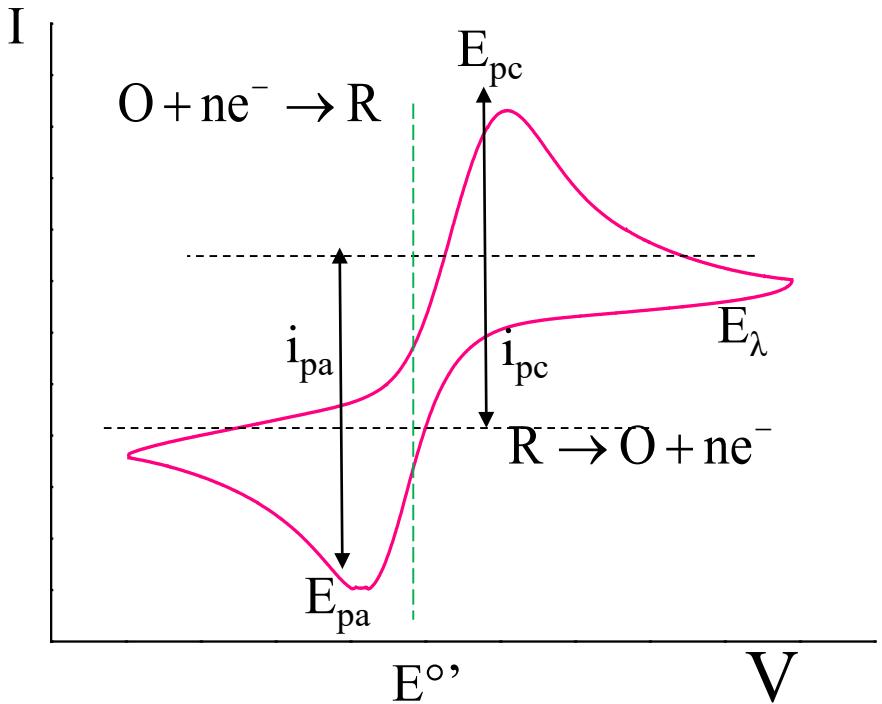
D: diffusion coefficient (cm^2/sec).

SR: scan rate

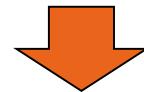




Peak Potential



$\Delta E_p = |E_{pa} - E_{pc}| = 59/n$ mV at 25°C
independent of SR



n, reversibility

Chemical fingerprint



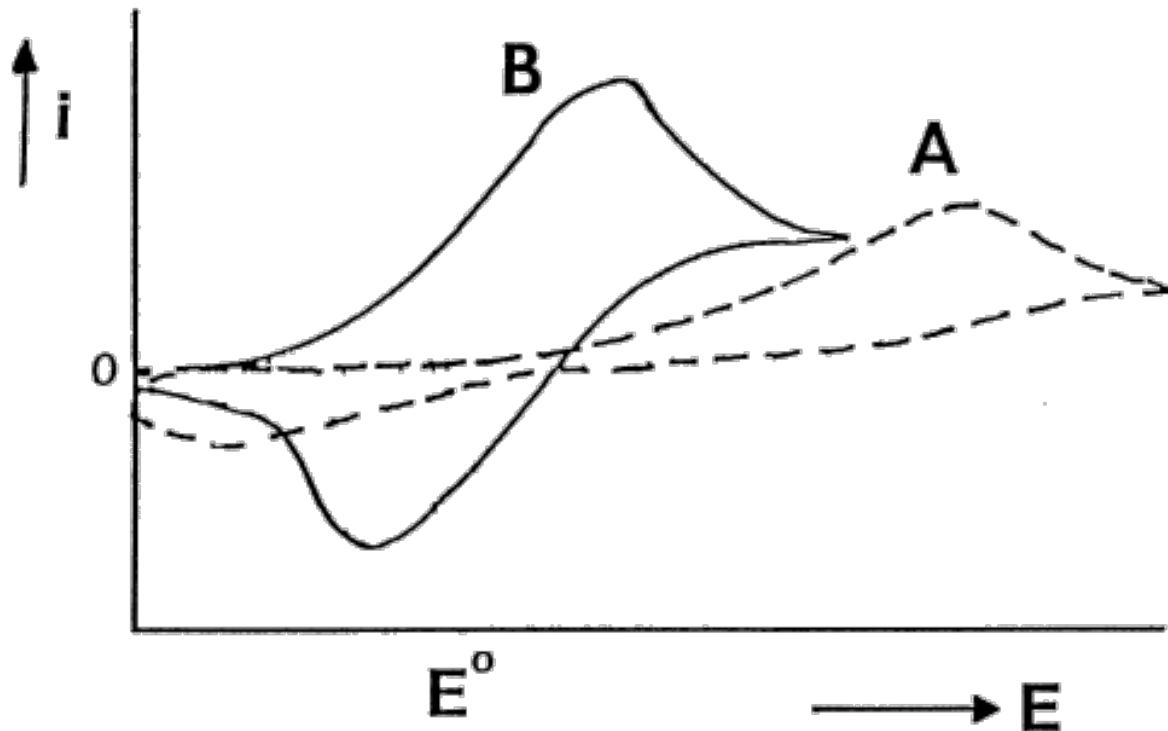
Quasi-Reversible or Irreversible

B - Quasi-reversible:

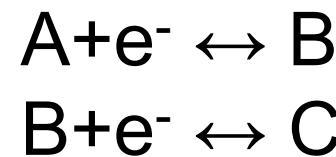
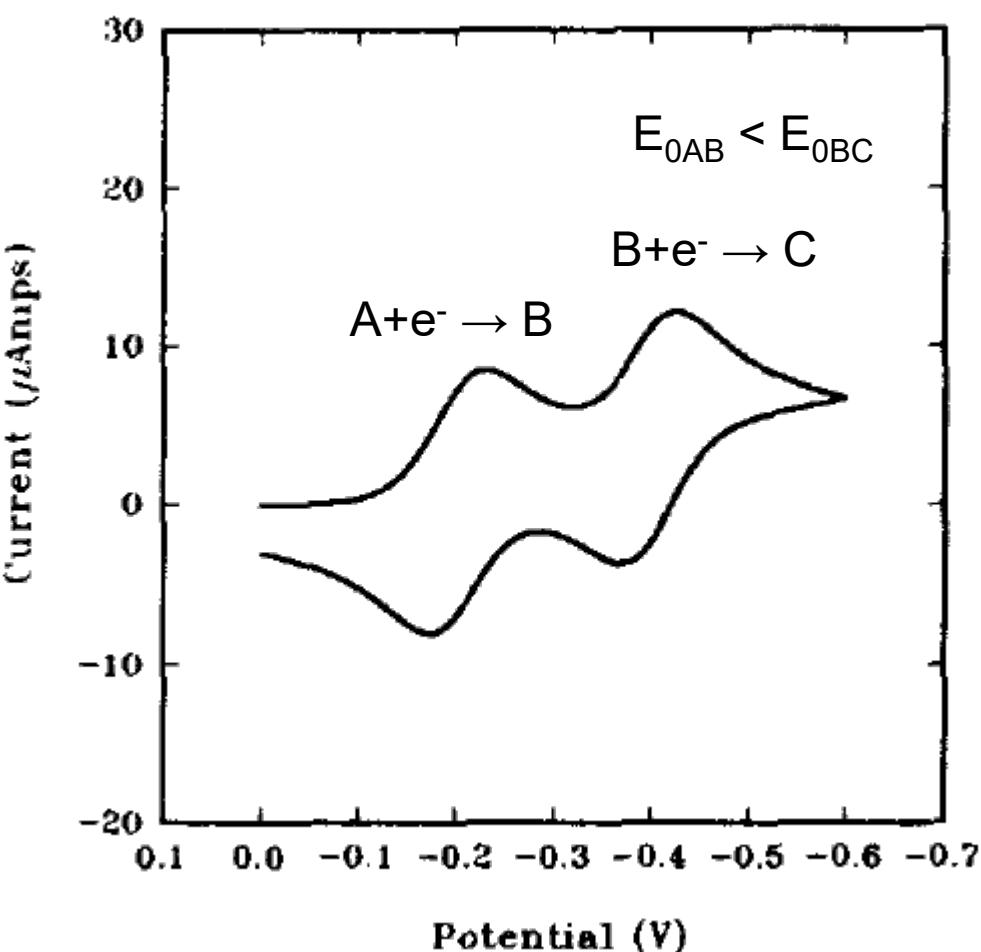
- $\Delta E_p > 59 \text{ mV}$ and ΔE_p increases with increasing SR

A - Irreversible:

- no return wave, 2 waves do not overlap

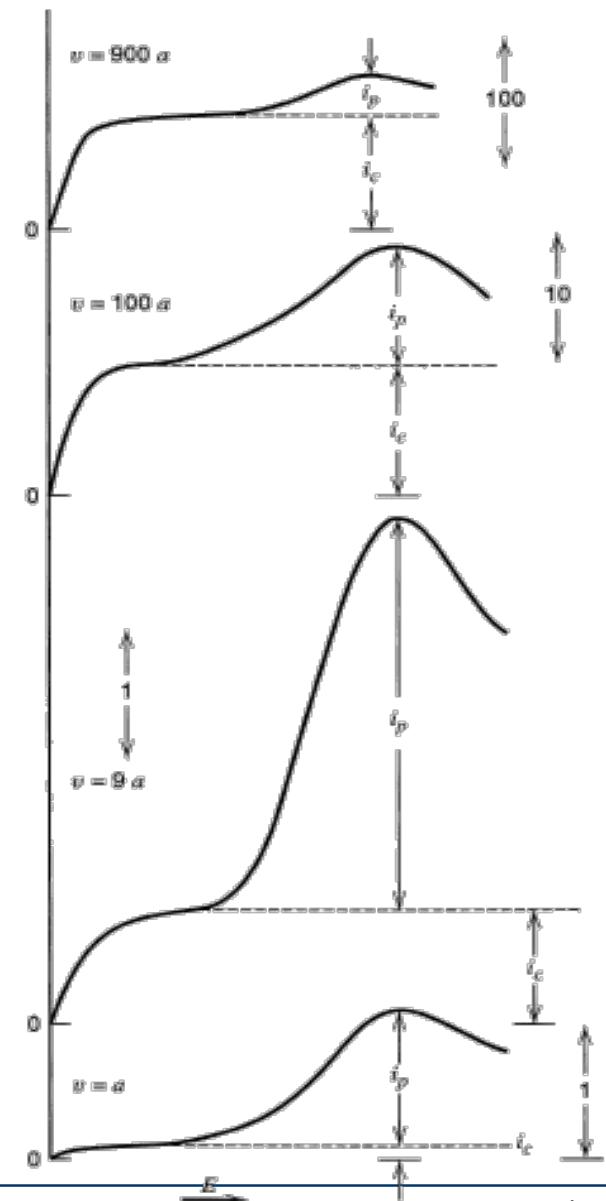


Multi-Electron Transfer

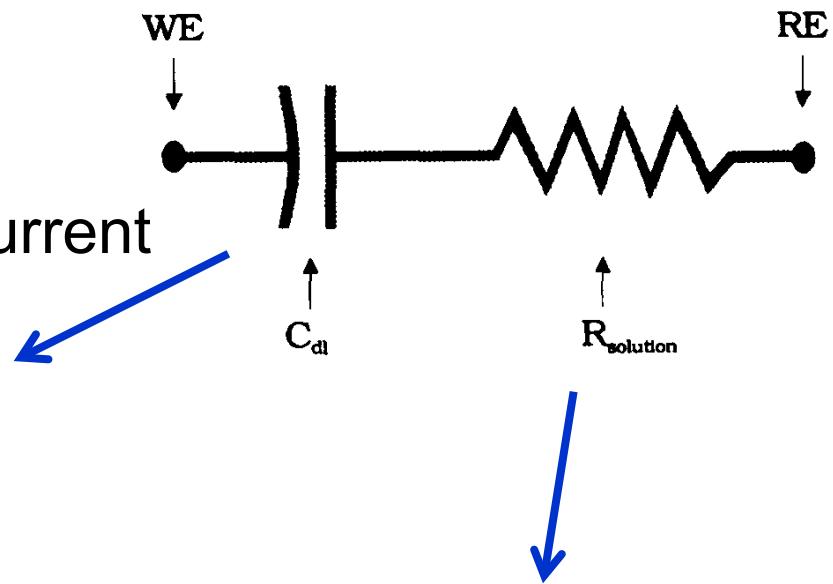


$$E_{0AB}$$
$$E_{0BC}$$

Spurious Effects



1) Capacitive current



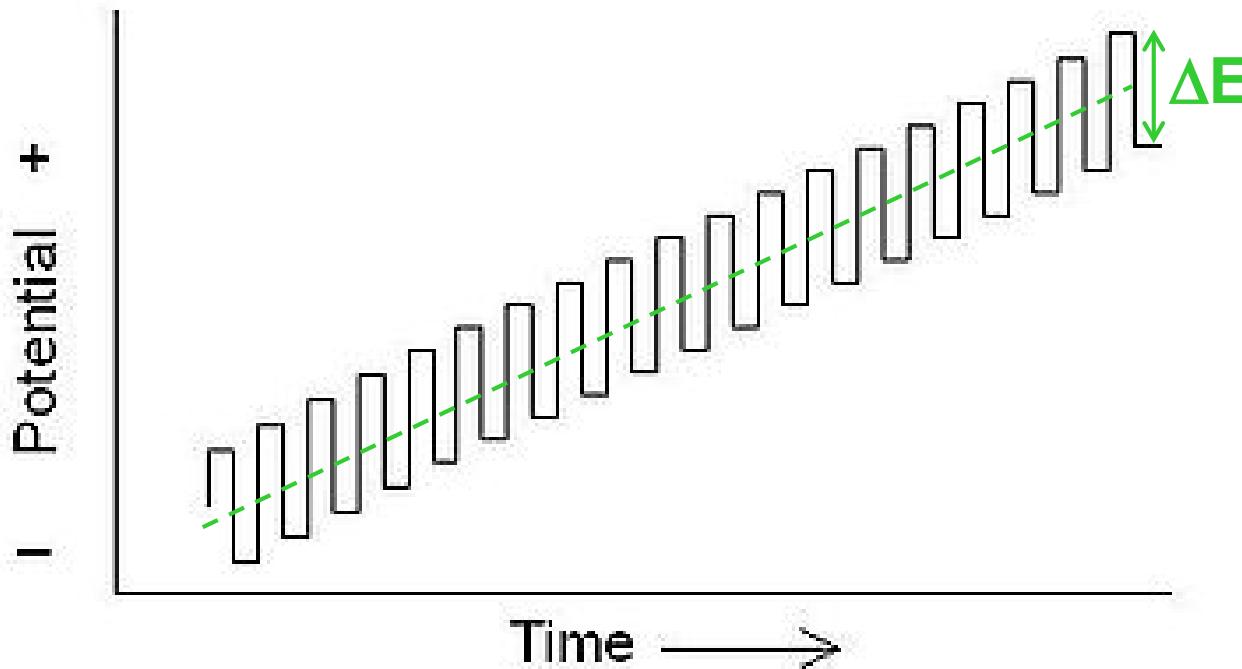
2) iR_{sol} drop

3) $C_{dl}R_{sol}$ time constant

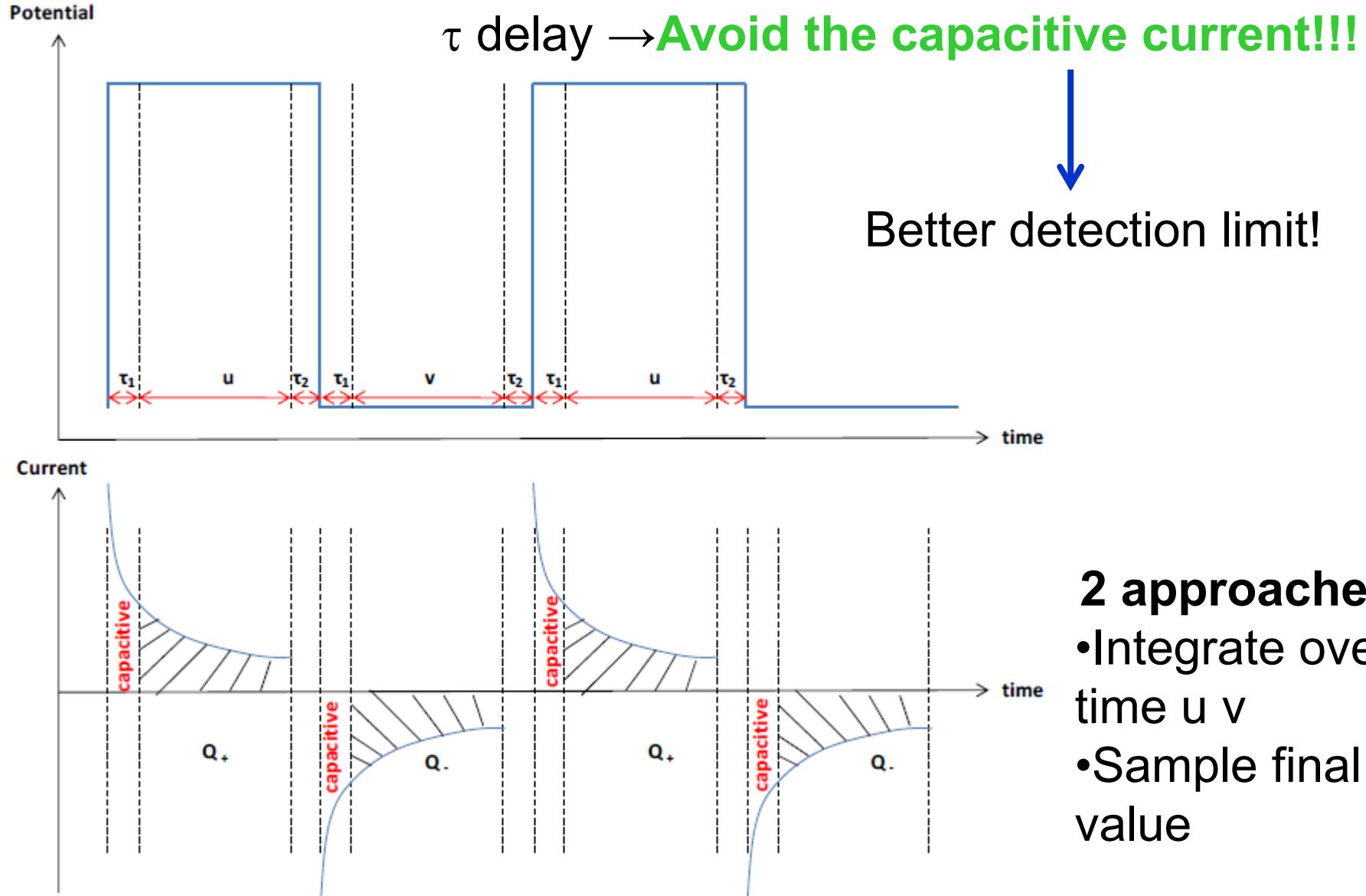
Square Wave Voltammetry

Evolution of linear sweep voltammetry: superposition of a **square wave** with large amplitude ΔE and take $i_{\max} - i_{\min}$

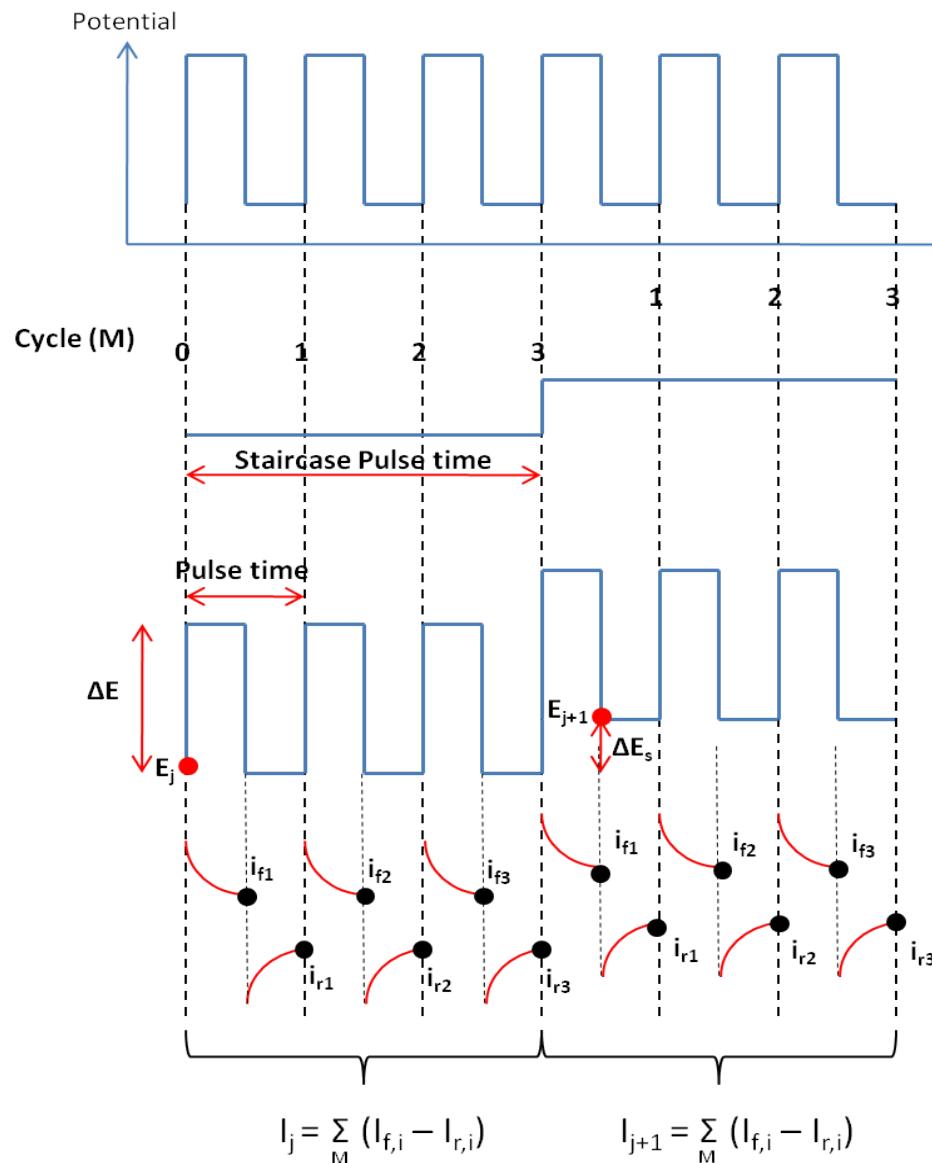
Obtain the *derivative* of the voltammogram (*differential square wave voltammetry*)



Square Wave Voltammetry



Multiple Square Wave Voltammetry

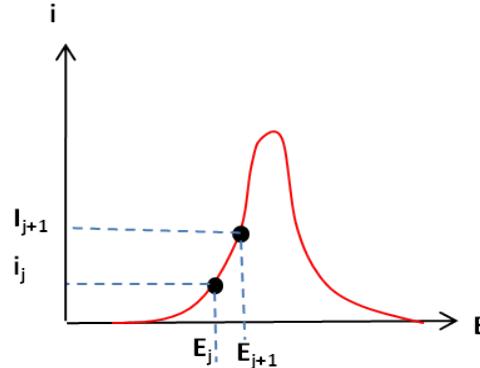


Generic pulse

Sampled DC Voltammetry

Multiple Square Wave Voltammetry

$$M = \text{Staircase pulse time} / \text{Pulse time}$$



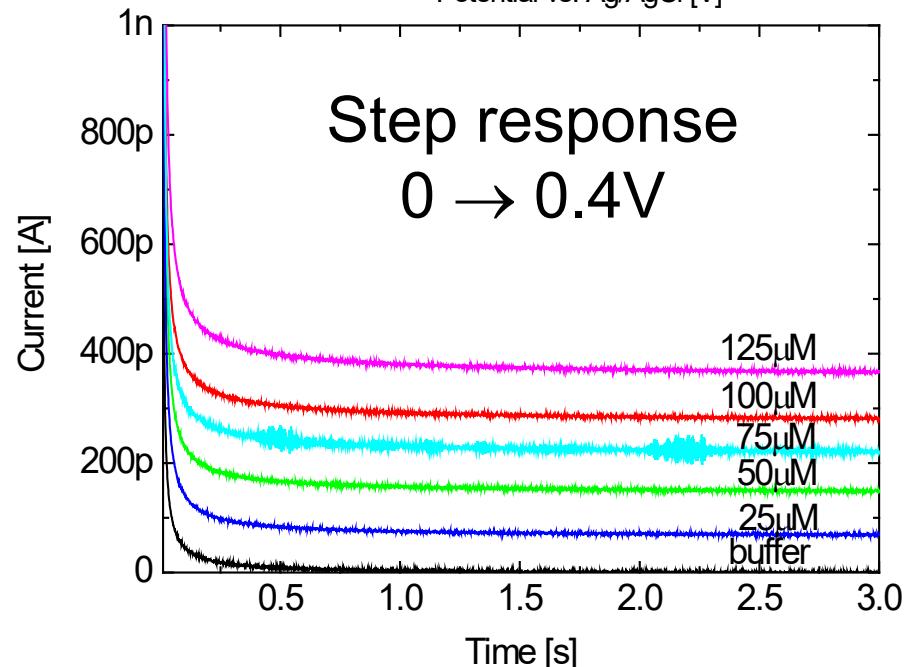
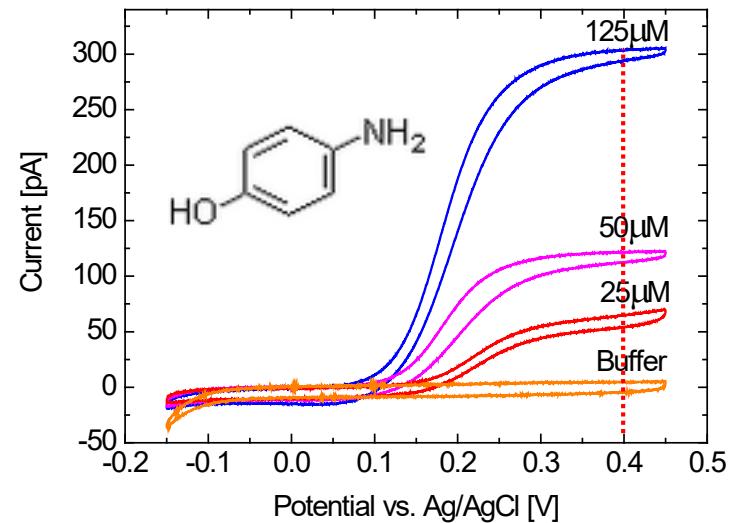
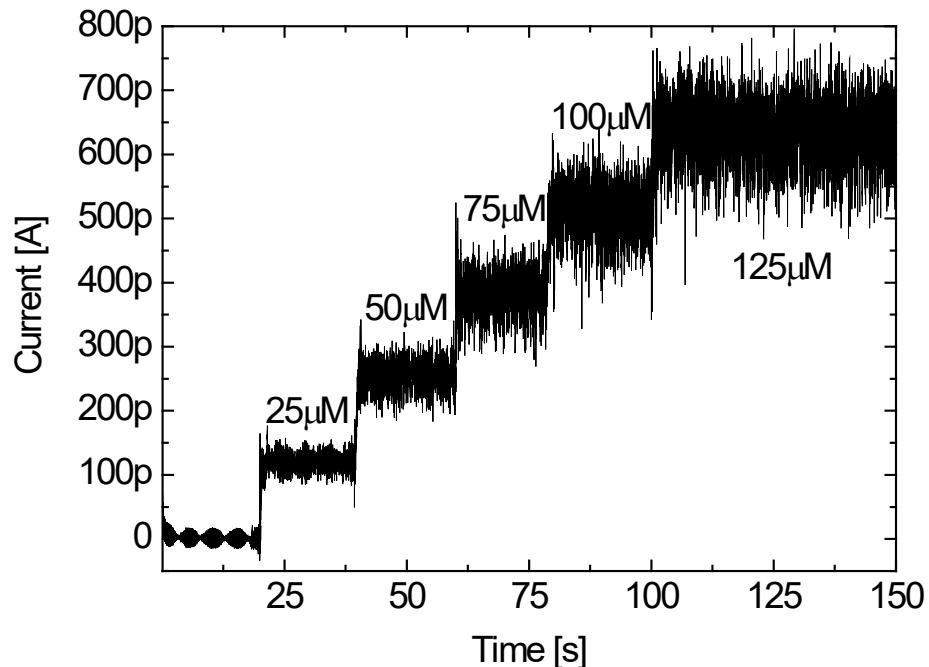
N. Fatouros, J. Electroanal. Chem., 213



Amperometry

Recording current over time at a fixed WE potential
 $i \propto \text{concentration}$

Fixed voltage 0.4V



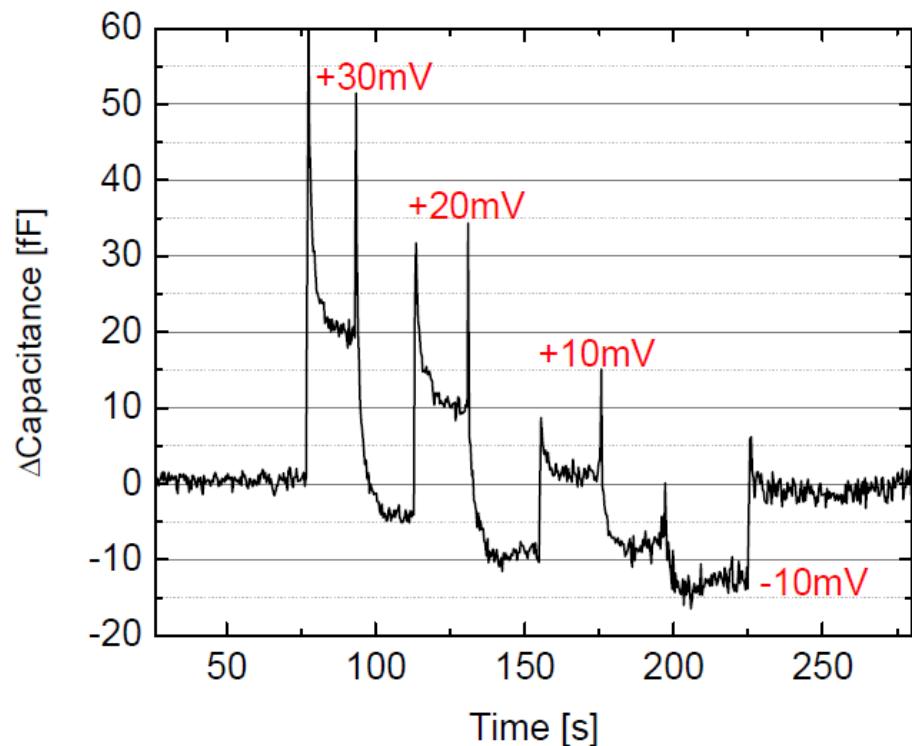


Electrochemical Impedance Sensing

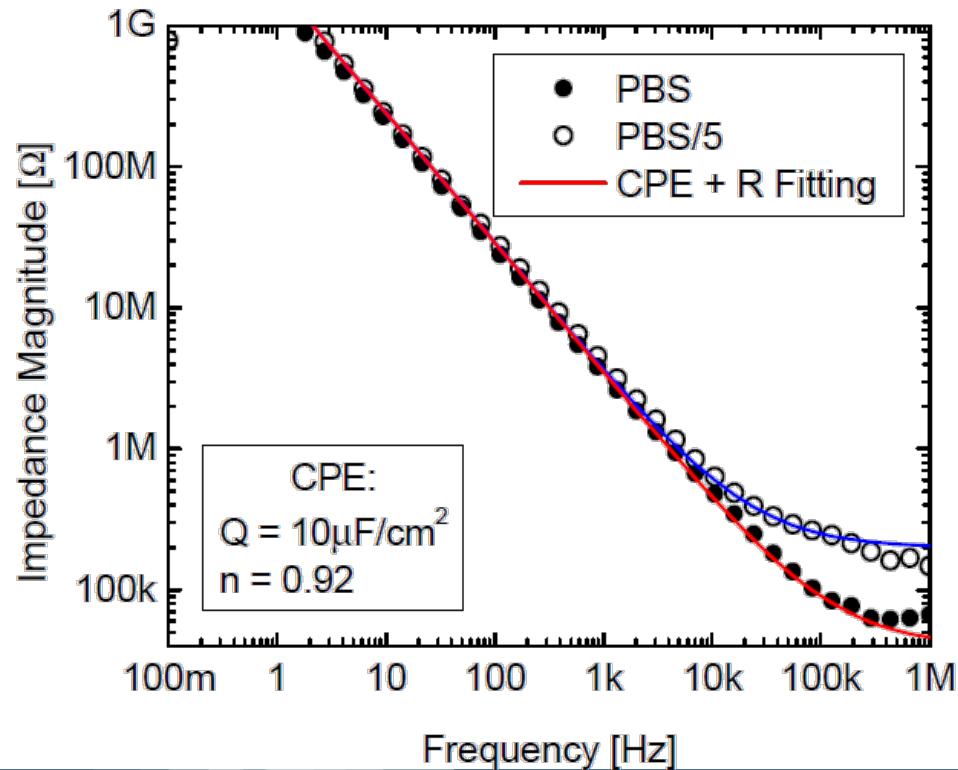
Sinusoidal excitation:

- Small signal (1-10mV) for linearity and minimal perturbation
- Wide frequency span: from <Hz to 100kHz-1MHz

Time tracking:

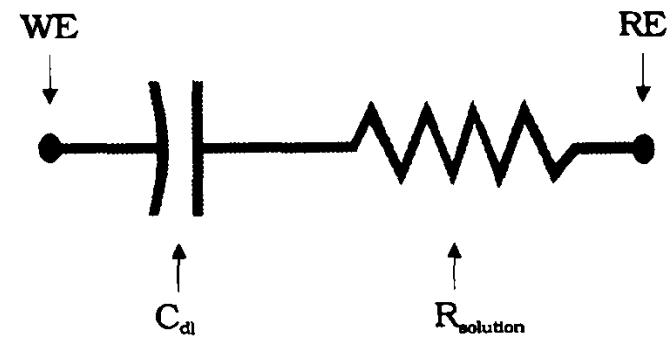
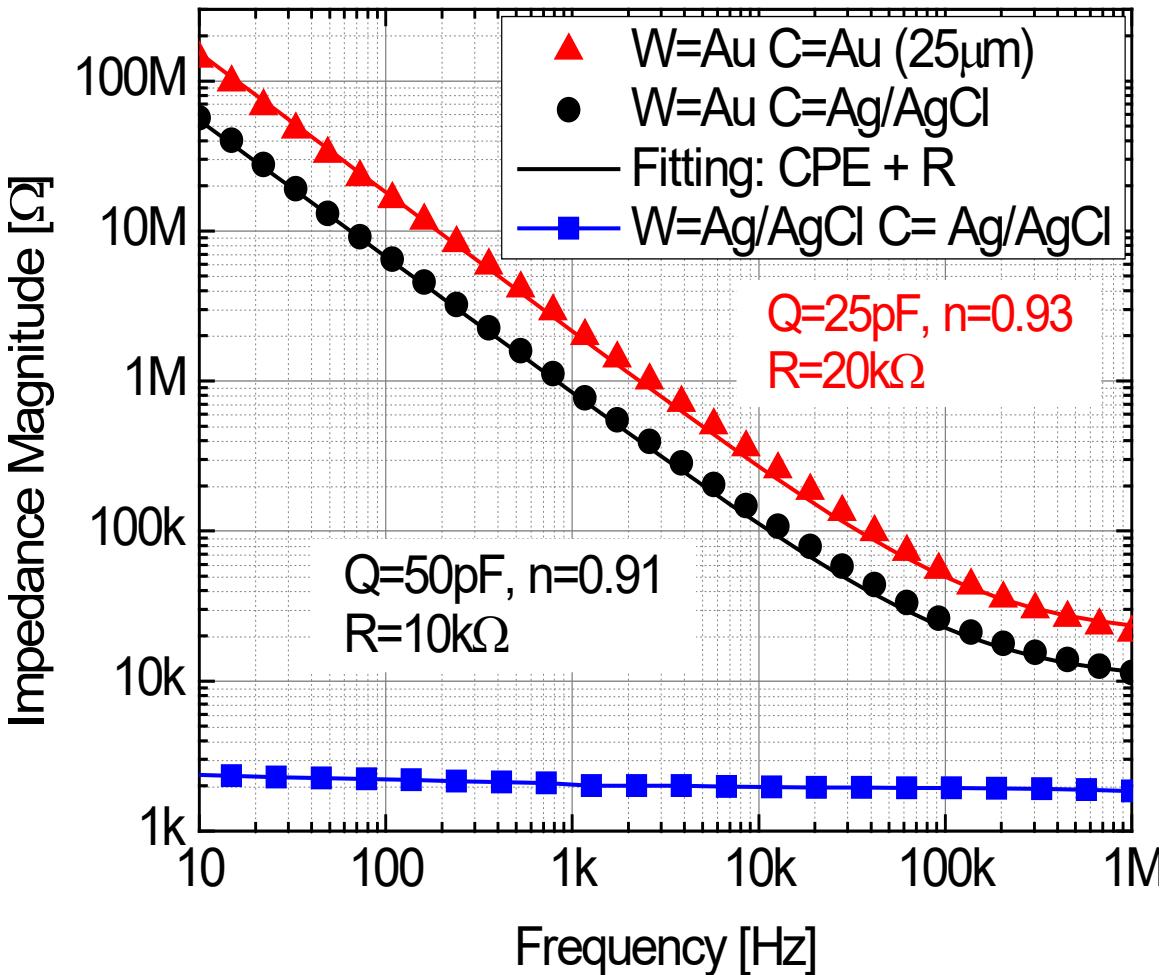


Frequency sweep:



Impedance Spectroscopy Application

Very sensitive to **interfacial properties**

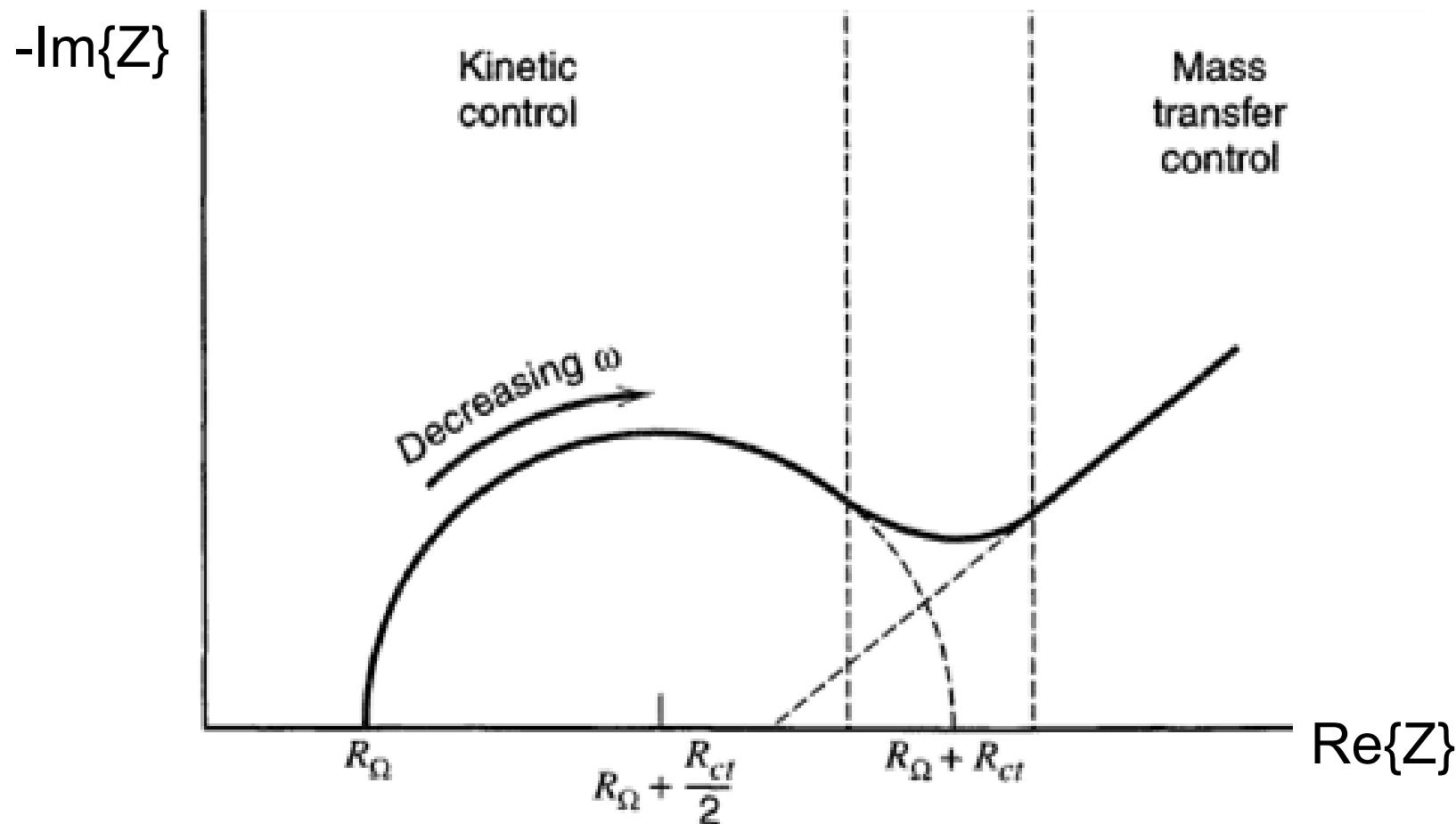


Applications:

- Coatings (paint)
- Corrosion
- Surface roughness
- Affinity biosensors
- Dielectric properties
- Battery SoC

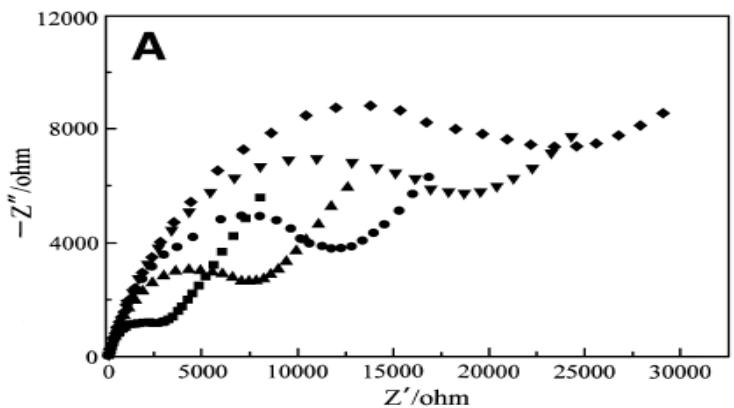
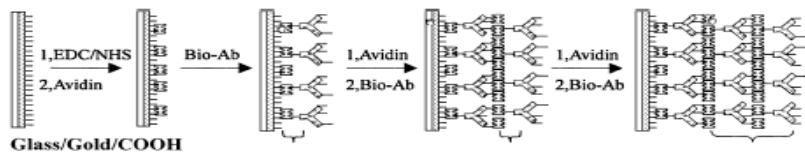
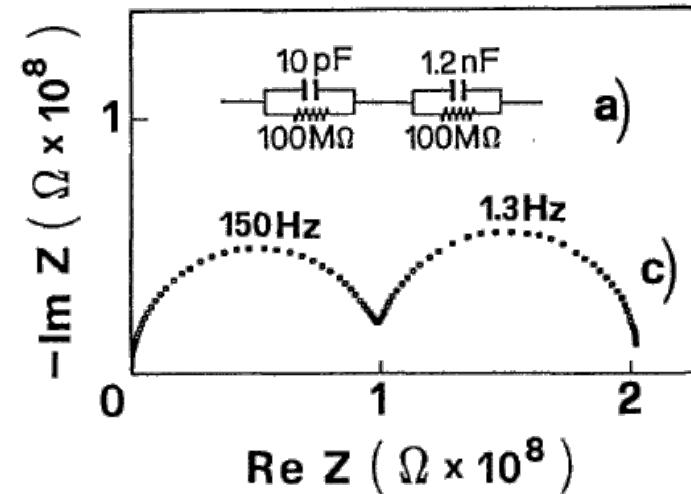
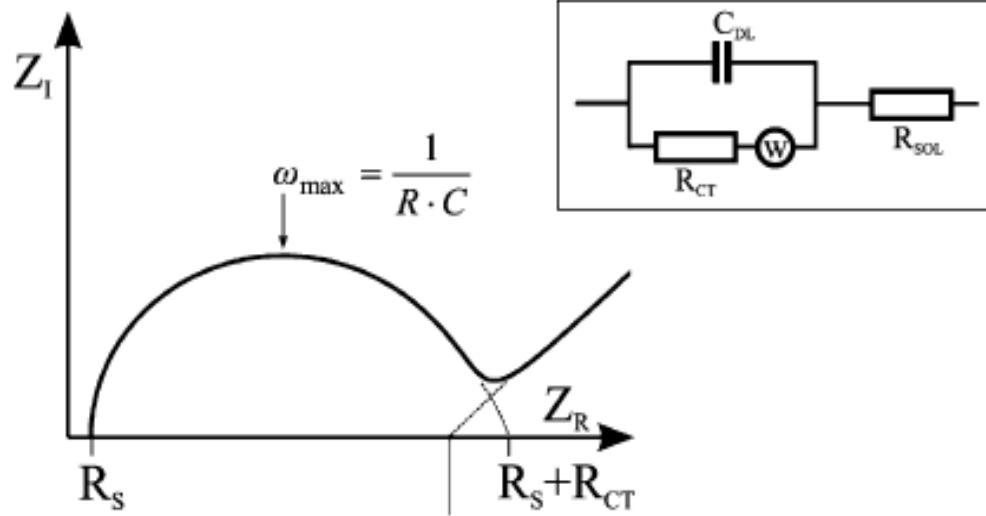
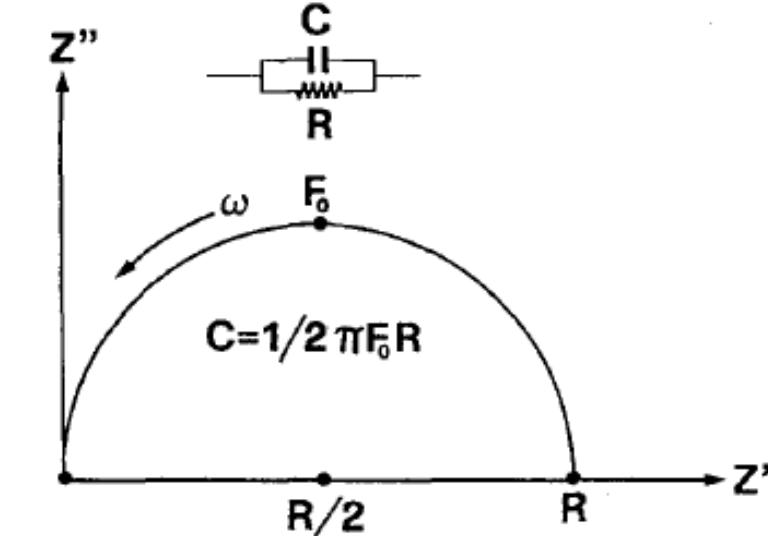
The Cole-Cole Plot

EIS spectra visualization: a very common representation in Electrochemistry, alternative to Bode (Nyquist diagram)

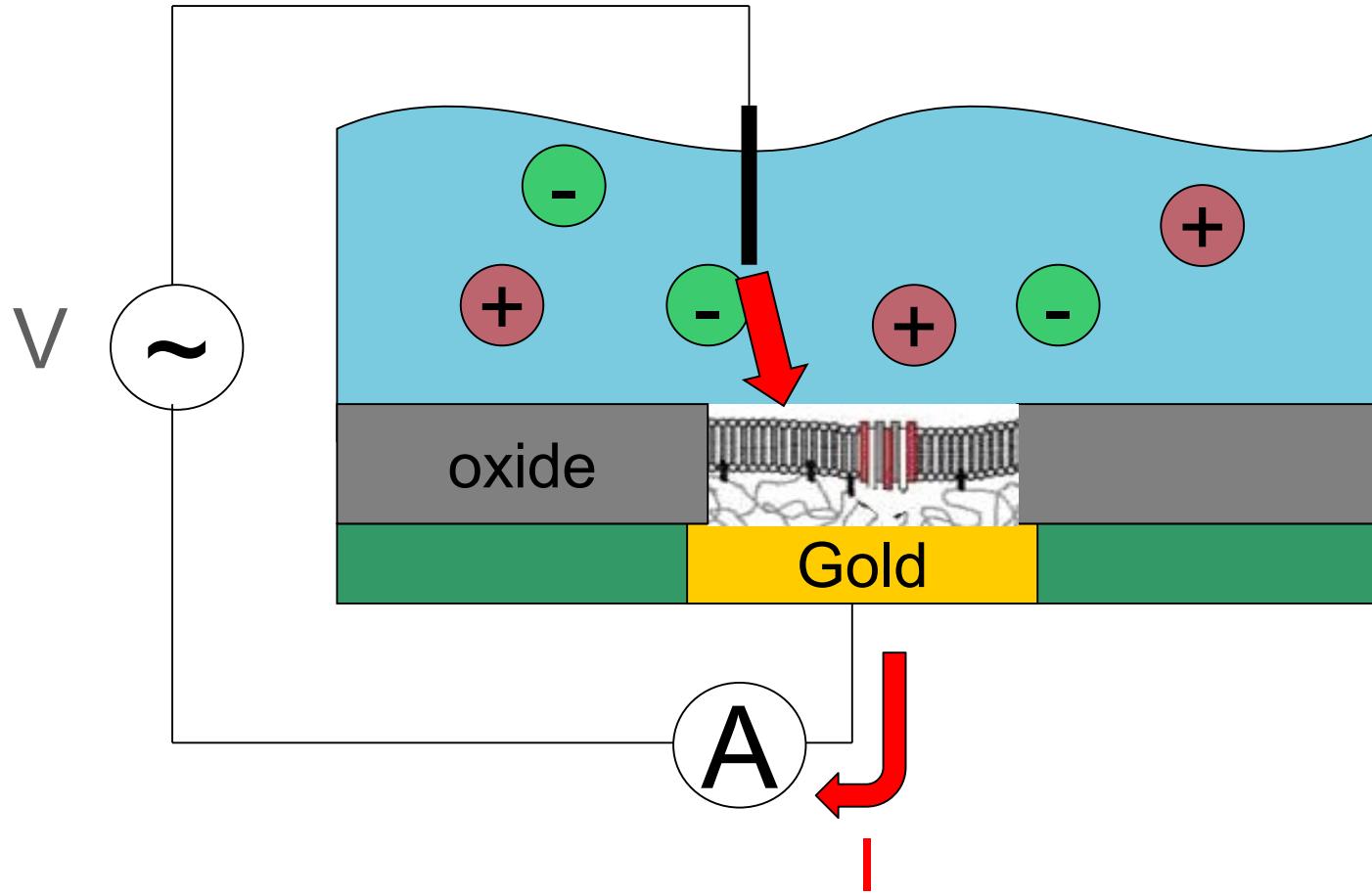




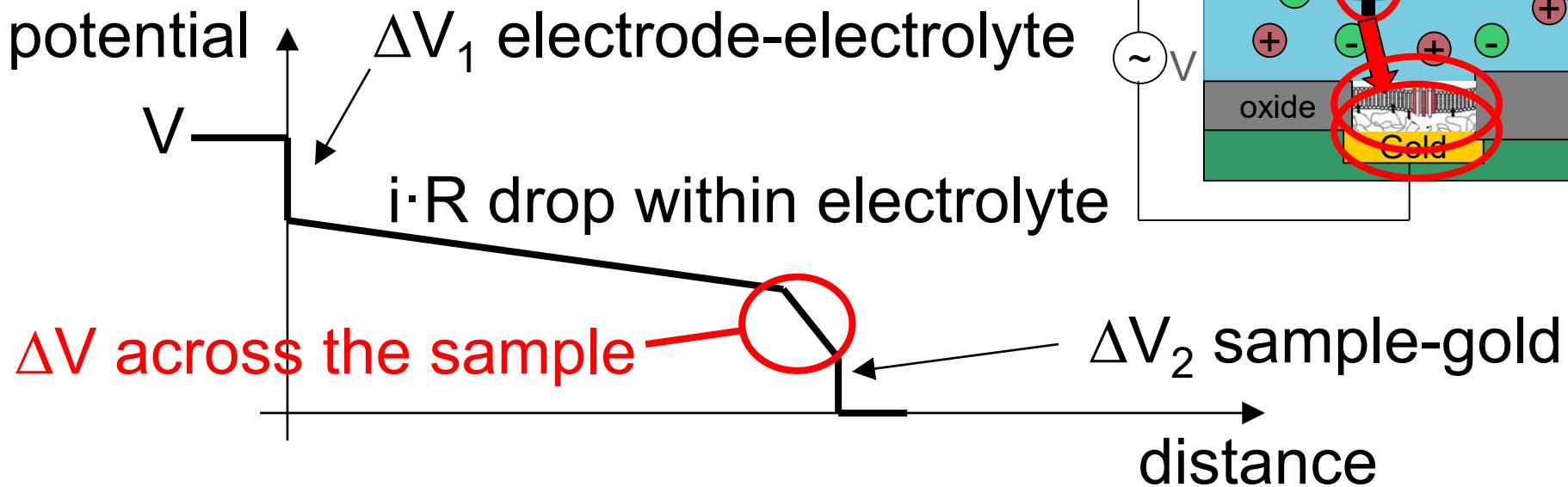
Cole-Cole Parameter Extraction



Two-Electrode Measurement



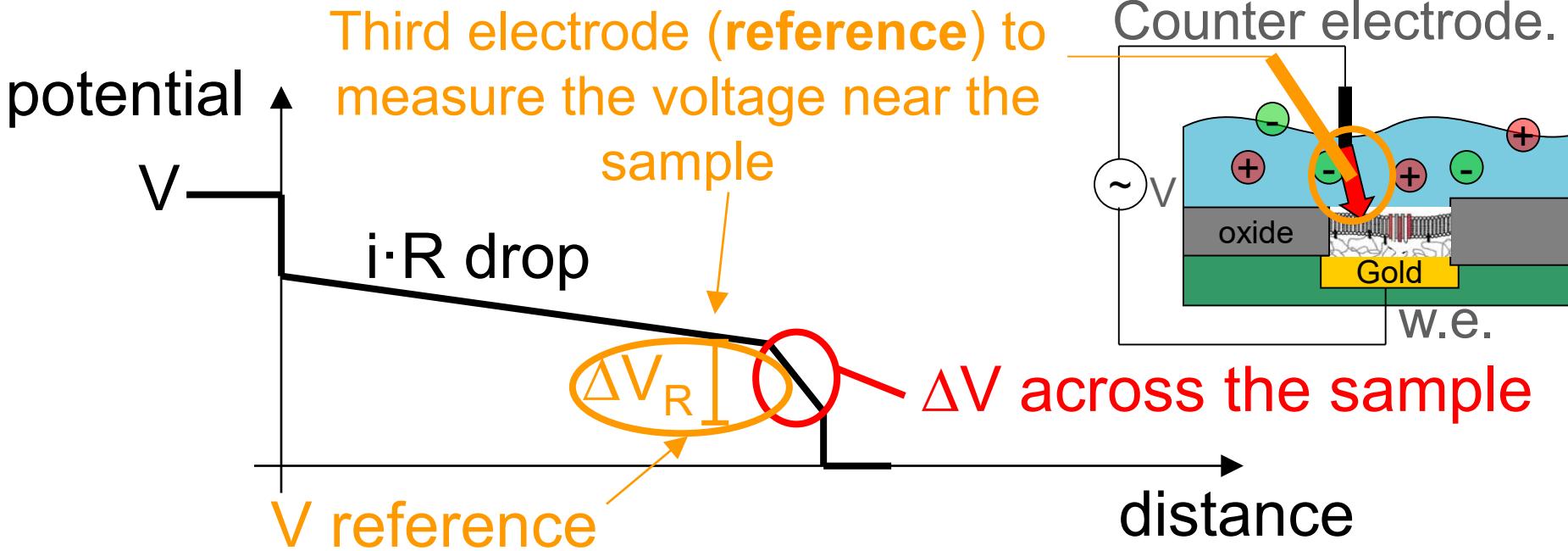
Two-Electrode Measurement



$\Delta V_1, i \cdot R$ and ΔV_2 change with current

ΔV across the sample is current-depend
→ not well controlled

Three-Electrode Setup

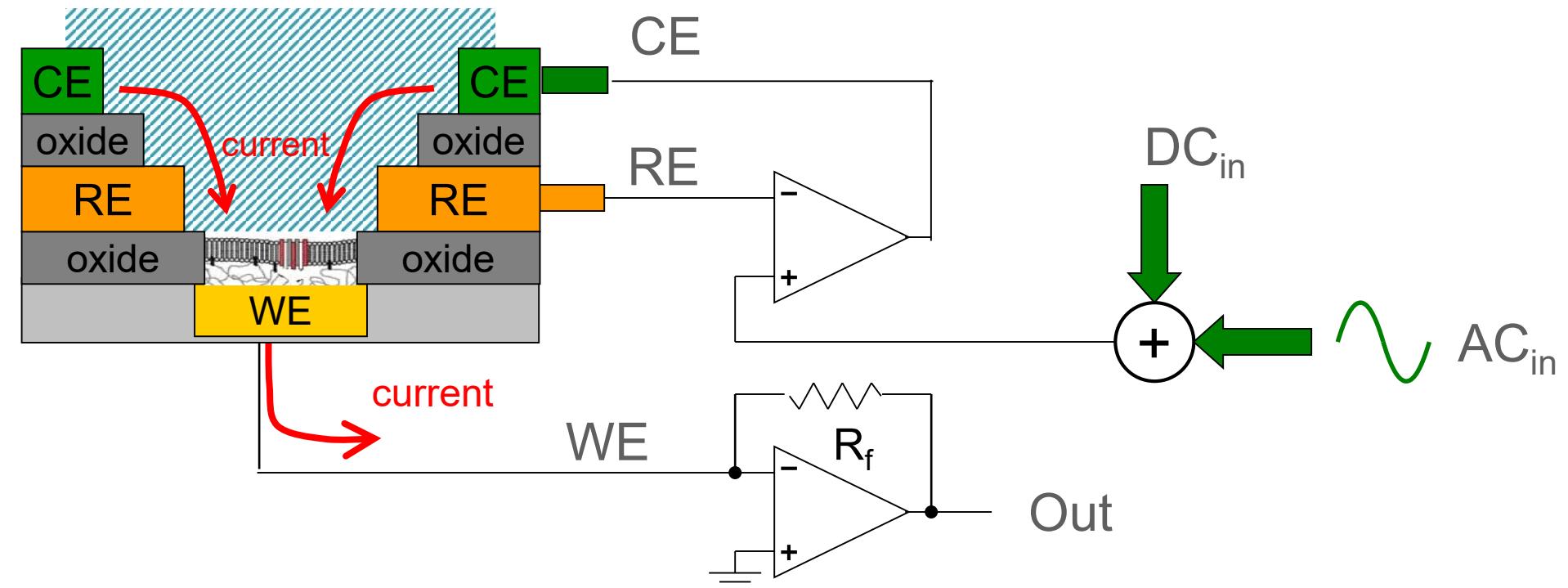


- Avoids internal polarization of reference electrode
- ΔV_R constant: **no current**; silver-silver chloride, calomel...
- reference electrode near the sample to compensate for major portion of cell iR drop



A New Instrument: the Potentiostat

Combining current detection and voltage-control loop





Reference Electrodes

Purpose: provide **stable potential** against which other potentials can be reliably measured

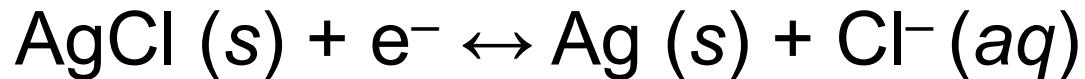
Criteria:

- stable in potential (time, temperature)
- reversible
- reproducible
- potential shouldn't be altered by passage of small current = not polarizable
- easy fabrication and handling
- convenient for use

The Silver/Silver Chloride Electrode

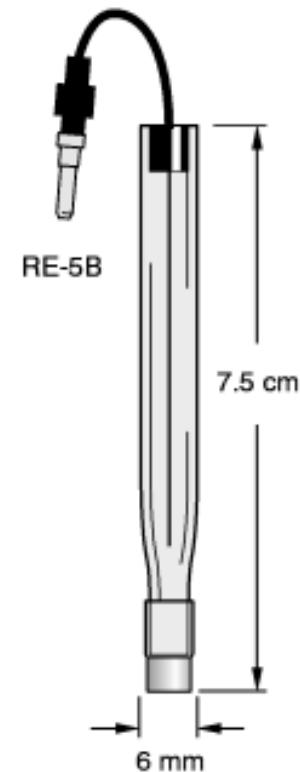
Ag wire coated with AgCl(s), immersed in NaCl or KCl solution.

It is stable in liquid that has large quantity of Cl⁻ such as the biological fluid.



$$E^\circ = +0.222 \text{ V}$$

Stable to +275°C



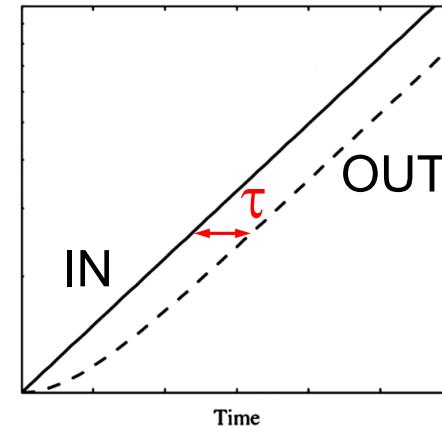
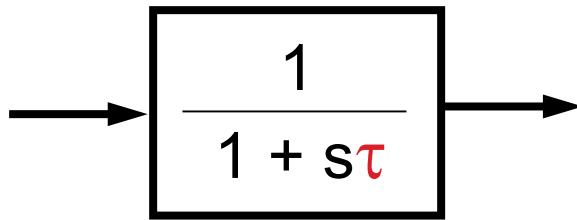
From BAS www-site



Instrument Design Specifications

Generation (cyclic voltammetry):

- Accuracy: $\sim 1\text{mV}$ (59mV characteristic feature)
- Bandwidth: $\text{BW [Hz]} = 40 \cdot \text{SR [V/s]}$



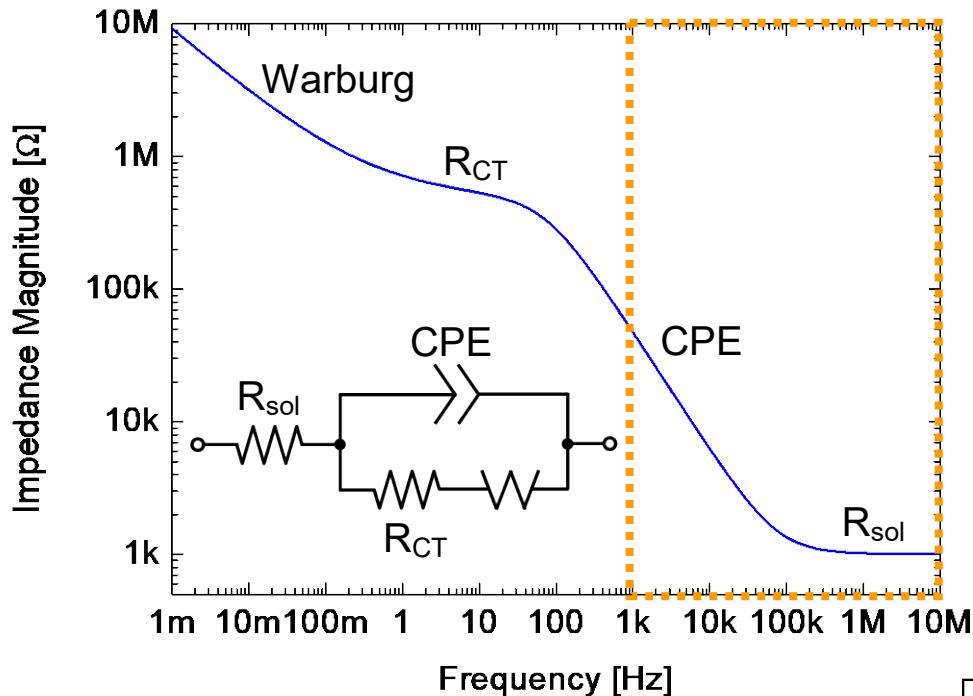
$$\Delta V_{\text{error}} = \tau \cdot \text{SR} = 4\text{mV} \rightarrow 1/(2\pi \cdot \tau) = \text{SR}/(2\pi \cdot 4\text{mV})$$

- Capacitive load $> 1\text{nF}$

Sensing:

- Sensitivity: scales with electrode area, $\sim 1\text{pA} - 1\text{mA}$
- Bandwidth: adequate for impedance and voltammetry

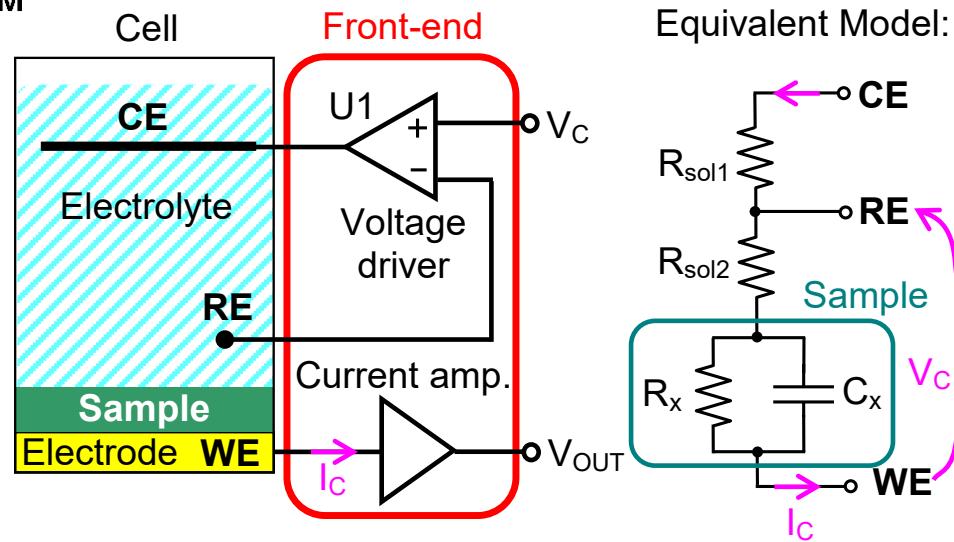
Small-Signal Equivalent Model



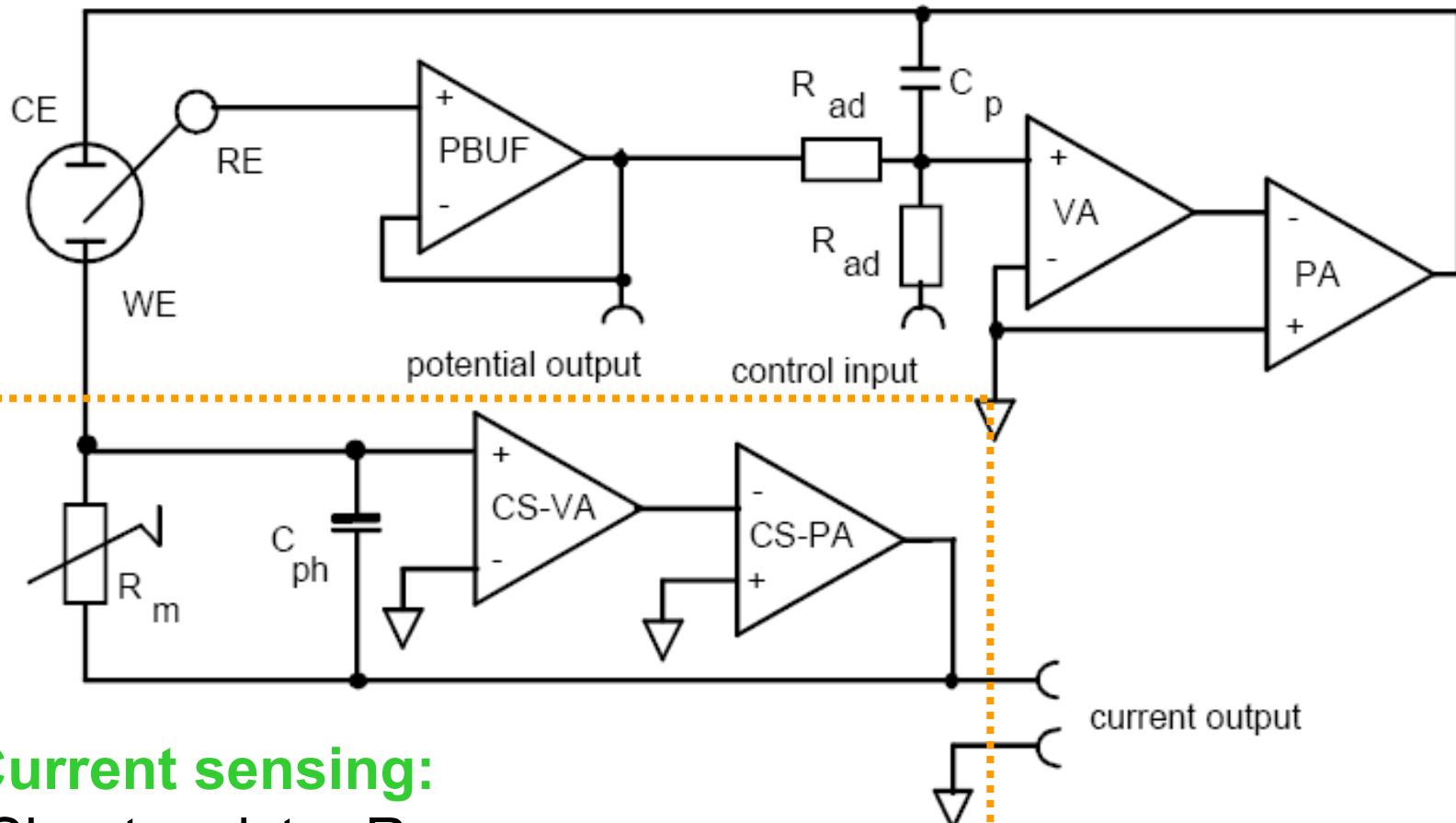
- $R_{sol} = \rho/4r$ (66Ωcm PBS)
- R_x = charge transfer
- $C_x = 0.1\text{pF}/\mu\text{m}^2$ (PBS)

Modulated by the sample

A simplified model of the interface can be adopted for design purposes (stability)
+ stray capacitances



Standard Potentiostat



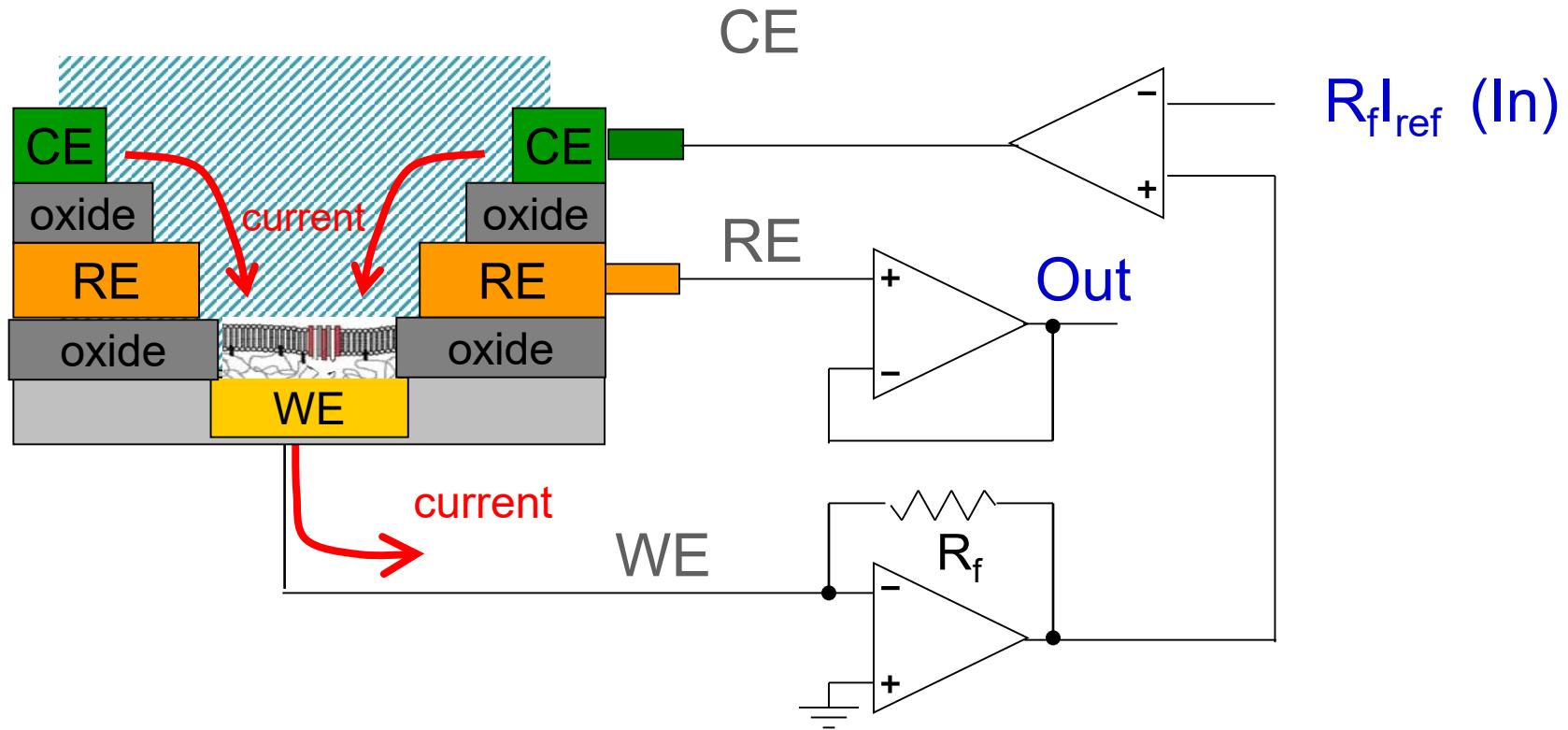
Current sensing:

- Shunt resistor R_m
 - Transimpedance R_f
- Switches change range R_m/R_f



Galvanostatic Regulation

Set the current and measure the voltage:

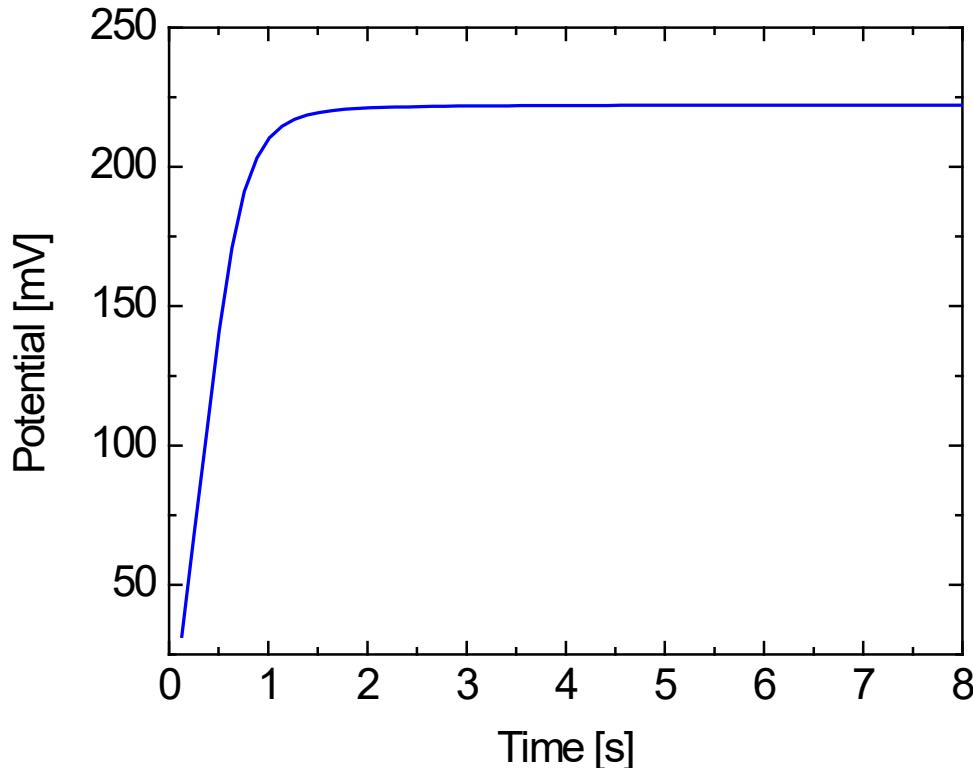
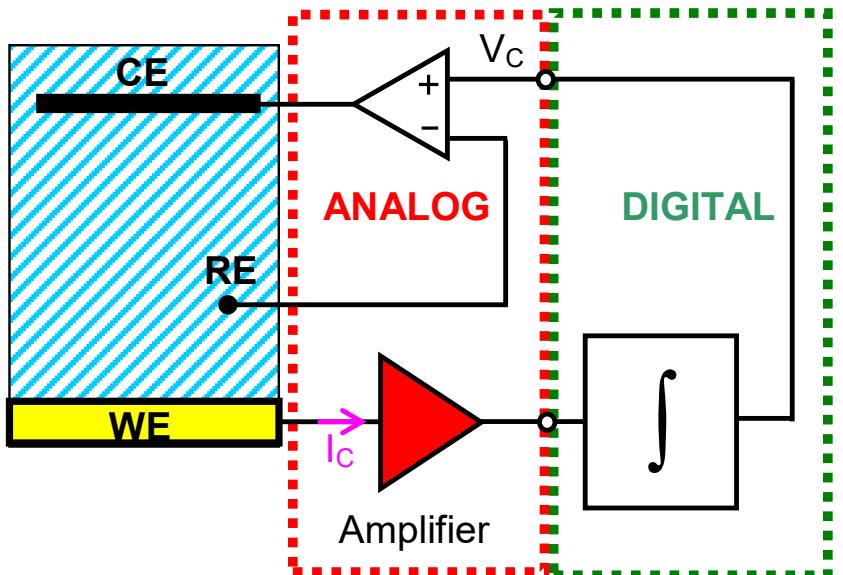


wide bandwidth more difficult (transimp. amp. in the feedback)



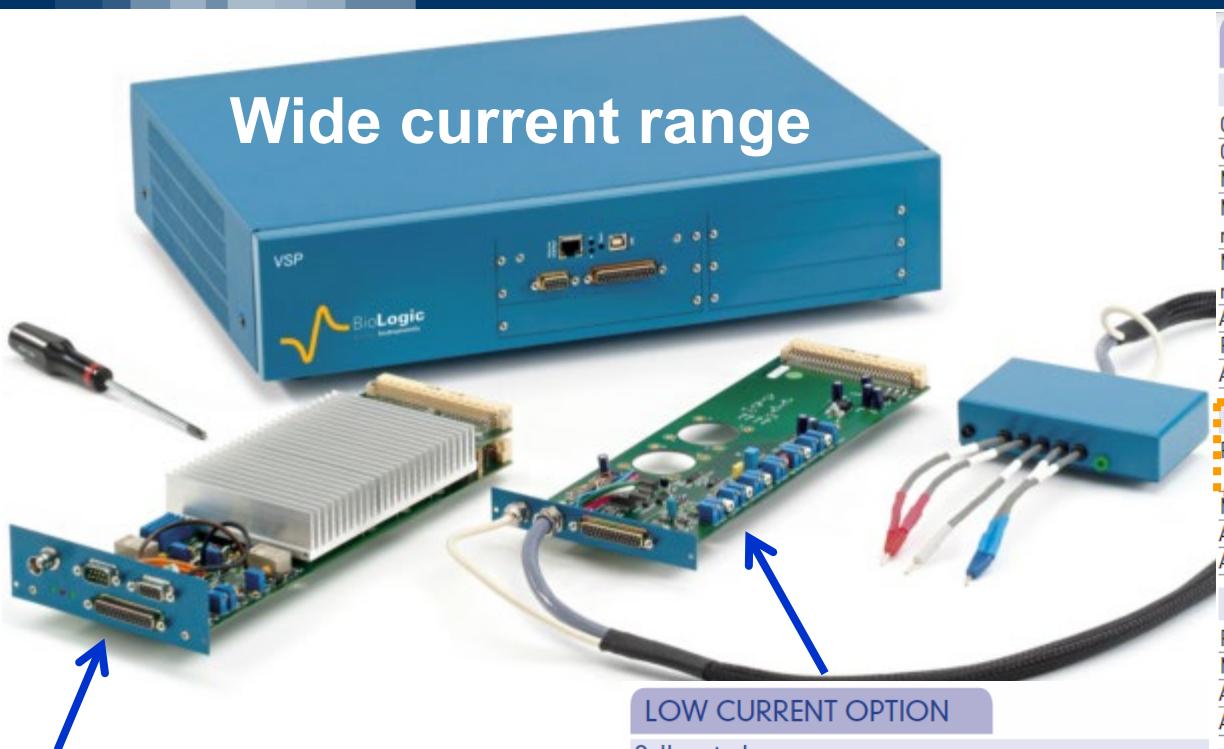
Potentiometry

A particular galvanostatic case: current set-point = 0
Measure the equilibrium potential of the interface



The loop must be stable

Commercial Workstations



4 A BOOSTER KIT

Cell control	
Maximum current	±4 A continuous
Potential ranges	±10 V at 4 A
Rise and fall time	Potentio mode: 15 µs Galvano mode: 100 µs
Measurement	
Potential accuracy (DC)	< 0.1% FSR*
Current accuracy (DC)	< 0.2% FSR*
Current noise	1 mA peak to peak [0-100 kHz] at 4 A
Potential noise	0.6 mV peak to peak [0-100 kHz]
Electrometer	
Impedance	10^{10} ohms
Inputs	3 potential leads with 2 differential voltages
Bandwidth	1 MHz

Current measurement	
Ranges	±1 nA, ±10 nA, ±100 nA, ±1 µA
Maximum resolution	0.004% of the range down to 76.3 fA
Accuracy	< 1% FSR* on the 1 nA range < 0.5% FSR* on the 10 nA range < 0.1% FSR* on the other ranges

Electrometer	
Impedance	10^{14} ohms in parallel with 1 pF
Bias current	60 fA typical, 150 fA max at 25 °C
Bandwidth	1 MHz

SPECIFICATIONS

Cell control

Connection	2, 3, 4 or 5 terminals (+ ground)
Compliance	20 V adjustable from ±10 V to 0-20 V
Maximum current	±400 mA continuous
Maximum potential	300 µV on 20 V
resolution	programmable down to 5 µV on 200 mV
Maximum current	0.004% of the dynamic range
resolution	760 pA on the 10 µA range
Accuracy (DC)	< 0.1% FSR*
Rise time	[10% - 90%] < 2 µs [No load]
Acquisition time	20 µs

Current measurement

Ranges	Automatic on every range ±10 µA to ±400 mA [7 ranges]
Maximum resolution	0.004% of the range
Acquisition speed	200000 samples/second
Accuracy (DC)	< 0.1% FSR*

Potential measurement

Ranges	±2.5 V, ±5 V, ±10 V, ±10 V adjustable
Maximum resolution	0.0015% FSR*, down to 75 µV
Acquisition speed	200000 samples/second
Accuracy (DC)	< 0.1% FSR*

Electrometer

Inputs	3 potential measurements
Impedance	> 10^{12} ohms in parallel with < 20 pF
Bias current	< 5 pA

EIS OPTION

Impedance	
Frequency range	10 µHz to 1 MHz
Amplitude	1 mVpp to 1 Vpp

General	
Dimensions	435 x 335 x 95 mm
Weight	8.0 kg
Power	85-264 V, 47-440 Hz
PC configuration	Pentium IV, Windows 2000, XP or Vista

Commercial vs. Custom Instruments

Pros:

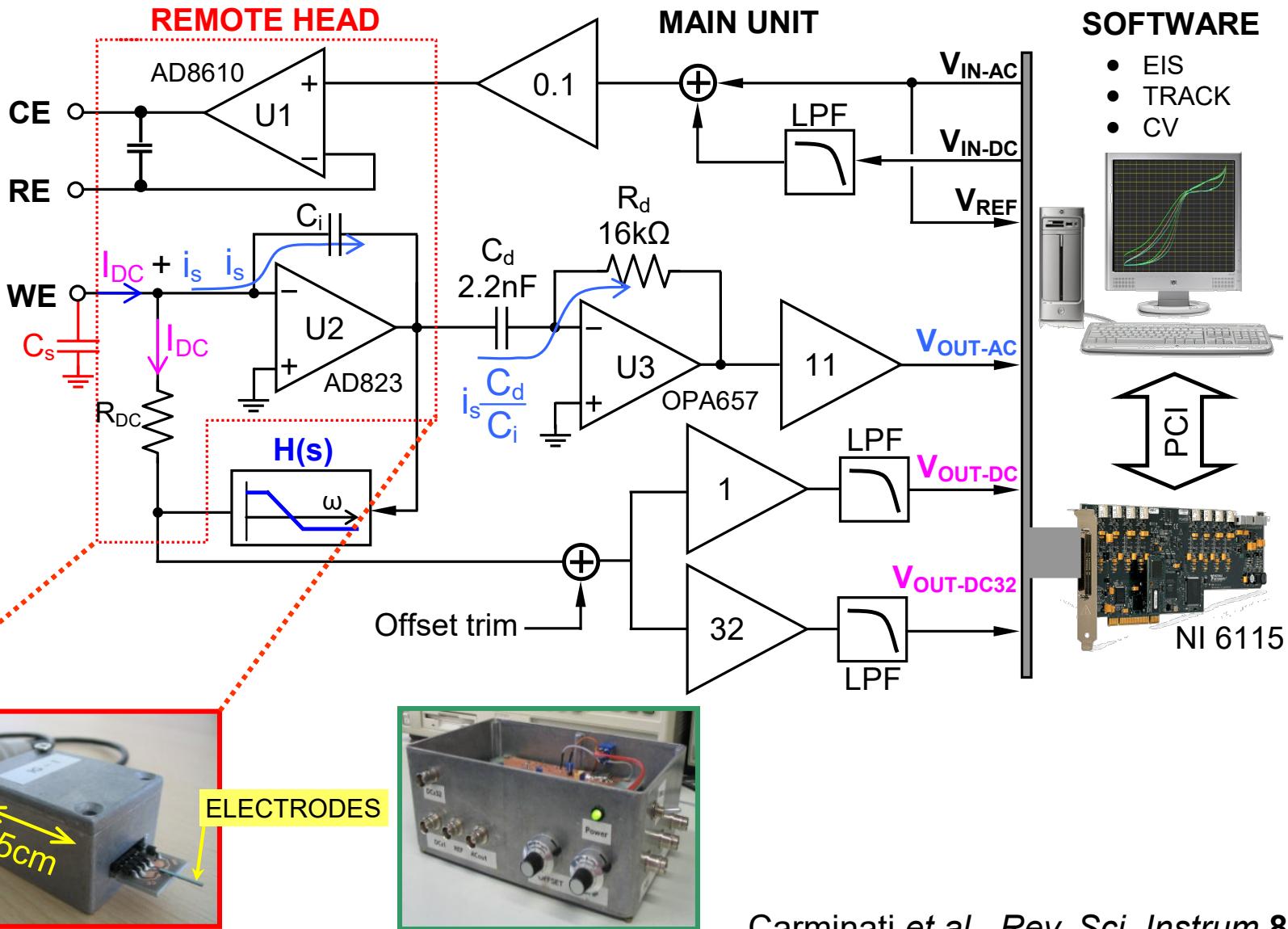
- Wide catalog of off-the-shelf products
- Versatile: wide range of currents and operating modes
- Professional software

Cons:

- Bulky (portable models are emerging)
- Few channels, rigid configuration/parameters
- Not optimized (performance can be improved for a specific application)

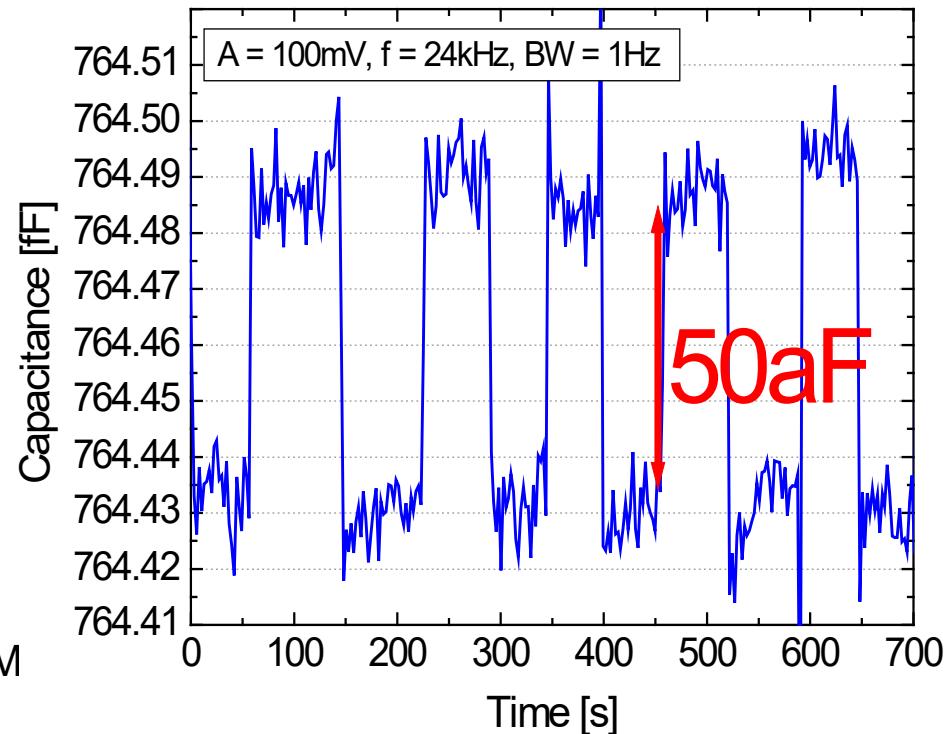
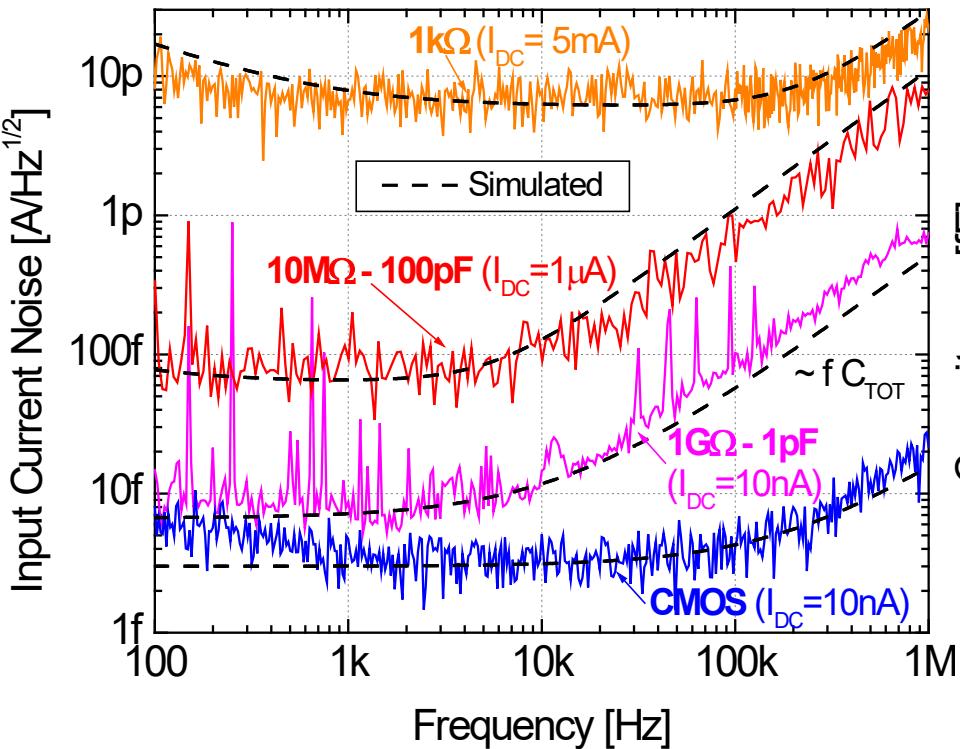


Enhanced Nanoscale Potentiostat



Achievable Performance

HEAD	R_{DC}	C_i	G_{DC}	G_{AC}	BW	Noise	Max. I_{DC}
CMOS	45M Ω	0.1pF	45M Ω	66M Ω	2MHz	3fA/ sqrt(Hz)	10nA
Integrator different.	1G Ω	1pF	1G Ω	400M Ω	1MHz	7fA/sqrt(Hz)	10nA
	1G Ω	10pF	1G Ω	40M Ω	1MHz	10fA/sqrt(Hz)	10nA
	10M Ω	100pF	10M Ω	4M Ω	1MHz	70fA/sqrt(Hz)	1 μ A
	standard transimpedance with $R_{feedback} = 1k\Omega$				10MHz	6pA/sqrt(Hz)	4mA



Multichannel Systems

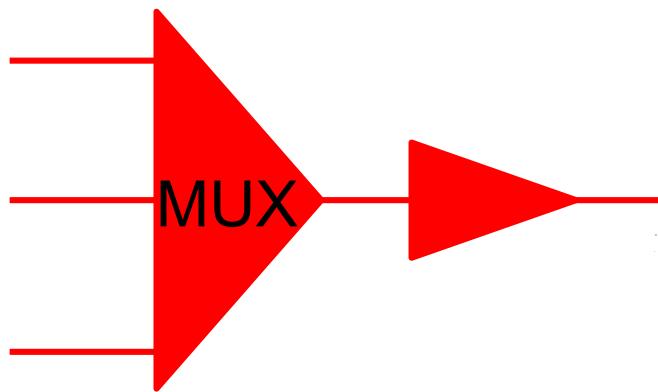
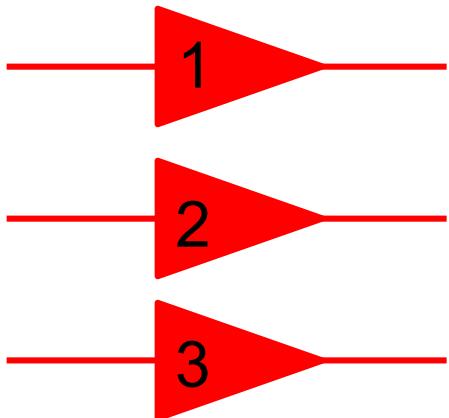
Multiple working electrodes:

- to control the potential of different interfaces
- to address multi-electrode systems



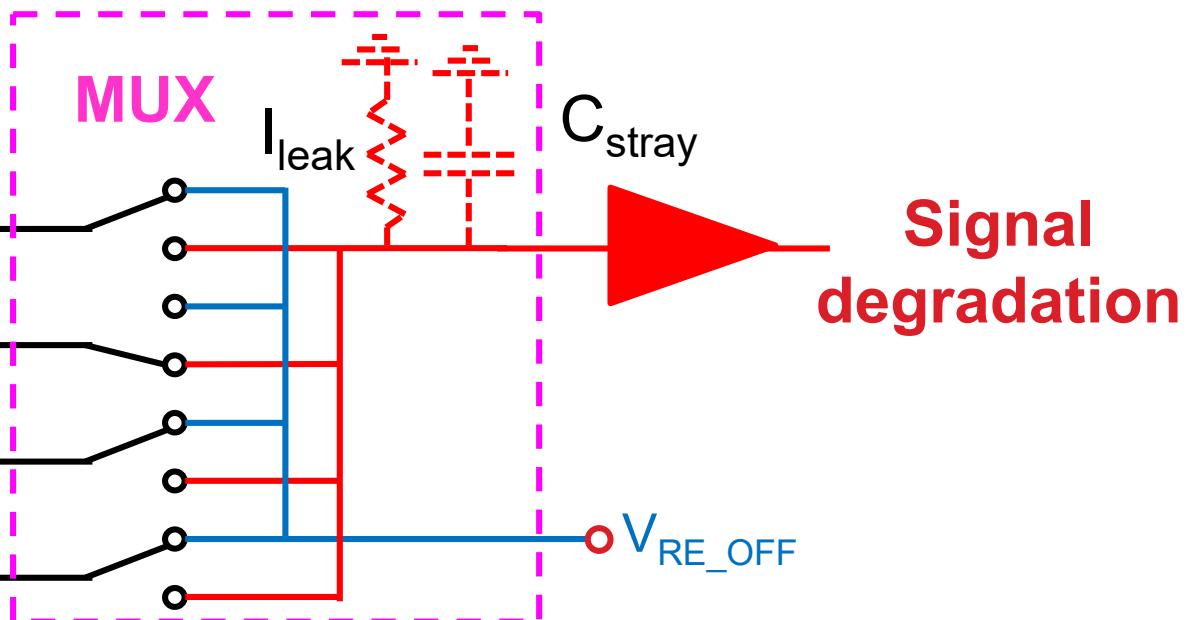
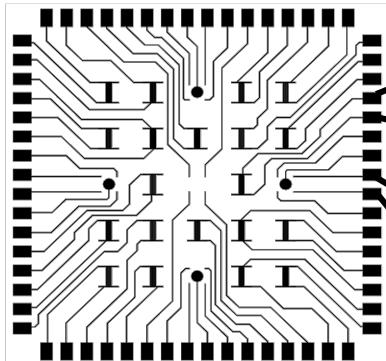
Trade-off: parallel replication vs. multiplexing

- cost and size (routing, acquisition channels)
- input signal degradation
- scan time

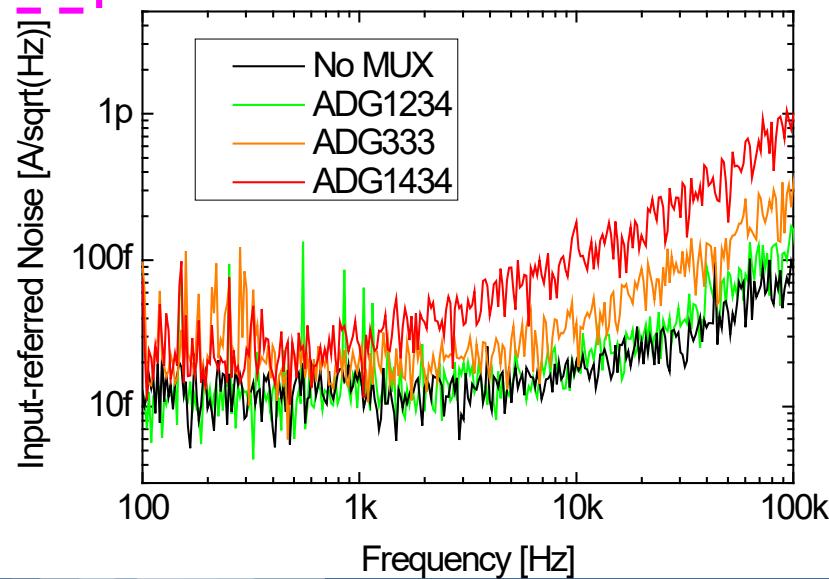


Critical MUX Design

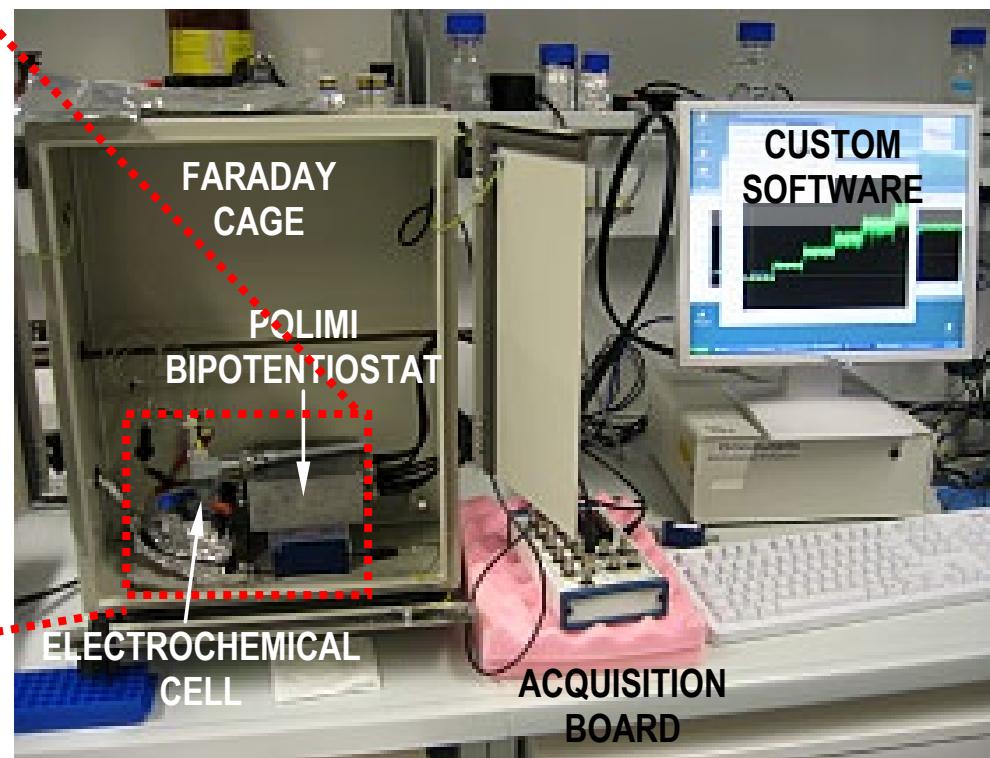
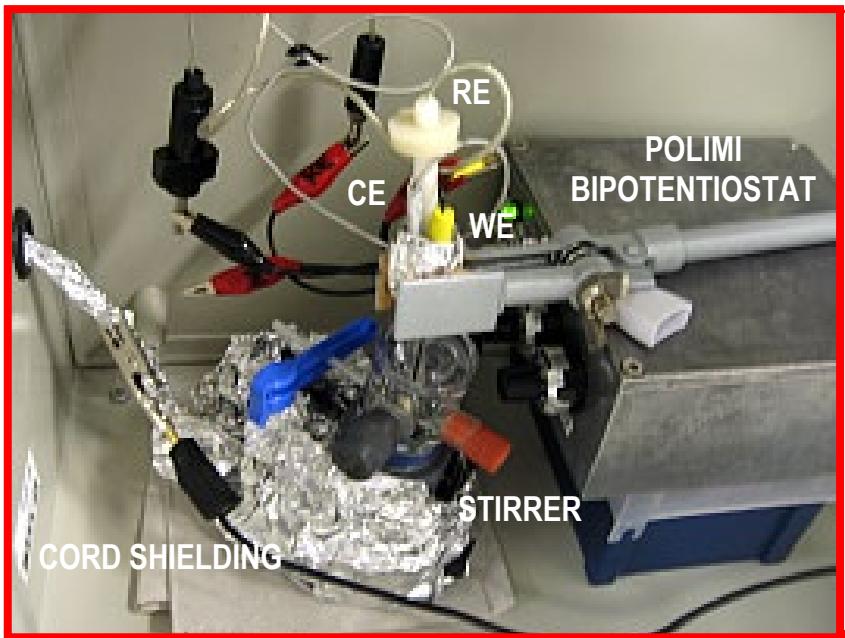
Channel addressing



- Use of single switches
 - Minimize parasitics
 - Bias disconnected electrodes
- ↓
- Control the potential
 - Reduced cross-talk (coupling)



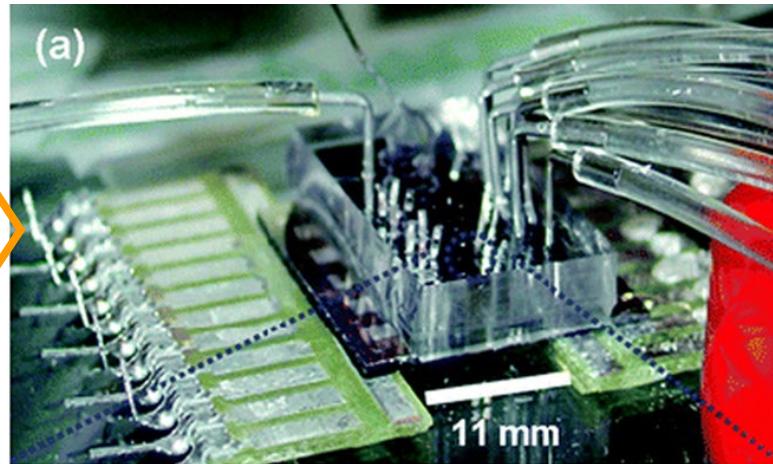
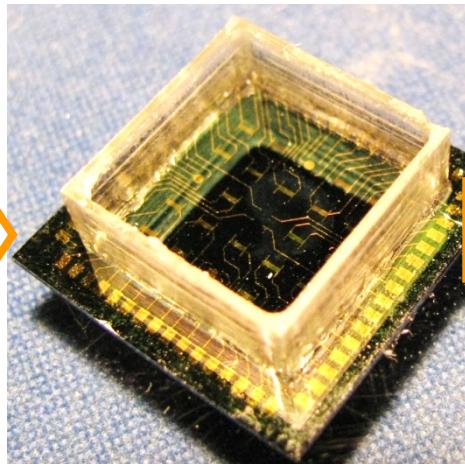
A Standard Electrochemical Setup



Practical critical issues for signal integrity:

- Shielding
- Long cables → stray capacitance
- Stirrer motor noise

Setup Miniaturization Trends

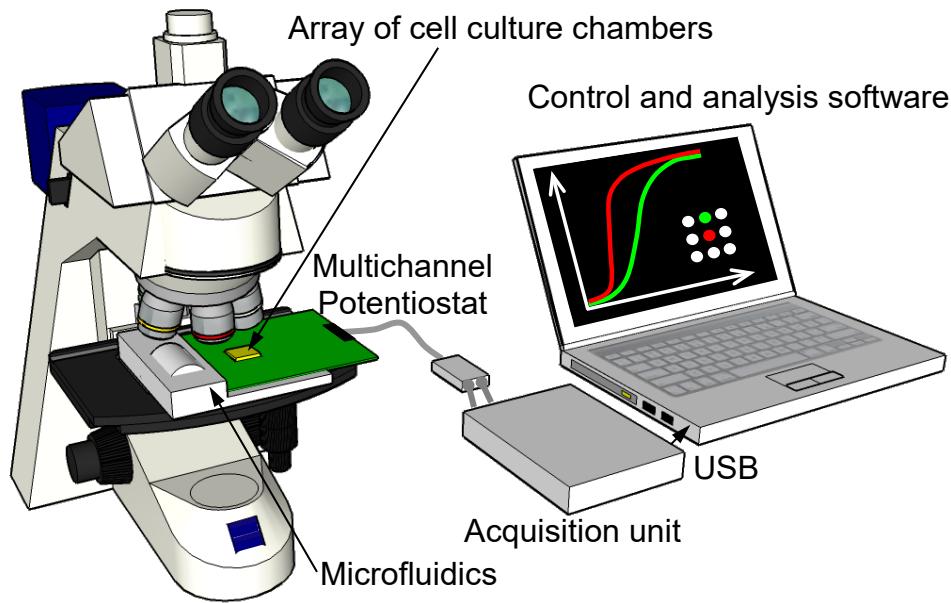


- From macro to **micro-electrodes**
- From static to **microfluidics**
 - *precise manipulation of fluid samples*
 - *same size scale of biology*
 - *less reagent waste*
 - *faster reactions*
 - *miniaturization/portability*

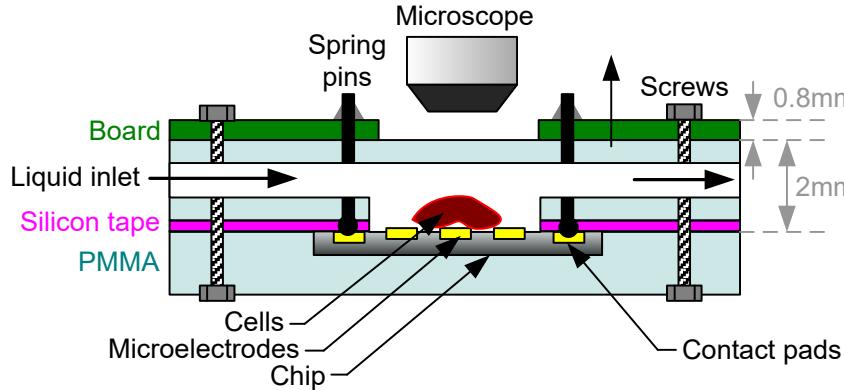


Lab-on-a-Chip!

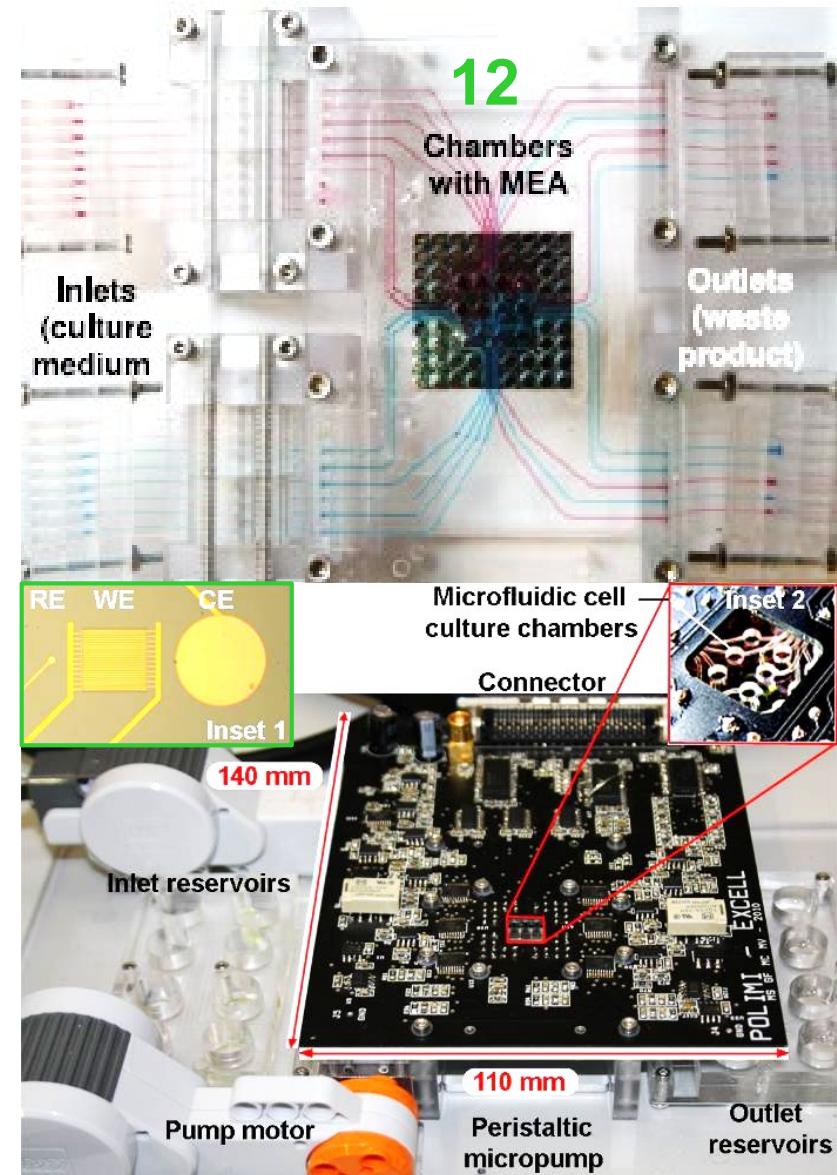
Electronics Integrated with the Setup



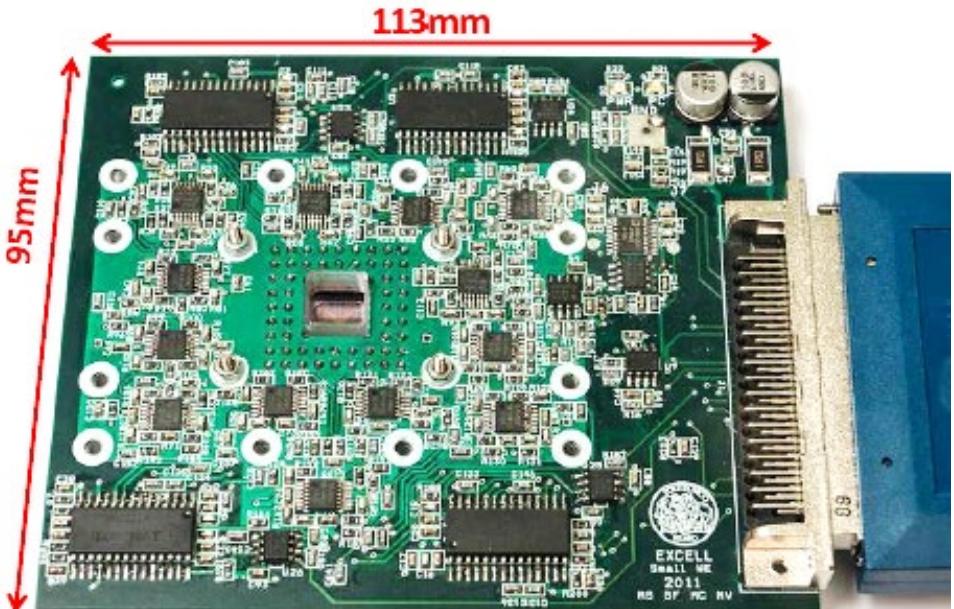
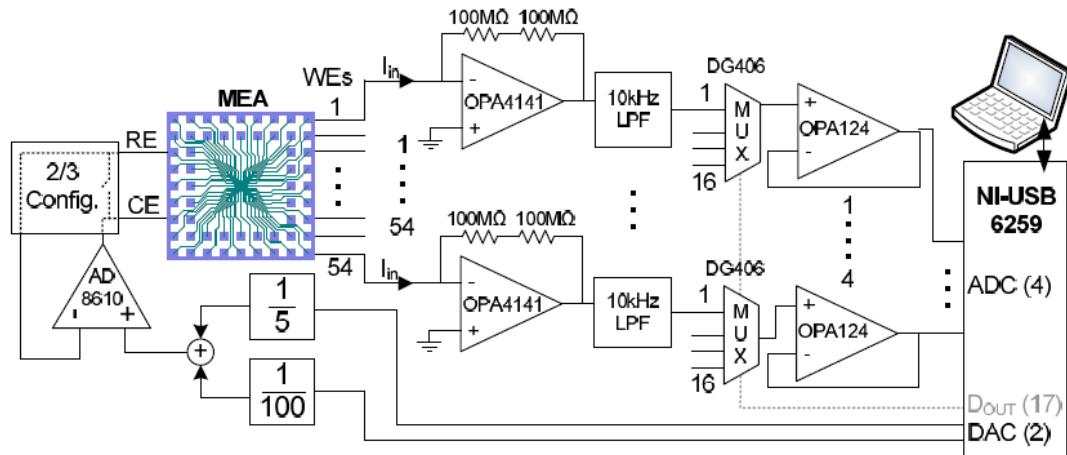
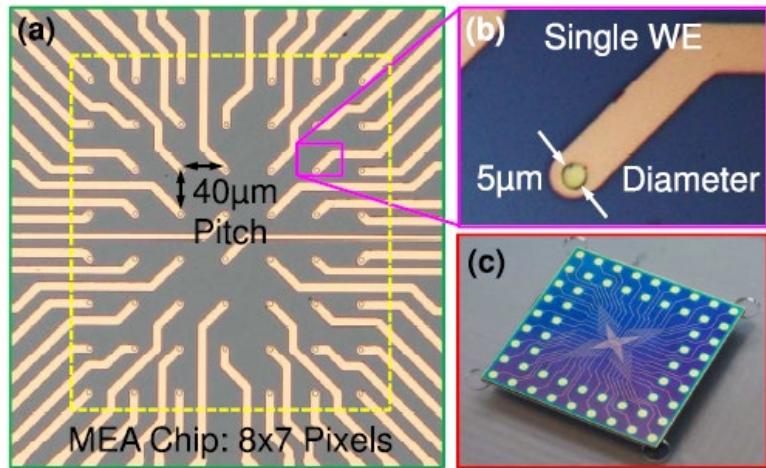
24 Channels, 100kHz BW



M. Vergani *et al.* TBCAS 2012



Example: 54 Channels

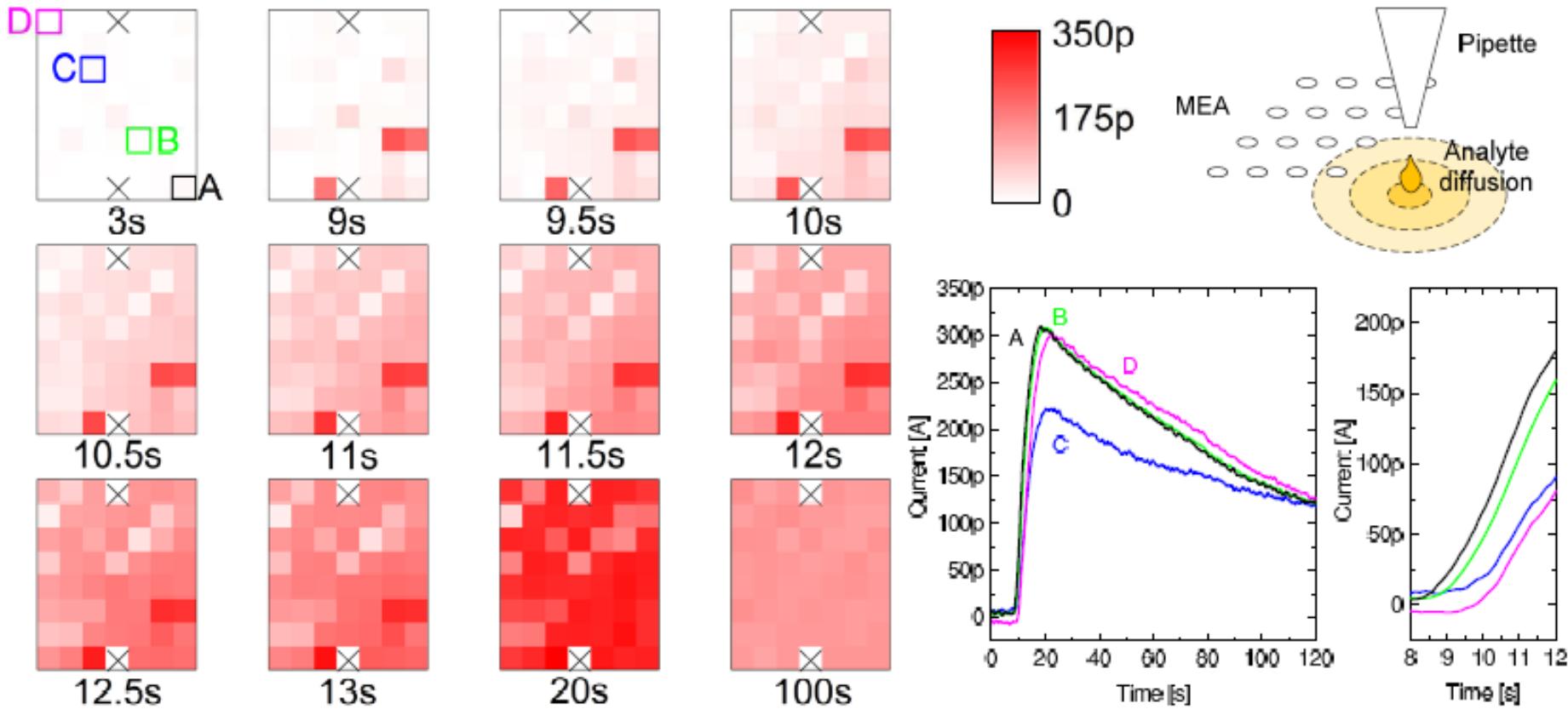


54 Channels, 8kHz BW
3pA resolution
Connectivity issues
Power issues: 3.8W



Example of Electrochemical Imaging

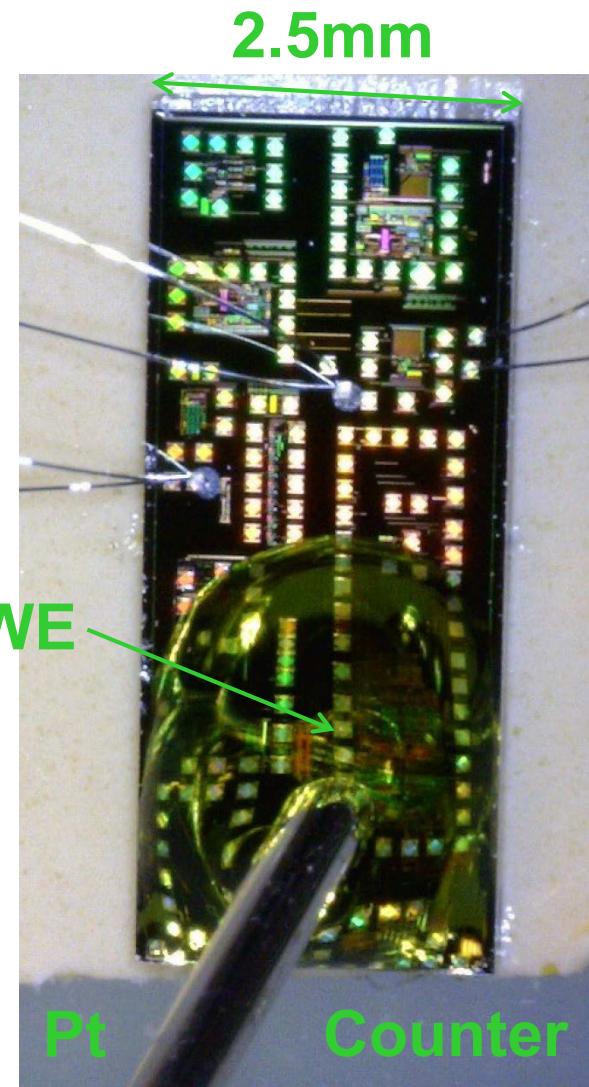
Tracking in real time the diffusion of the redox molecules:



From Discrete to Integrated Systems

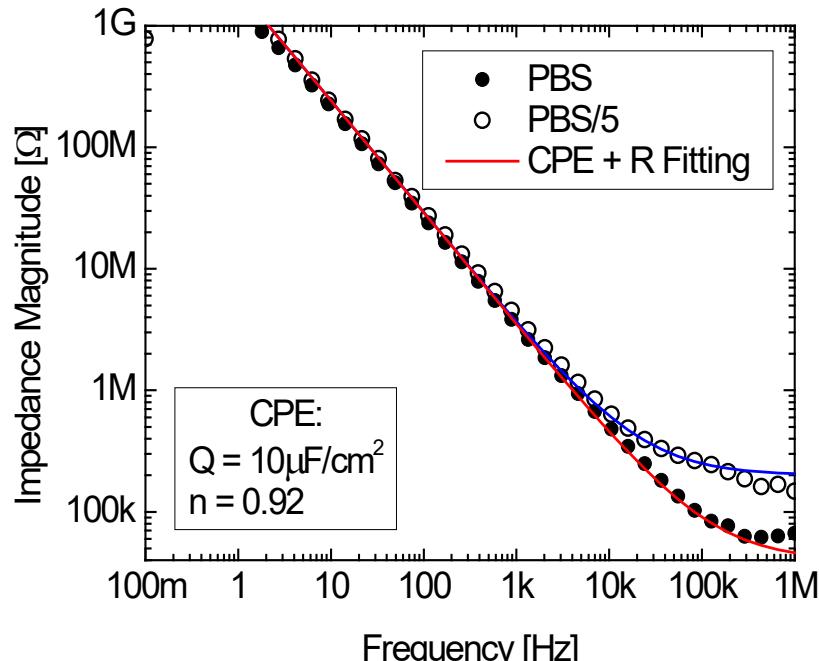
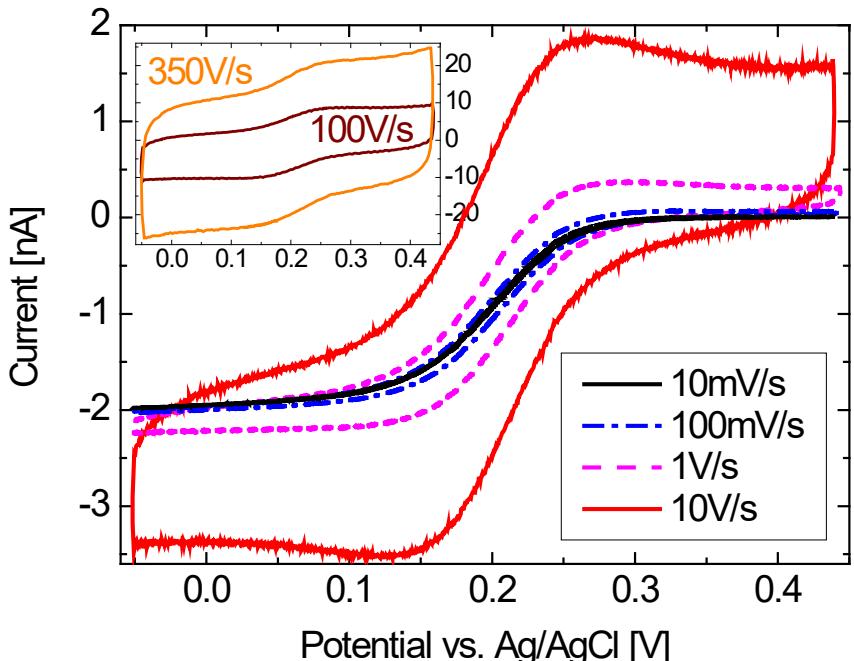
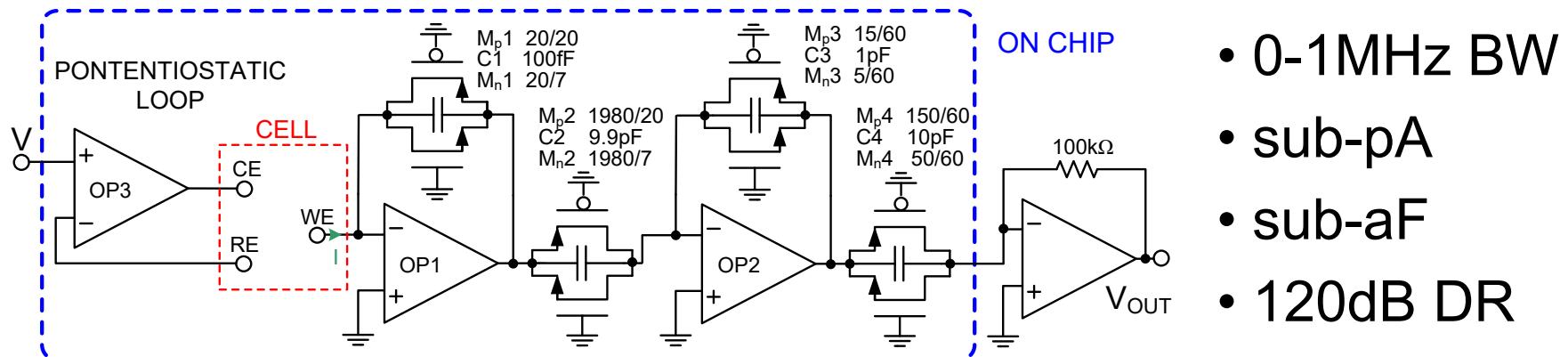
Moving to an **integrated circuit** allows:

- Miniaturization
- Parallelization (multichannel)
- Reduction of parasitics

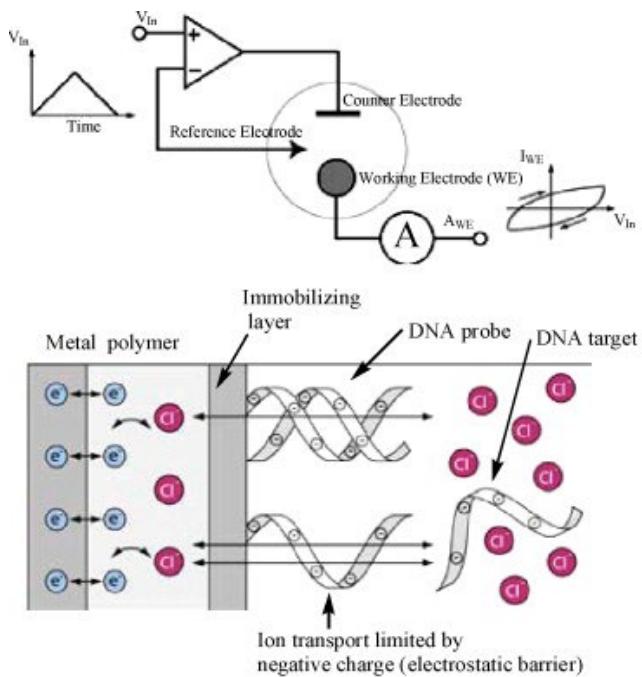


Single-Chip CMOS Potentiostat

Single channel, improving performance: matched-mosfets

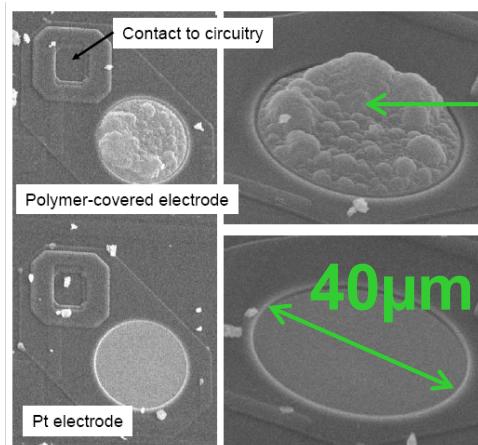
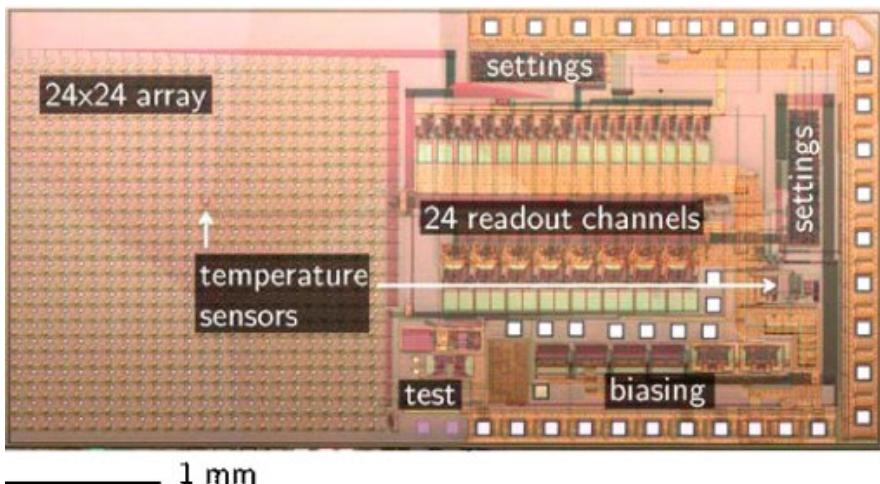
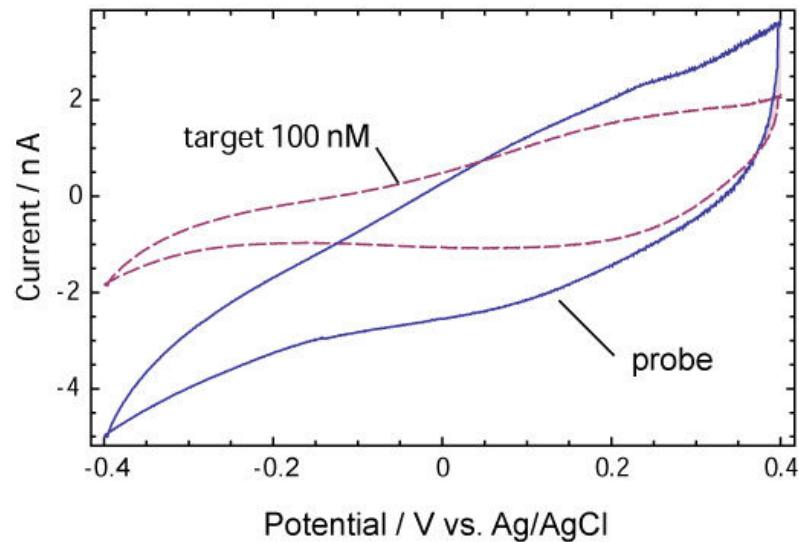


Multichannel CMOS Potentiostat



576 Channels

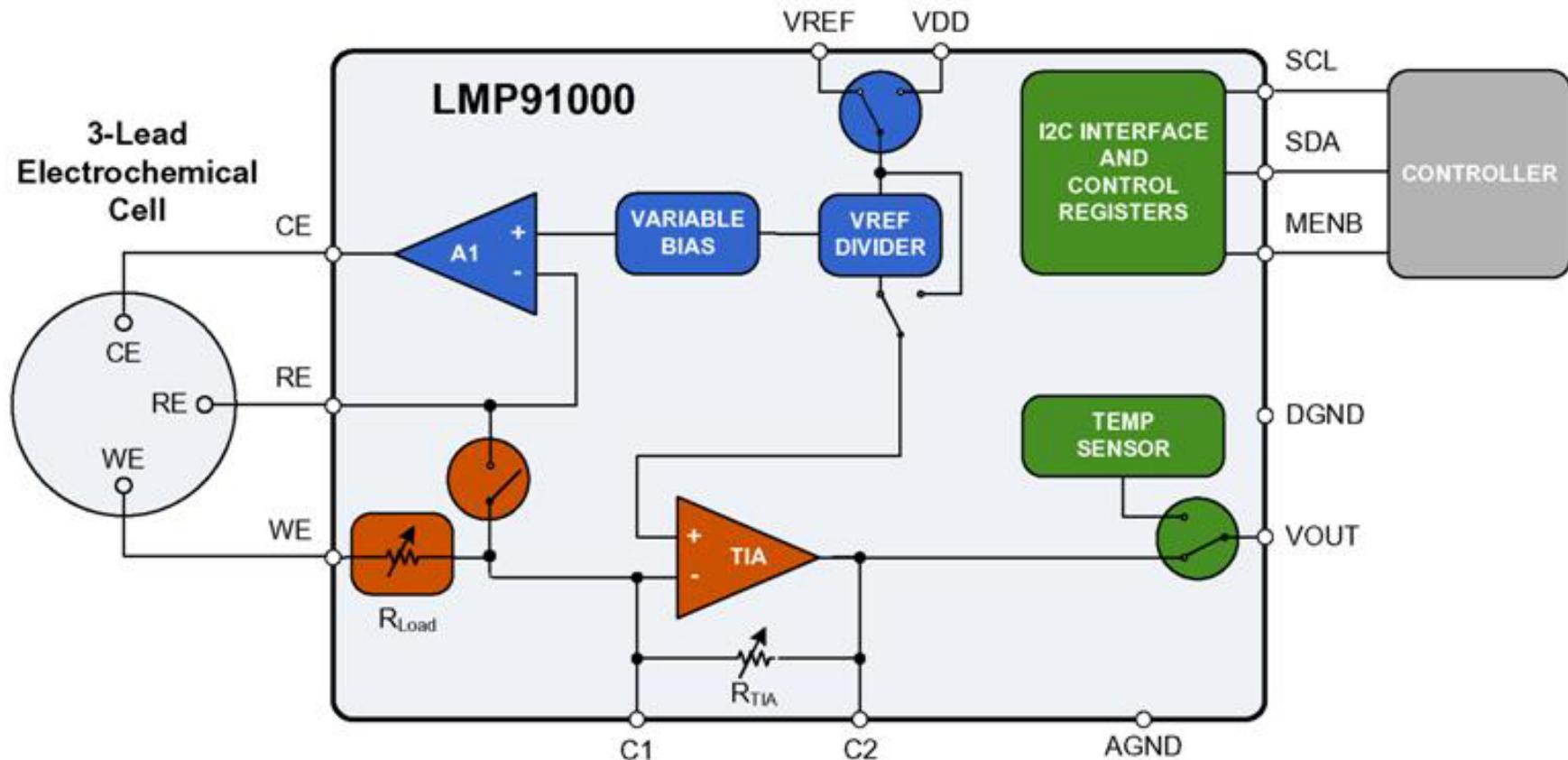
100 nM complementary 30-mer
average area change (N=46): -38%



F. Heer et al.
ISSCC 2008

Commercial Single-Chip Potentiostat

General-purpose interface for electrochemical sensors



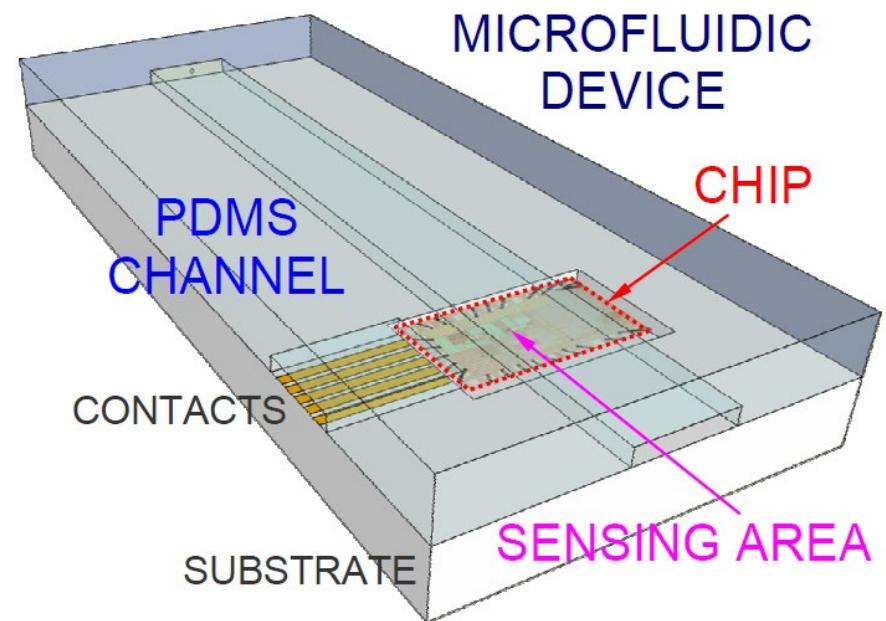
Challenges for using the chip PADs as electrodes:

Material issues:

- Packaging (world-to-chip)
- Pad **metal**: aluminum vs. gold
- Surface roughness and functionalization

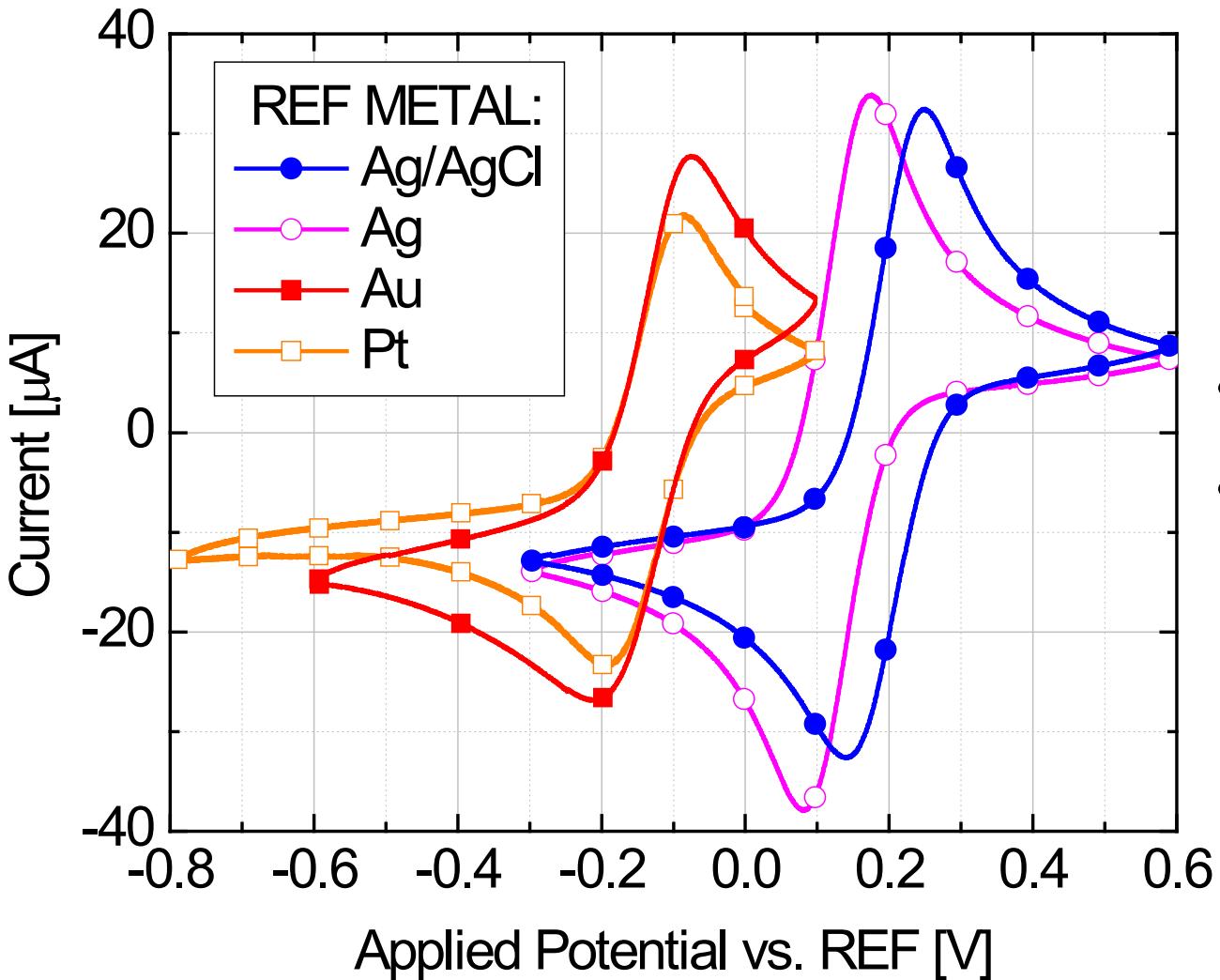
System issues:

- Addressing and multiplexing
- On-chip vs. off-chip elaboration



Pseudo Reference Electrodes

What happens if the RE is **not ideal**:



- Potential shift
- Distortion



Packaging

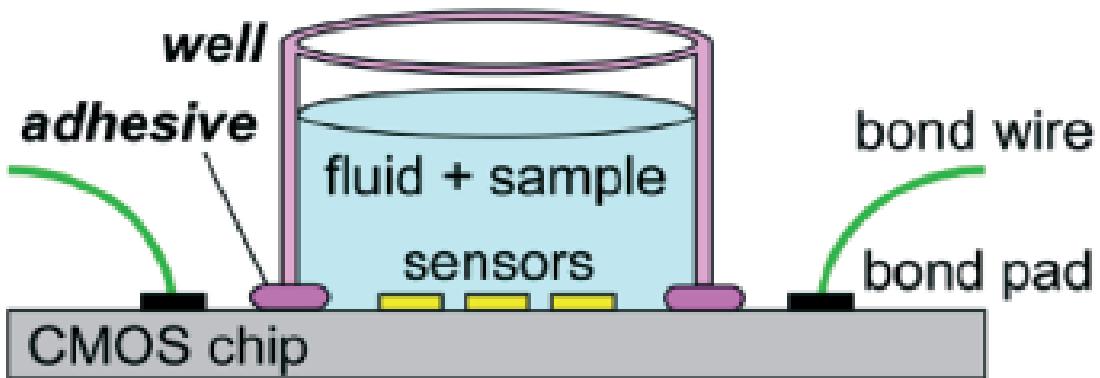
A suitable **package** should provide:

- Protection of the chip from the liquid
- Protection of the bonding wires (without breaking them)
- Patternable exposure of the electrodes to the liquid
- Long-term sealing for re-usable chips
- Connectors/interface with the rest of the system

A standard biochip packaging approach is still missing. Several artisanal solutions have been proposed. Industry need an automatable approach.

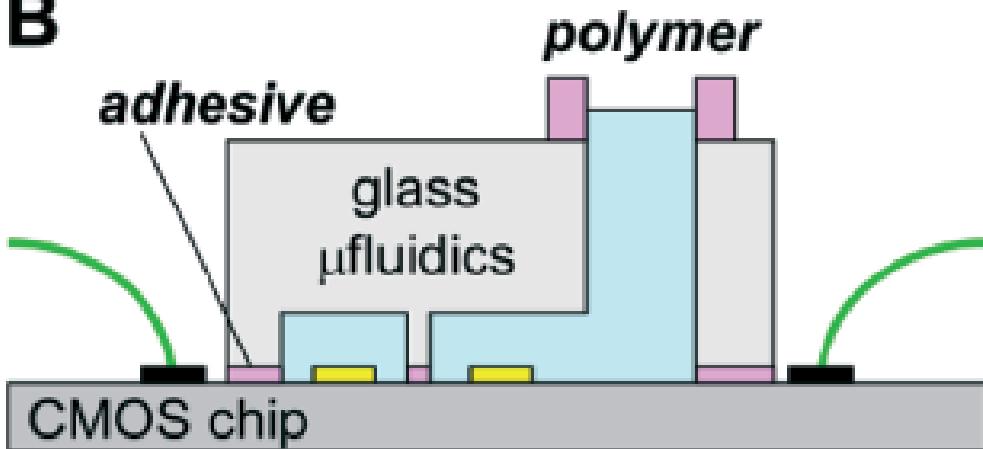
Packaging Approaches

A



Simplest
For large chips, but Si area is expensive

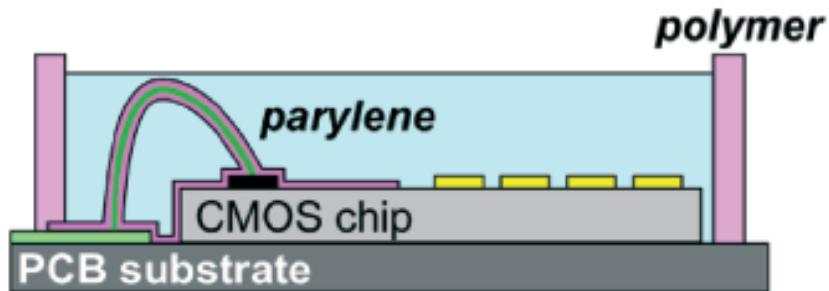
B



Rigid microfluidics
Sealing issues

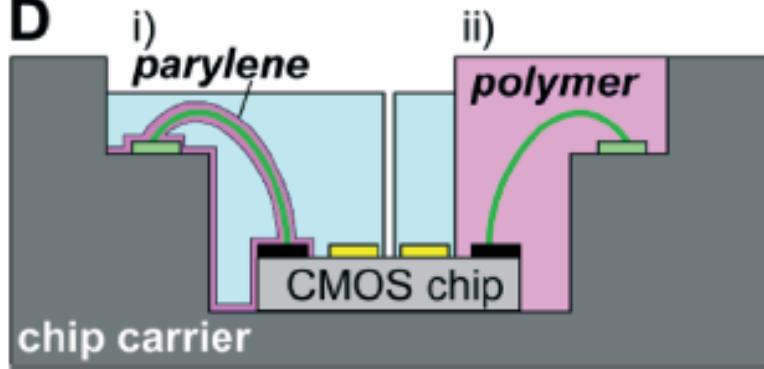
Packaging Approaches

C

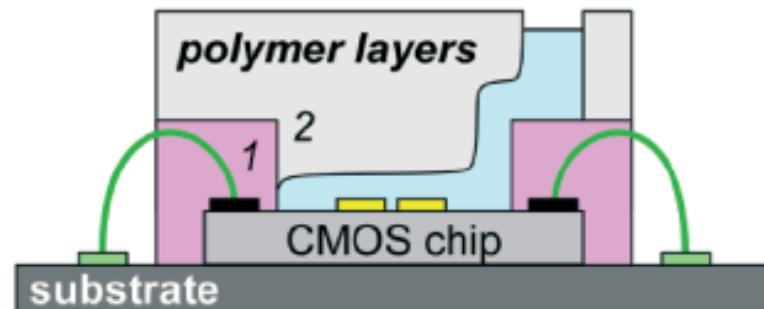


Cover with photo-patternable soft passivation

D



E



Sacrificial layer

Direct Sacrificial 3D Printing

