EPFL
École polytechnique fédérale de Lausanne

CHEMINA
Laboratory of Chemical Nanotechnology

Semiconductor Interfaces with Biology
Lesson 14

MSE 304

Emily Schafer

emily.Schafer@epfl.ch

December 19th 2025

In-Depth Evaluations Open

We will dedicate 5-10 minutes for you at the start of class to complete the survey next week

Log onto moodle and stay on the home page (dashboard, not the course page)

Click on the arrow to the top right of the screen which will reveal a block that contains the entitled “In-depth evaluation” tile

You can then select this course (MSE 304) and complete the feedback

You will also be able to access the course evaluations via the EPFL Campus App

In-Depth Evaluations – The Importance of Your Participation

This was the first time we ran this course with 80% new material compared to Prof. Francesco Stellacci’s course last year

Any feedback you provide will help us to improve the content for next year!

I am a tenure-track assistant professor (non-permanent position at EPFL) and your evaluations are necessary for my tenure case in the future. So your feedback is very important so I can continue to teach future students, thank you for your cooperation!

Plan of the Course: Fundamentals, Characterization, and Applications

1: Intro to Surfaces & Interfaces

2: Surfaces in the Real World - Adsorption

3: Surface Energetics & Interfacial Phenomena

4: Atomic Structure of Real Surfaces

5: Solid-Solid Interfaces

6: From Ideal Planes to Real Materials (Recap)

7: Characterization of Surfaces & Interfaces

8: Surface Chemistry

9: Surface Patterning and Polymer Chemistry

10: Probing Functional Interfaces

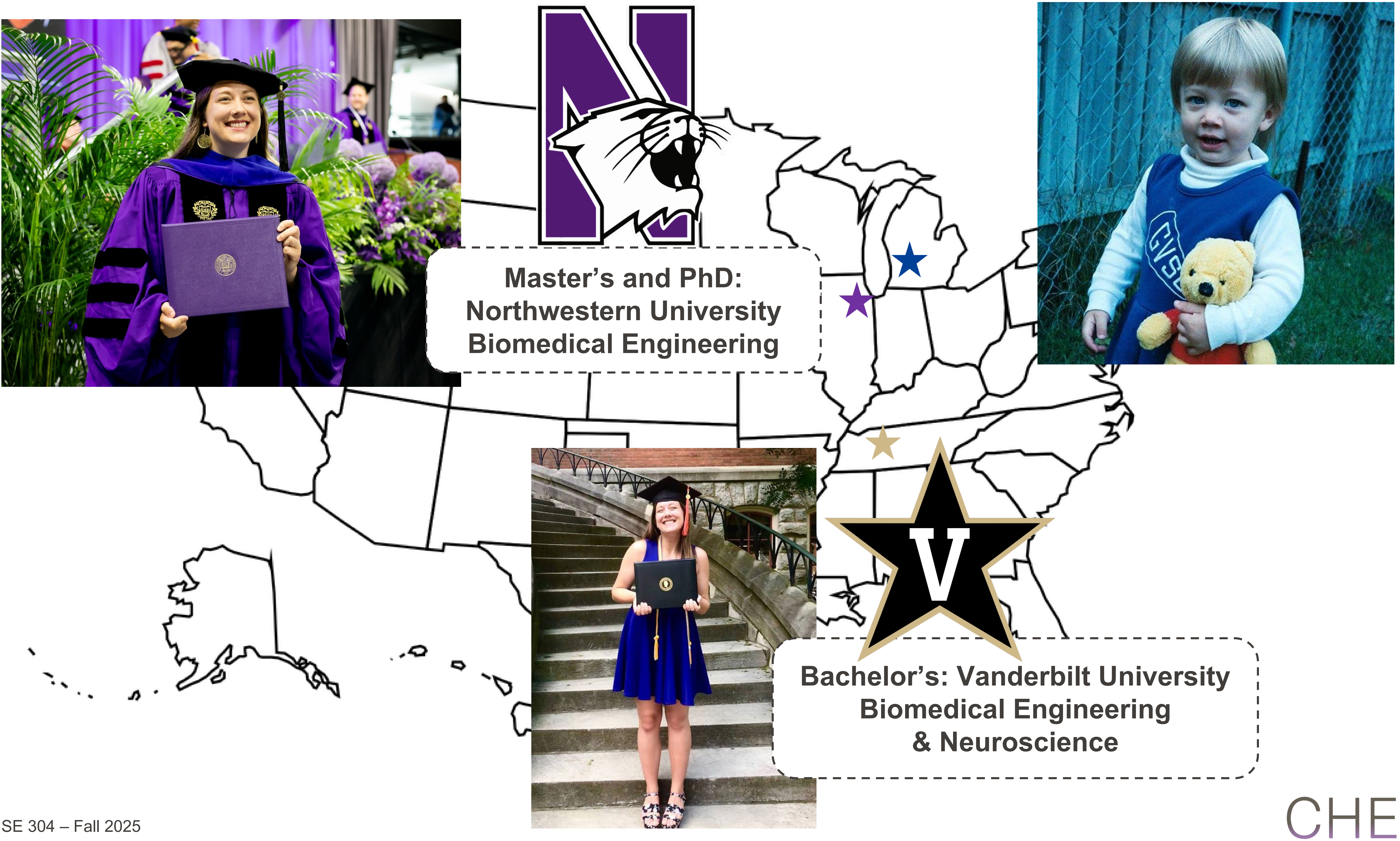
11: Surface Phenomena at the Nanoscale

12: Introduction to Biosensing

13: Biosensing Neurochemicals in the Brain

14: Chemistry of Semiconductor Surfaces & Beyond

About Me



Master’s and PhD:
Northwestern University
Biomedical Engineering

Bachelor’s: Vanderbilt University
Biomedical Engineering
& Neuroscience

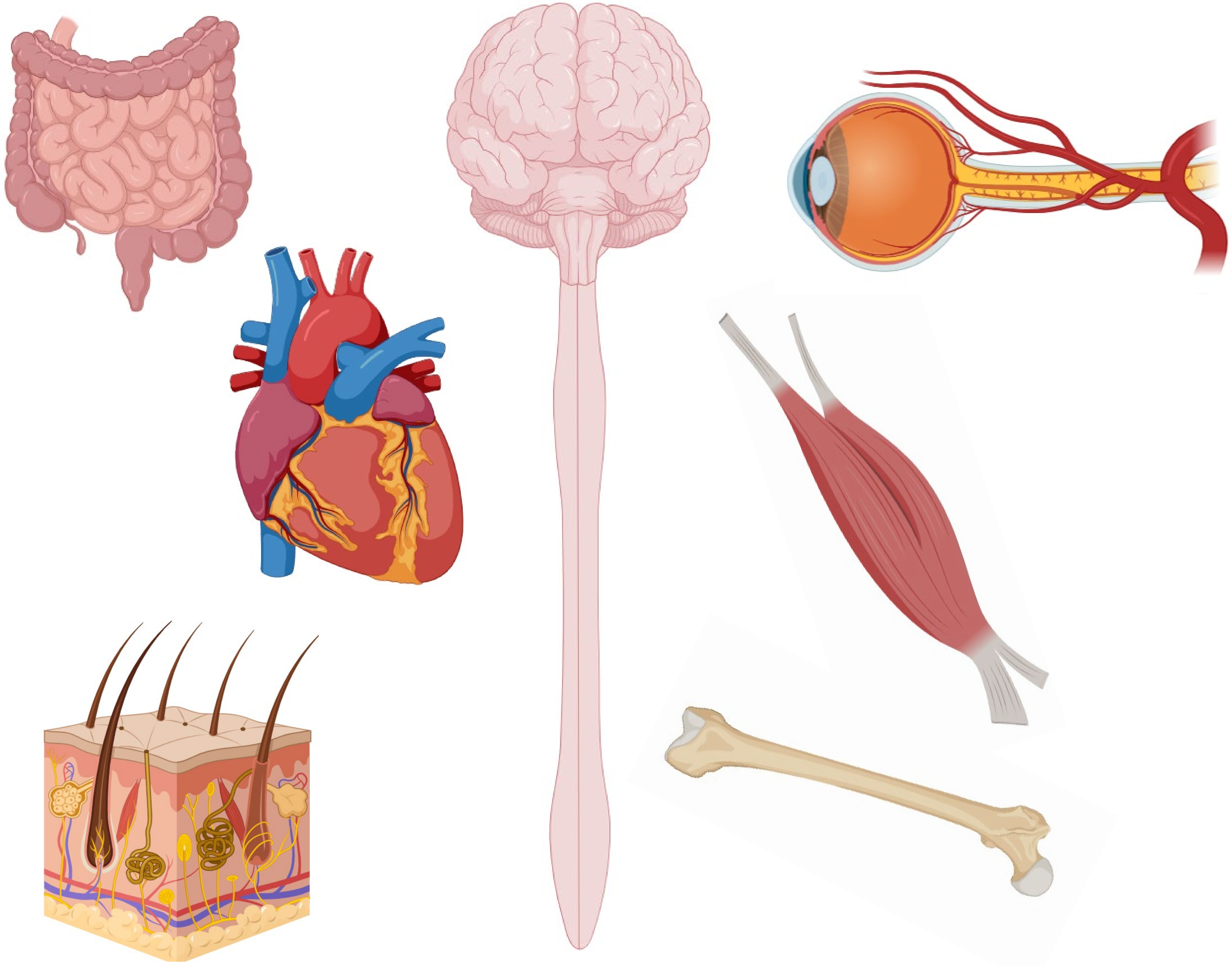
About Me

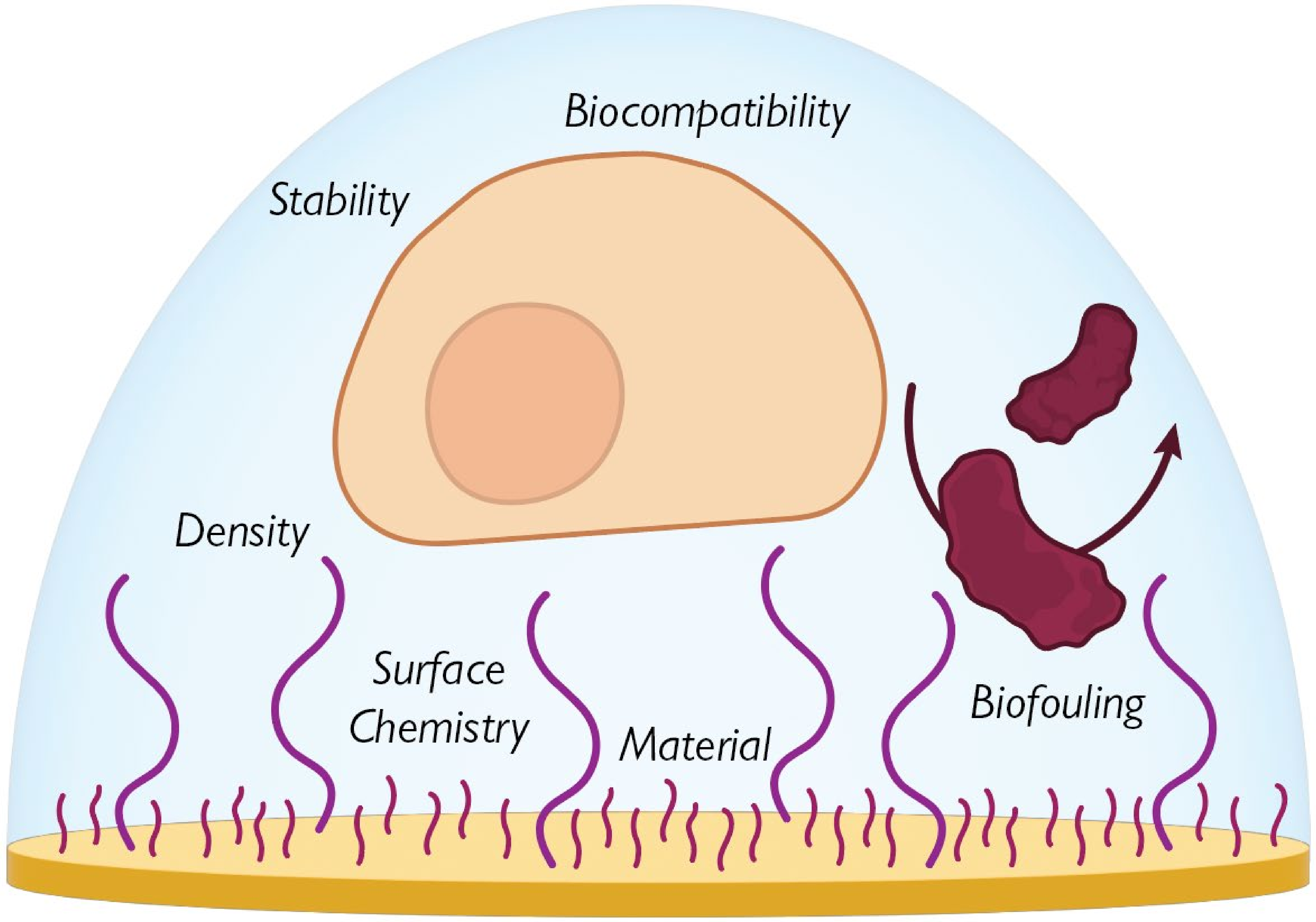
Neuro-X Postdoctoral Fellow at EPFL
CHEMINA Lab (based in Geneva)

Neuro X Institute

CHEMINA

Introduction to Bioelectronics





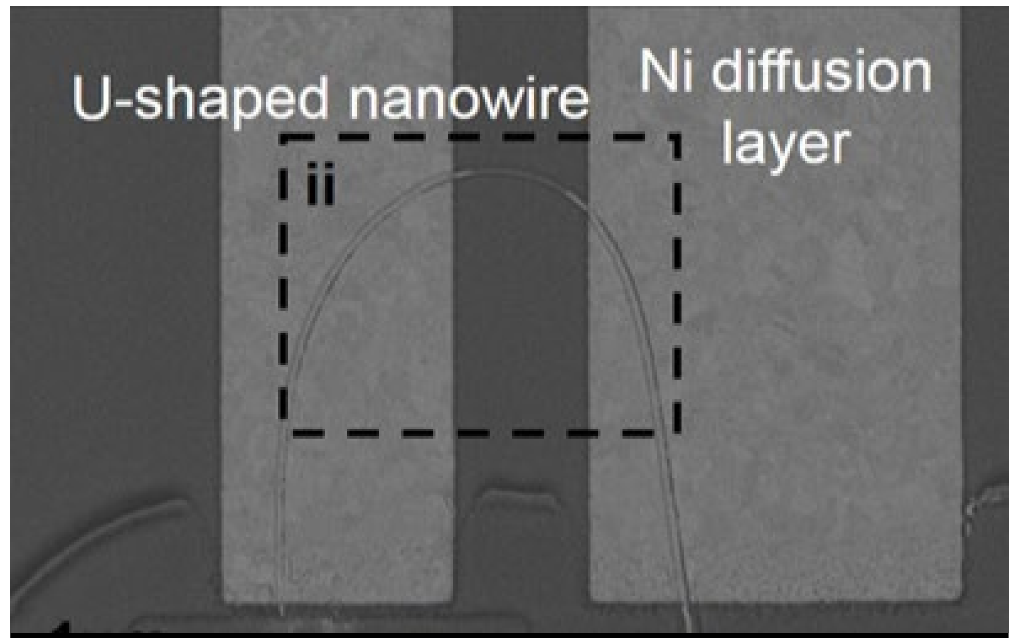
Bioelectronic Interface

Bioelectronics across Time and Length Scales

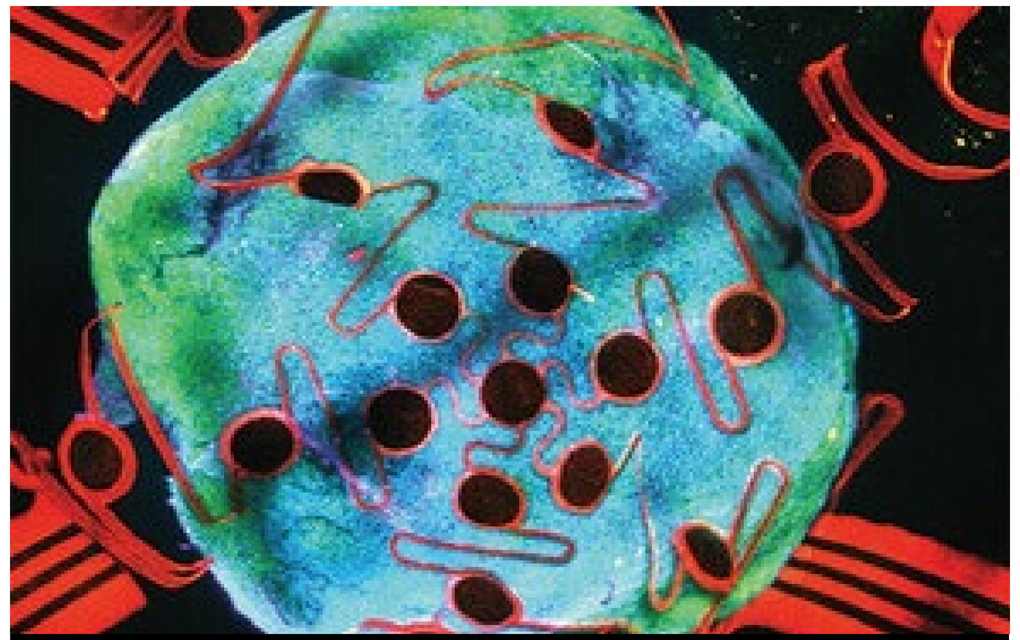
Biological signals vary across time scales and length scales … so bioelectronic interfaces must also!

Length

nanometer **micrometer** **millimeter** **meter**

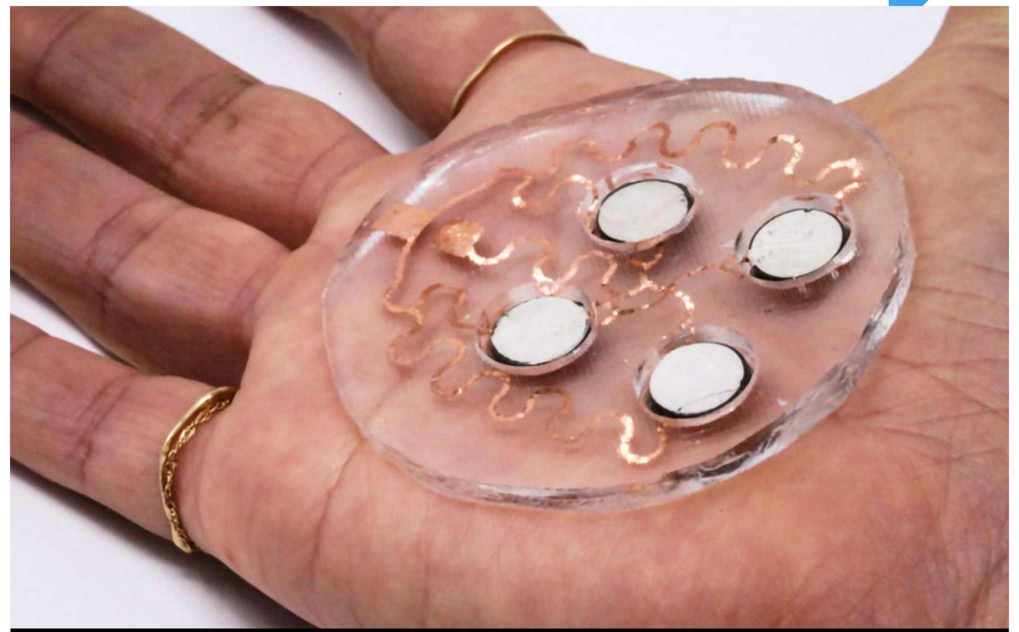


nanowire probes



microelectrode arrays

pacemakers



epidermal electronics

Zhao, *et al.*, *Nat Nanotechnol*, *14*, **2019**

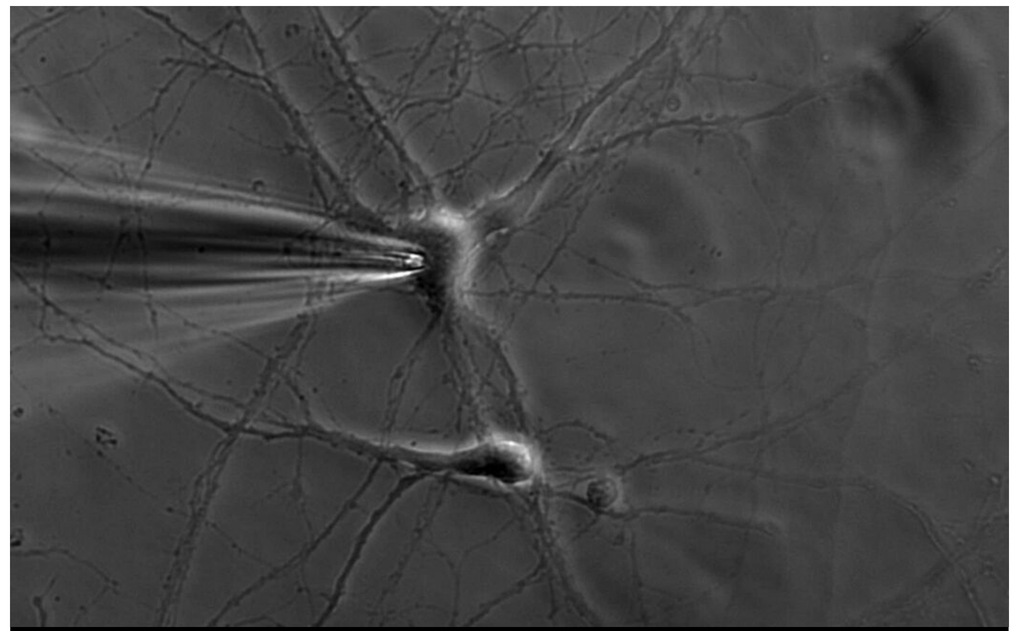
Kim, *et al.*, *Adv Mat*, *37*, *6*, **2025**

Choi, *et al.*, *Nat Biotechnol*, *39*, **2021**

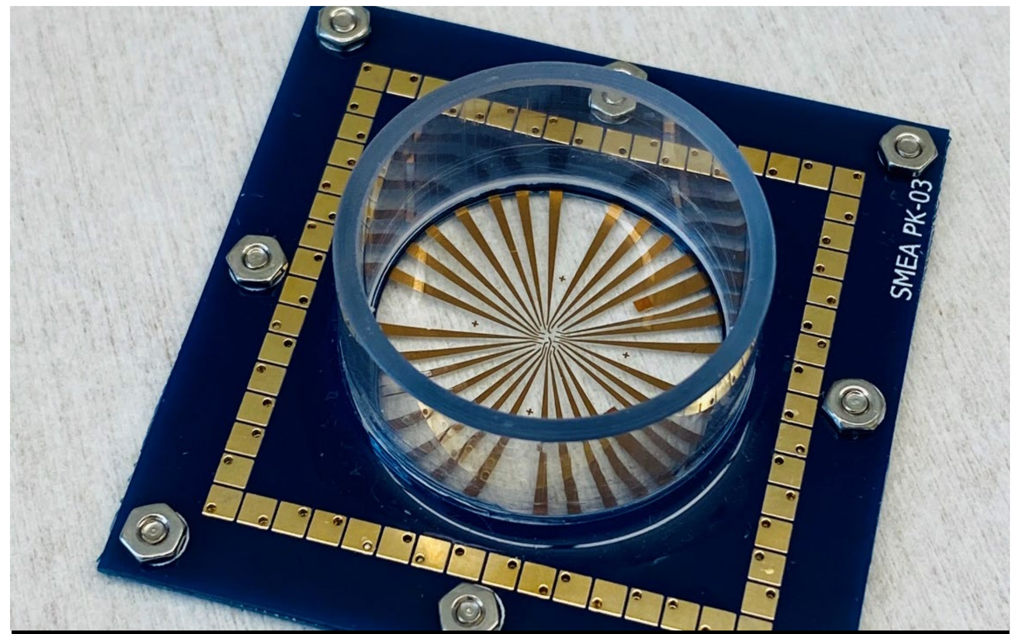
Yu, *et al.*, *Adv Mat*, *35*, *23*, **2023**

Time

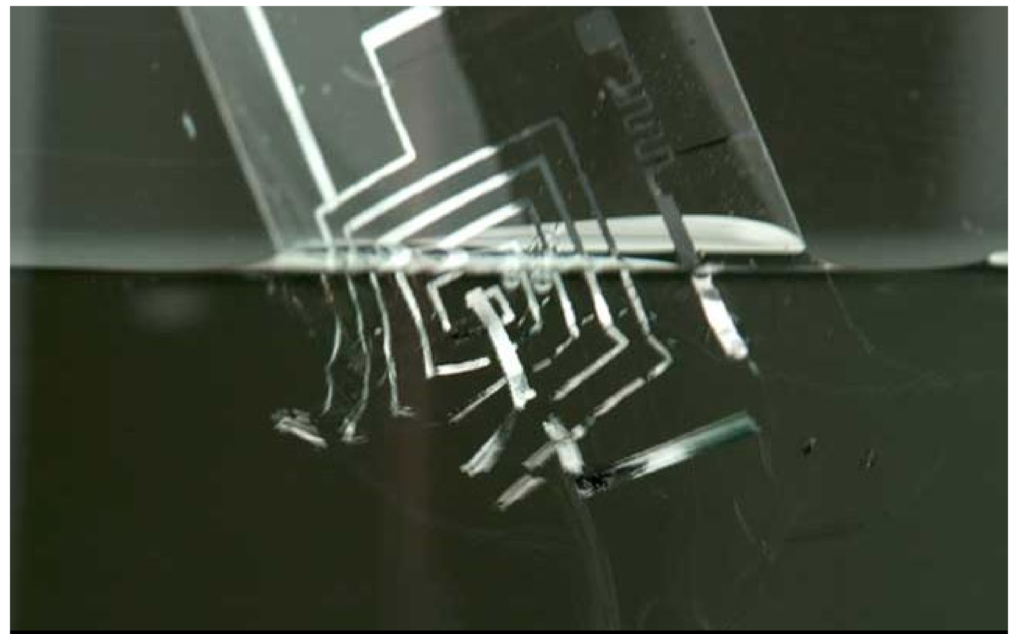
millisecond **second** **hour** **day** **year**



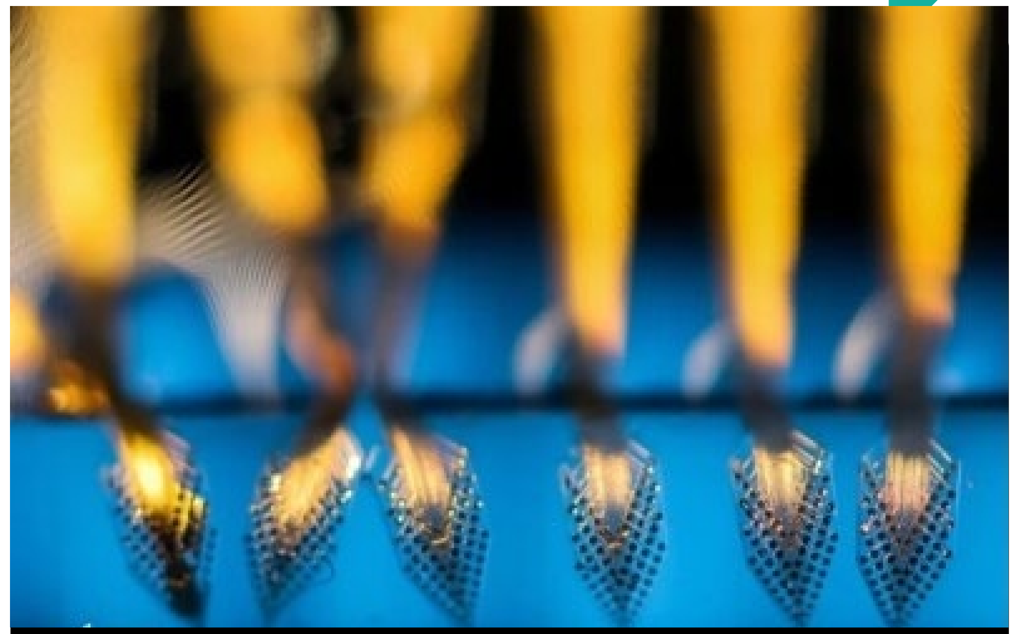
patch clamp



drug or protein sensors



transient electronics



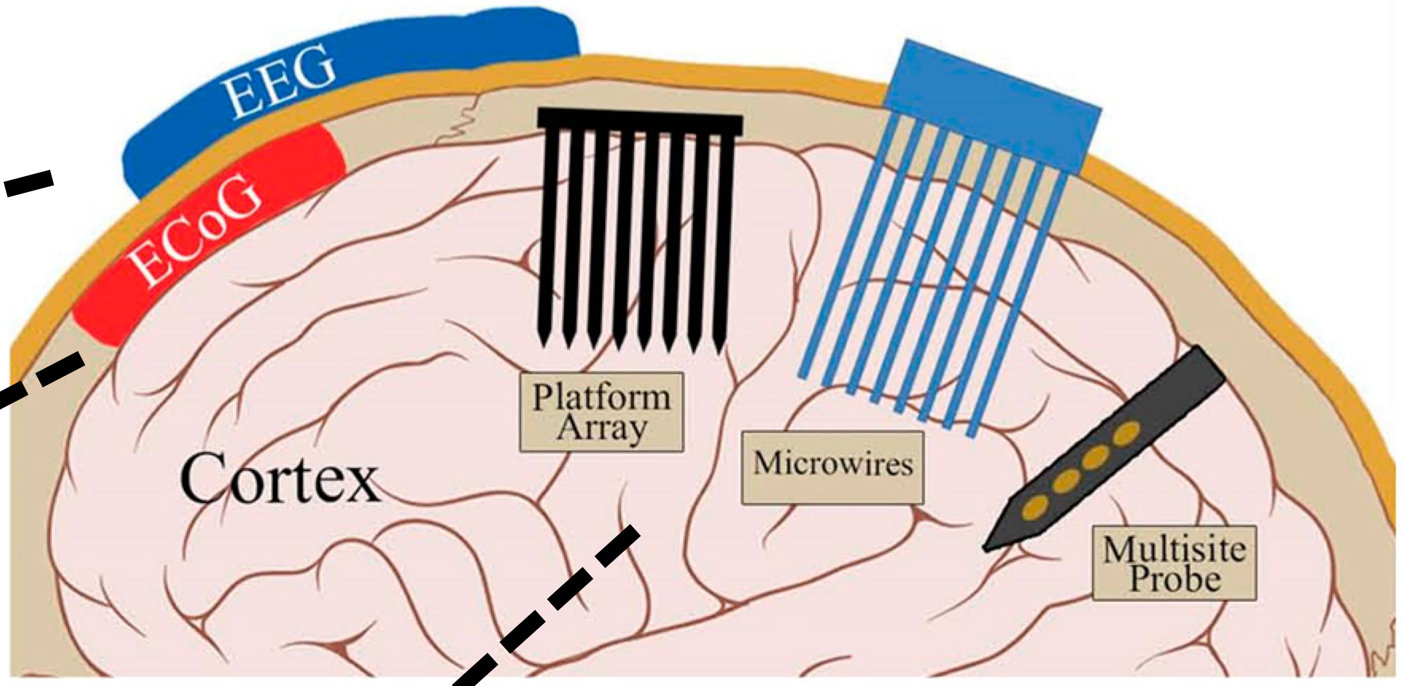
neural probes

Wikipedia

Hwang, *et al*, *Science*, *337*, *6102*, **2012**

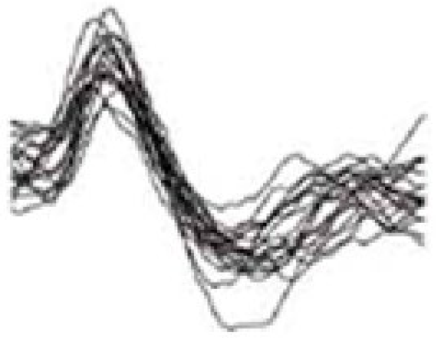
Le Floch, *et al*, *Nat Nanotechnol*, *19*, **2024**

Invasiveness vs. Resolution Tradeoff

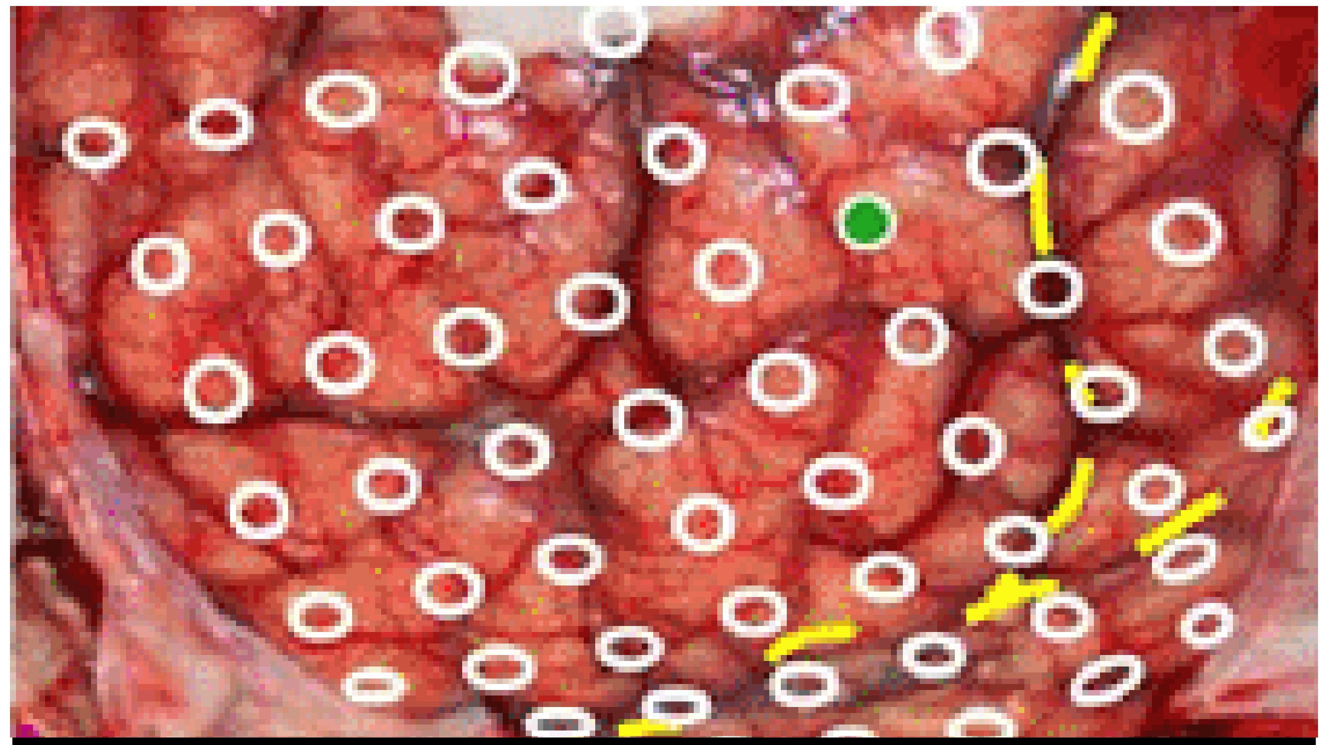


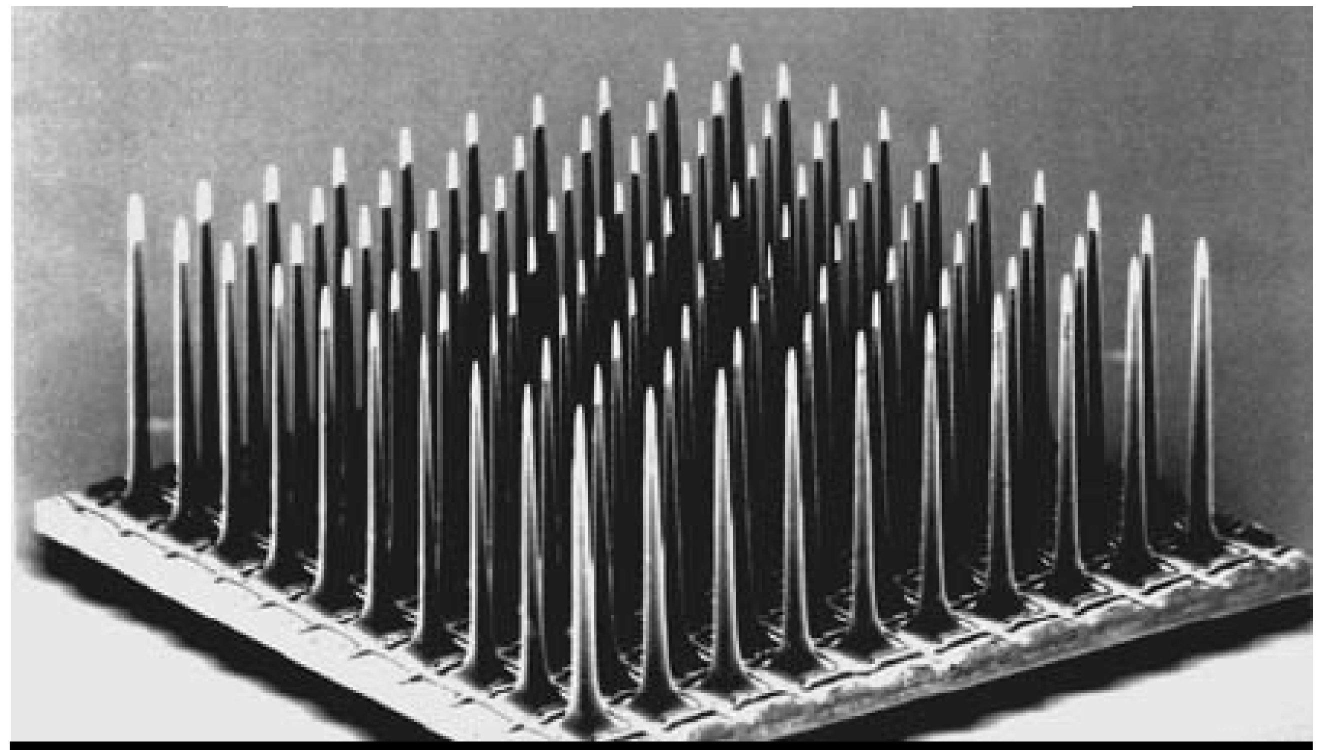

5-300 µV
< 100 Hz


0.01-5 mV
< 200 Hz


~500 µV
0.1-7 kHz

Electroencephalography (EEG)


Electrocorticography (ECoG)

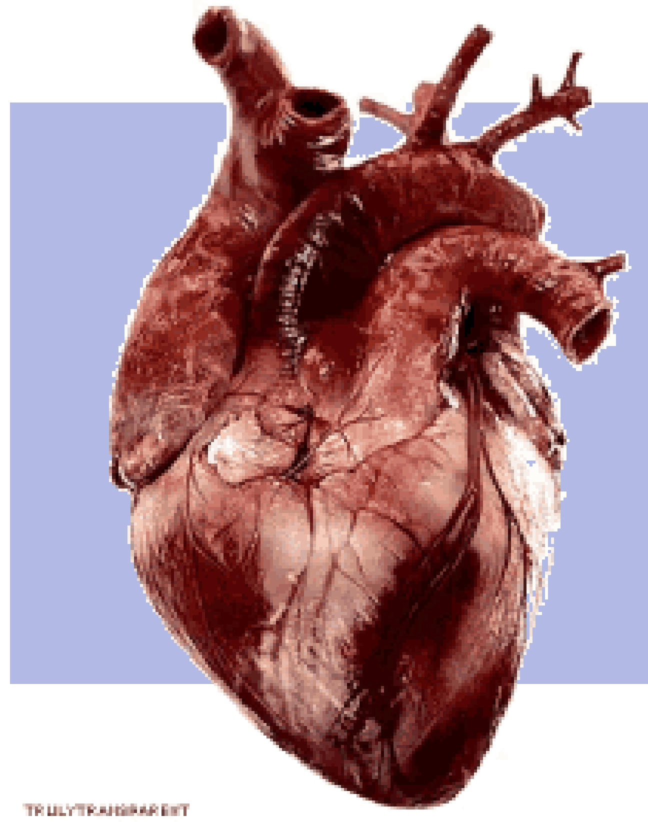

Penetrating electrodes


Non-invasiveness
Safety

Resolution
Signal Quality

Lago & Cester, *Appl Sci, 7, 12,* **2017**

Materials Selection Drives Bioelectronic Interface Performance



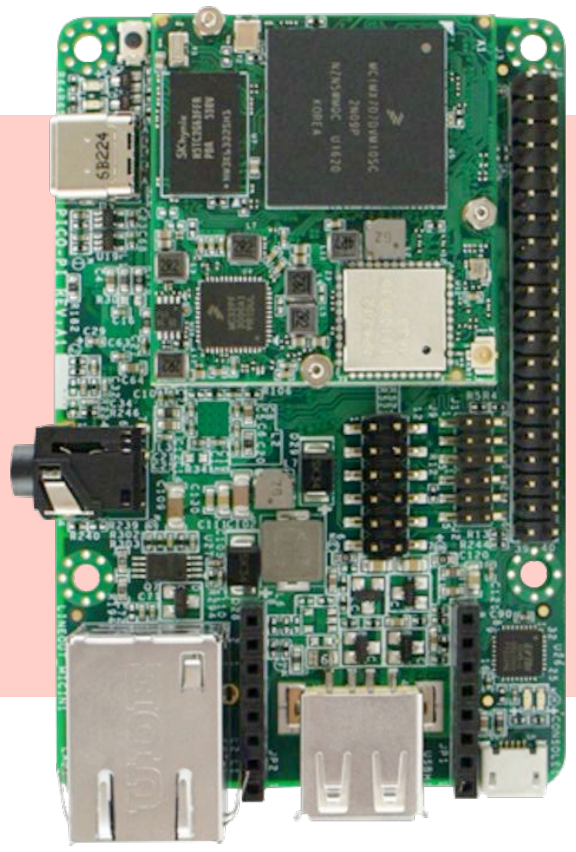
BIOLOGY

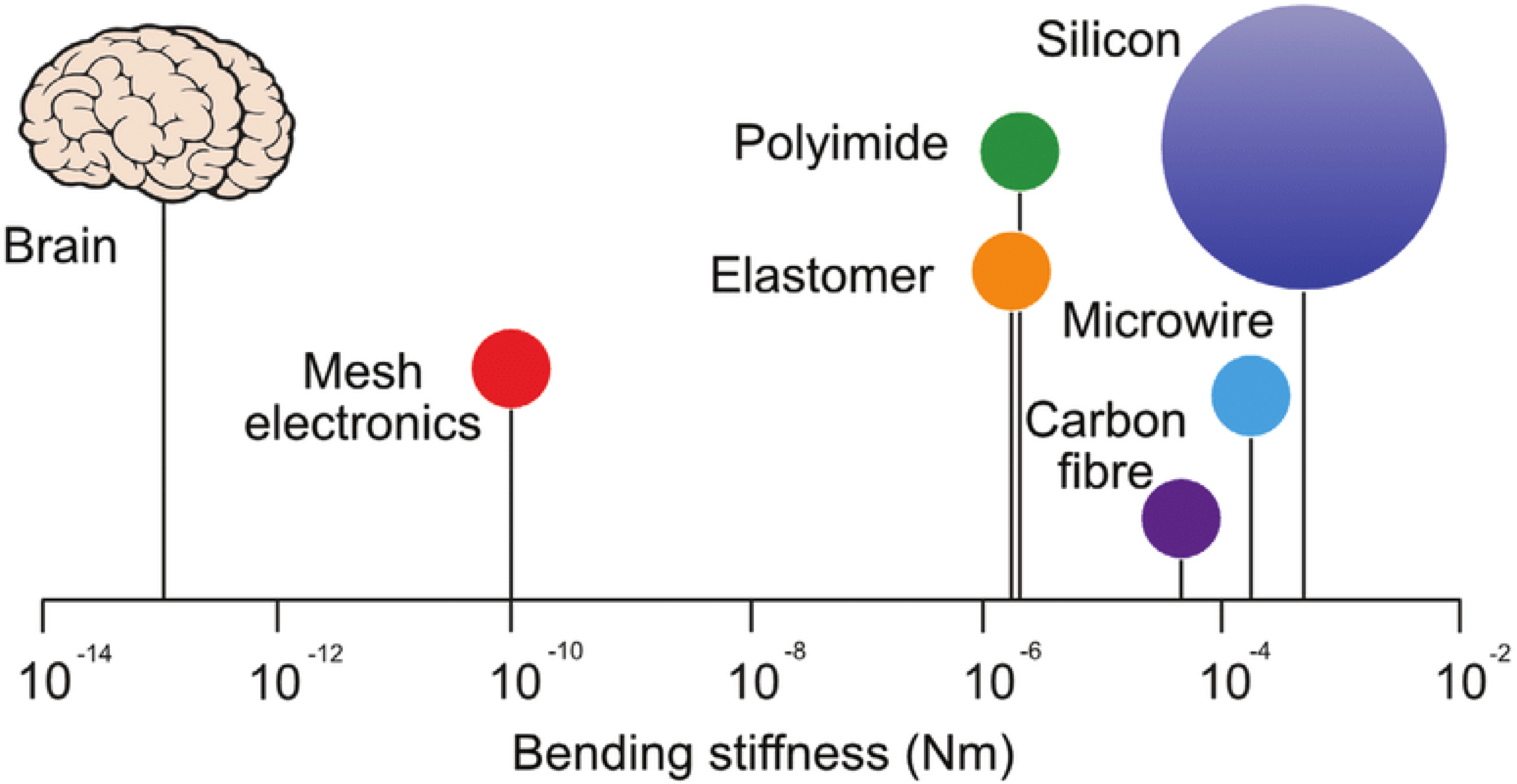
Soft and flexible
Dynamic

POLYMERS

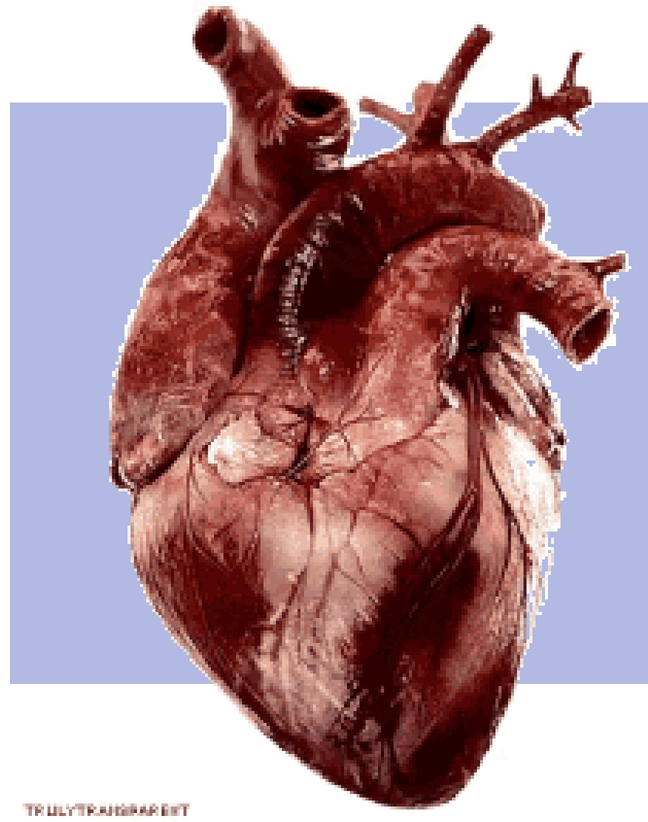
MICROELECTRONICS

Hard and rigid
Static





Materials Selection Drives Bioelectronic Interface Performance



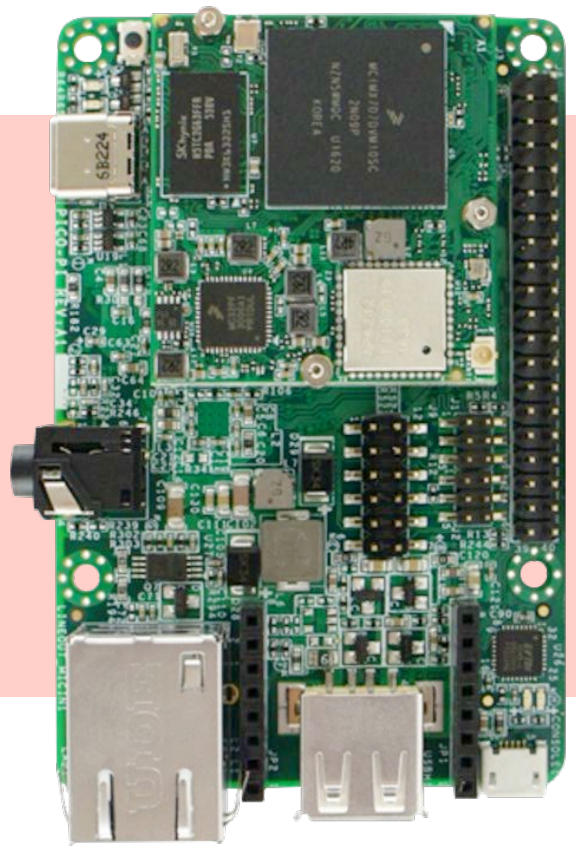
BIOLOGY

Soft and flexible
Dynamic

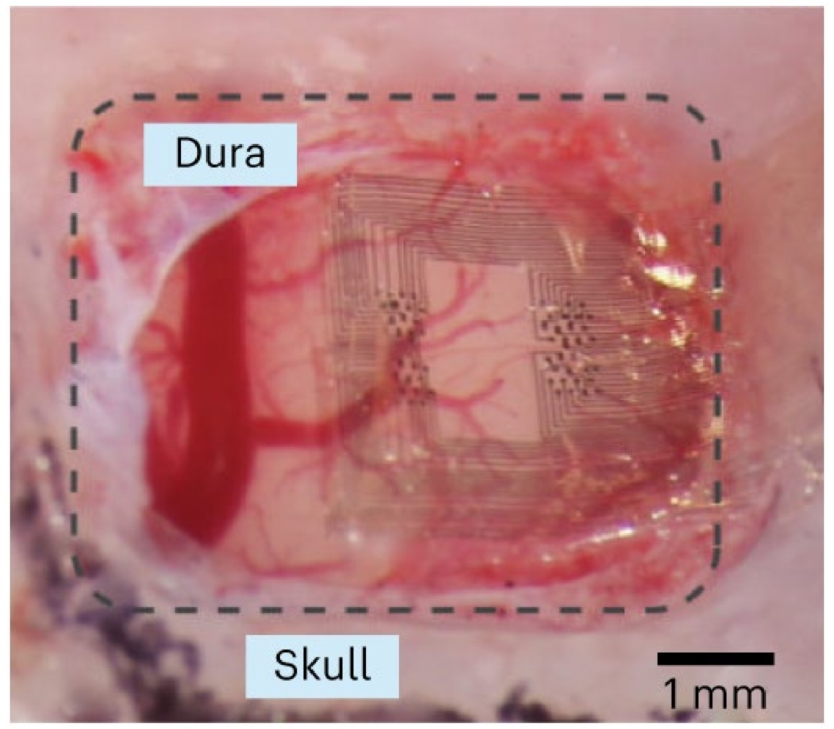
POLYMERS

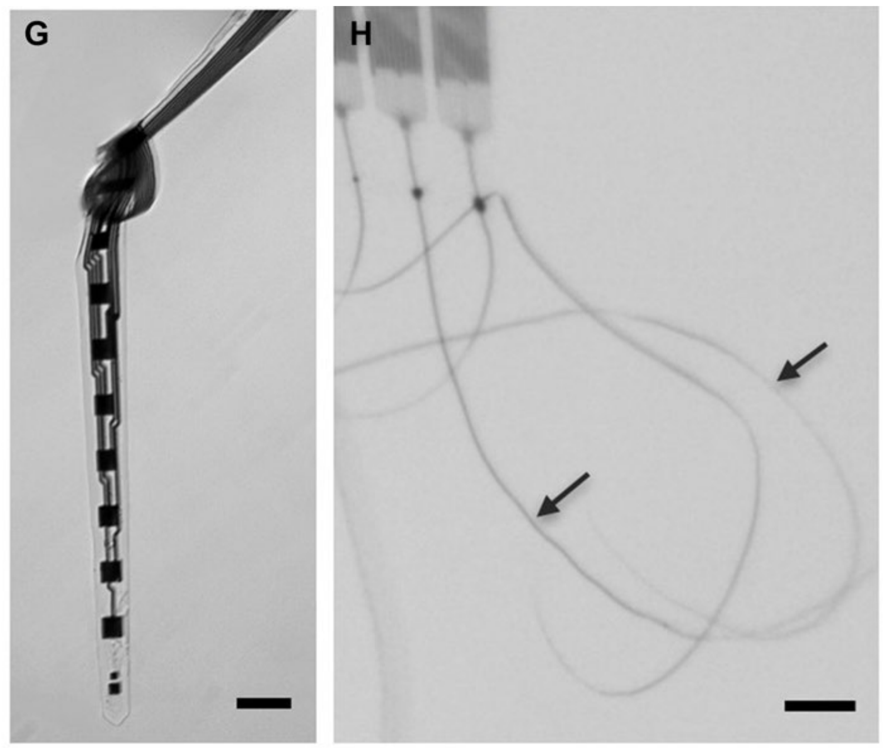
MICROELECTRONICS

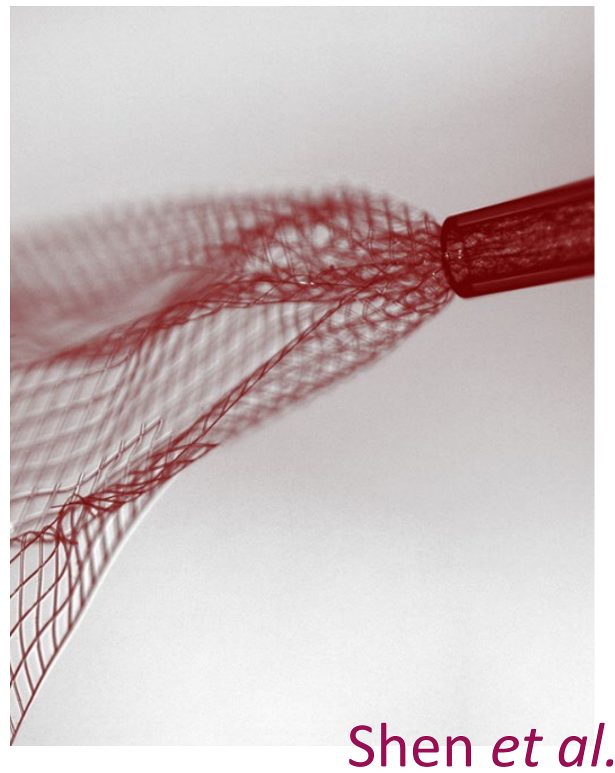
Hard and rigid
Static



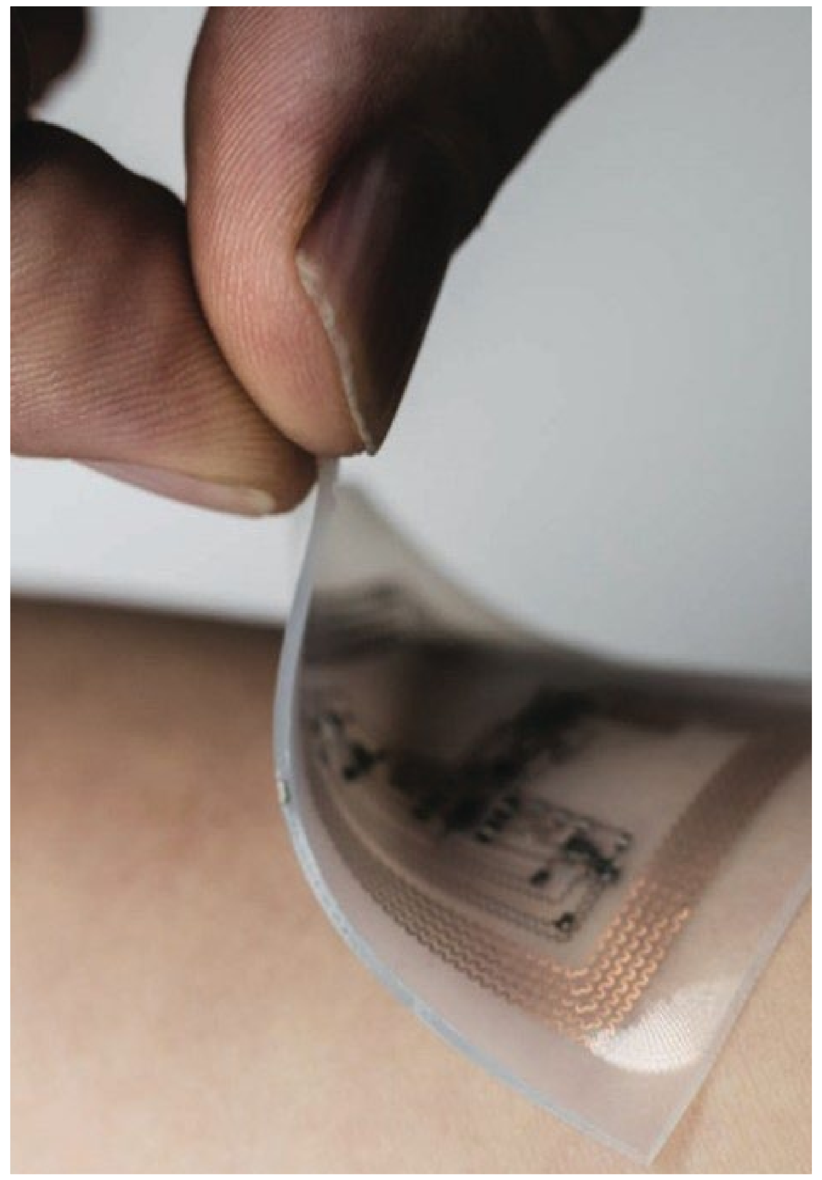
In vivo
“within the living”

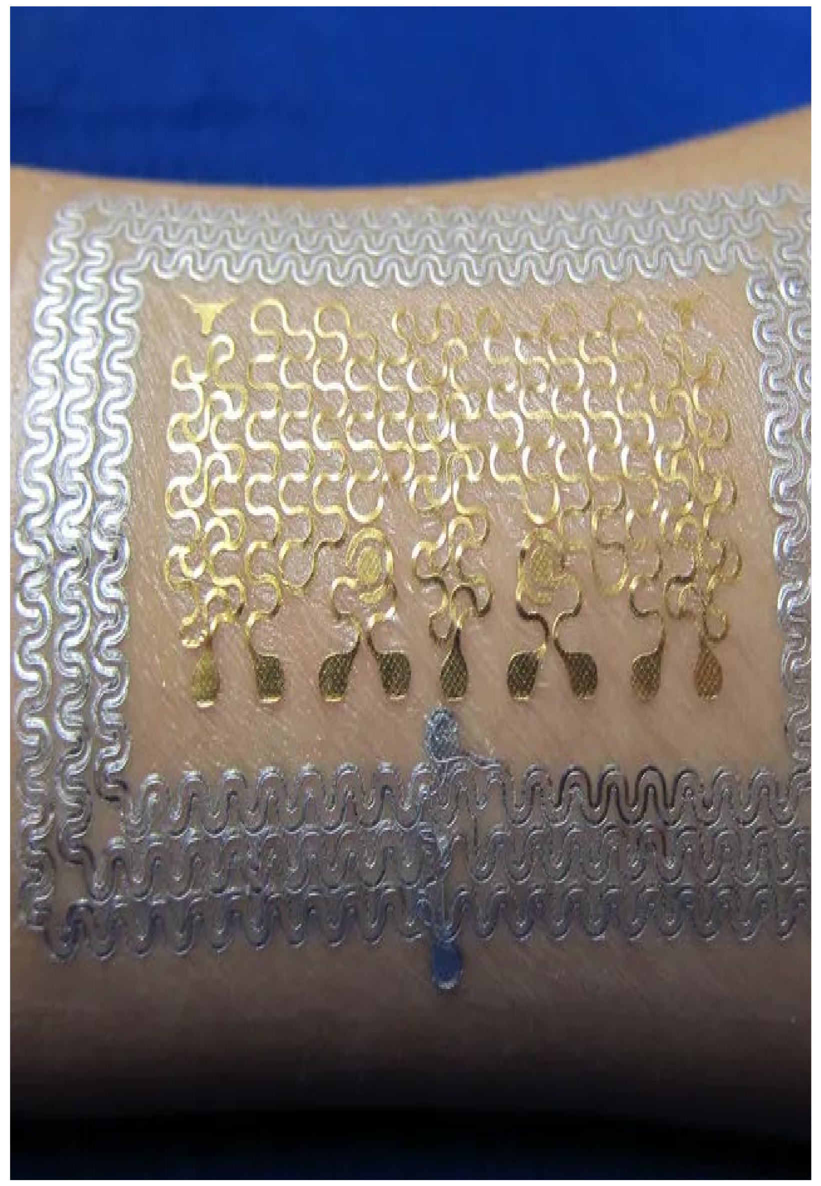




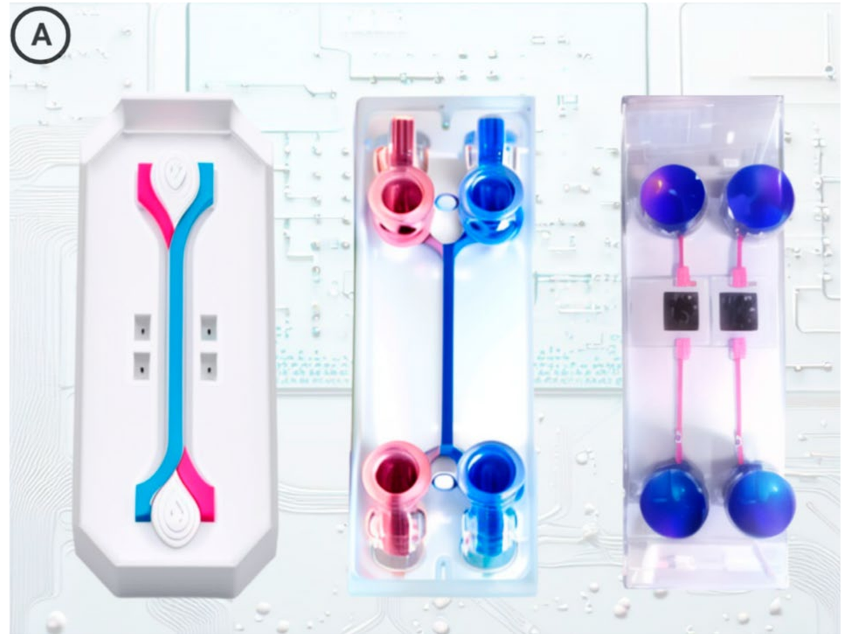


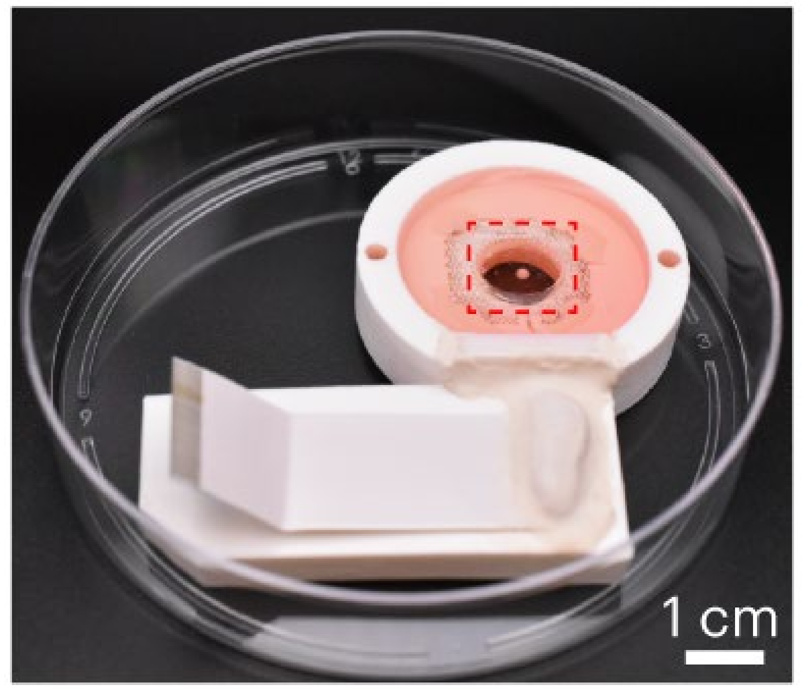
Wearables

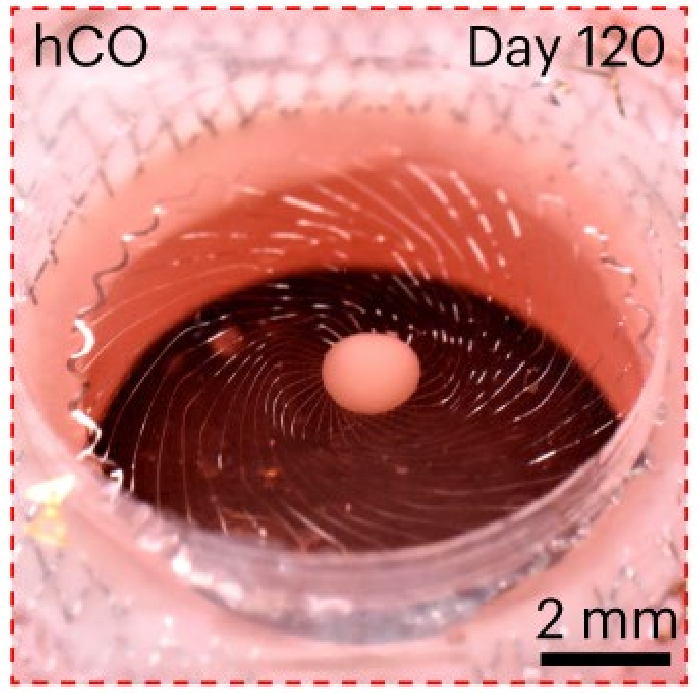




In vitro
“in glass”





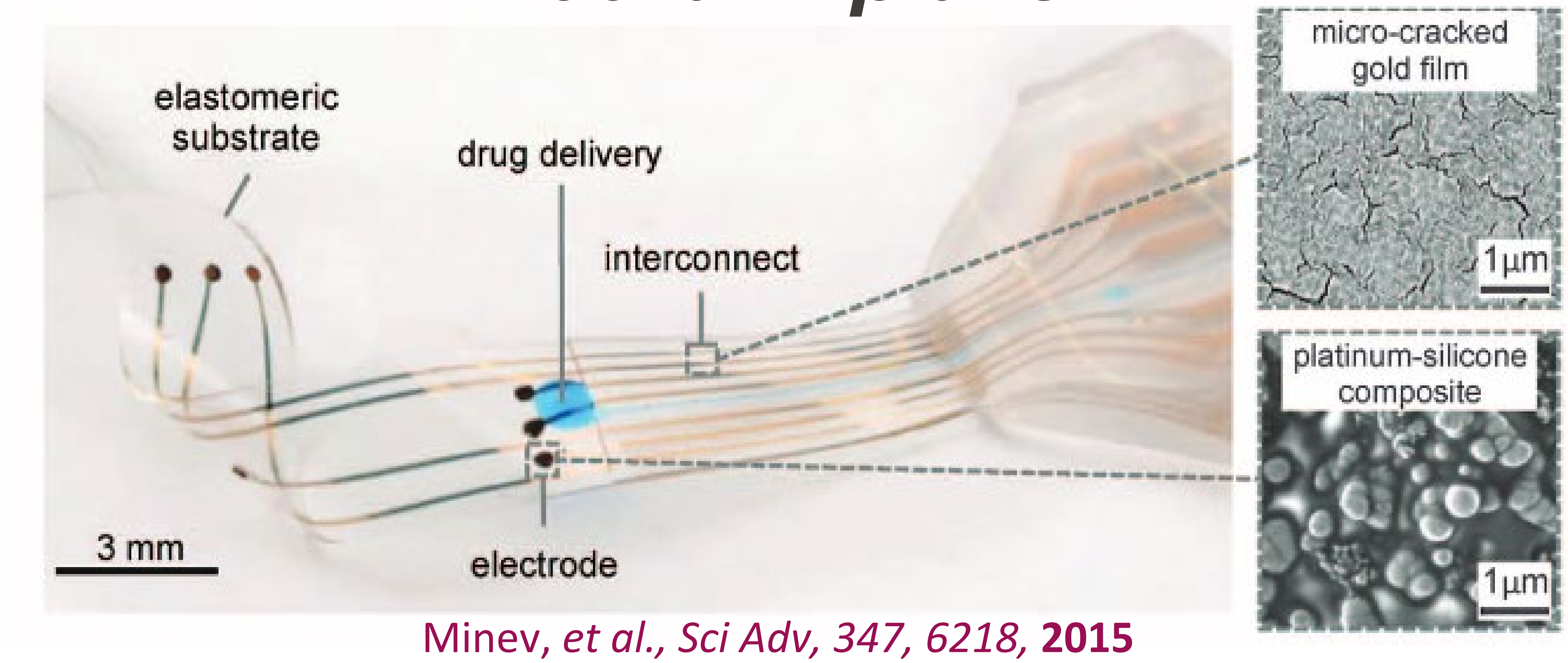


Shen *et al., Nat. Biomed. Eng., 7,* **2023**
Luan *et al., Sci. Adv., 3, 2,* **2017**

Yang, *et al., Nat Biotech,* **2024**
Ha, *et al., Adv Sci, 6, 14,* **2019**

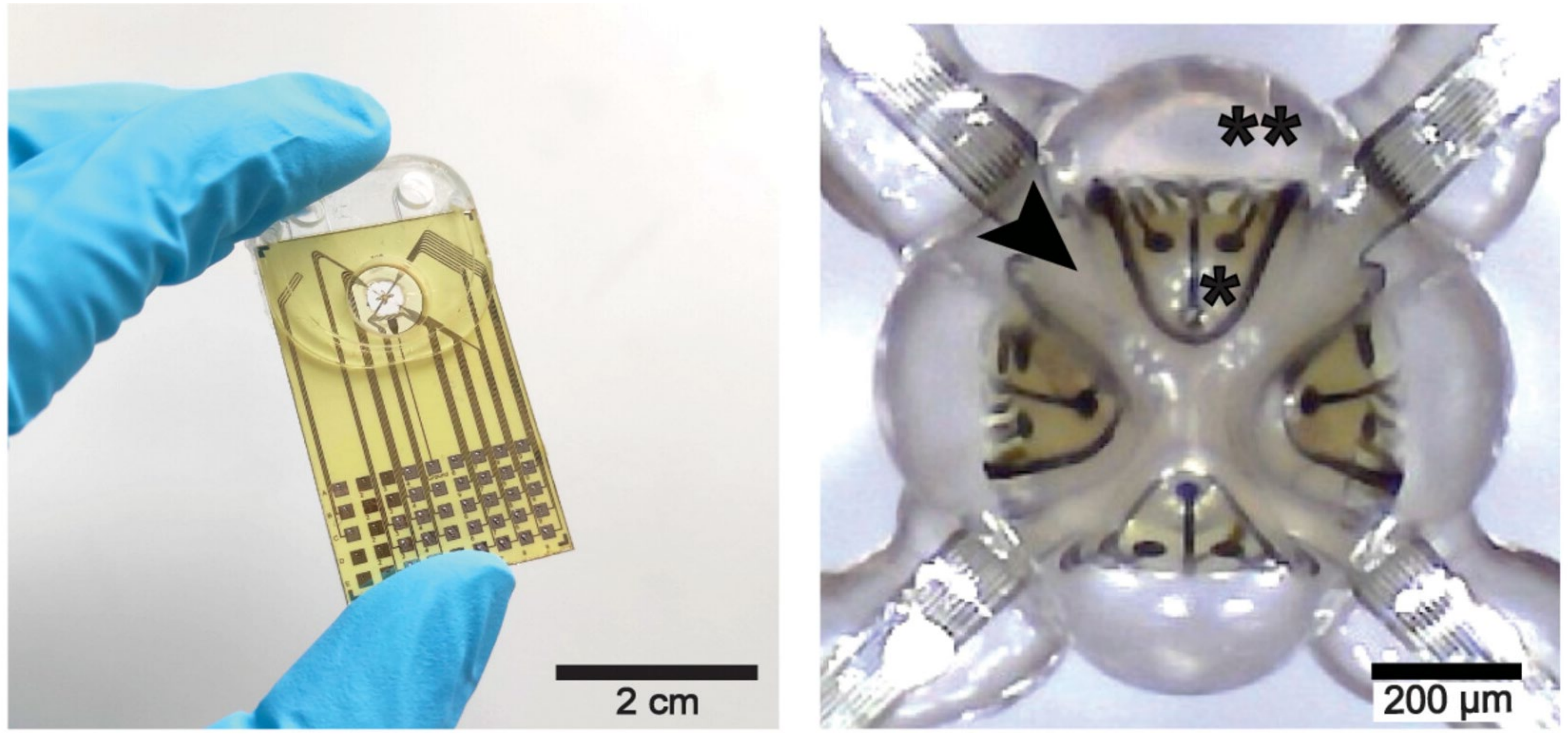
Laboratory for Soft Bioelectronics at EPFL

E-dura implant



Minev, *et al., Sci Adv, 347, 6218,* **2015**

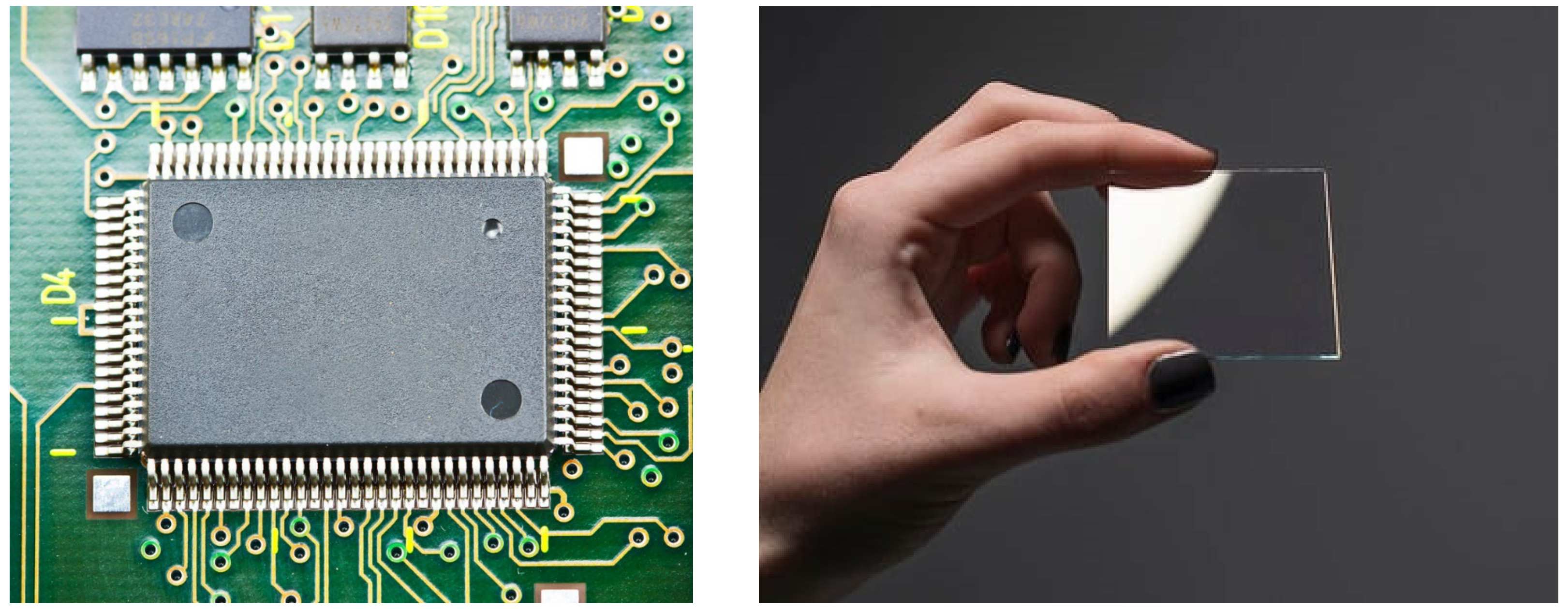
E-flower electrodes



Martinellli, *et al., Sci Adv, 10, 42,* **2024**

Materials Selection Drives Bioelectronic Interface Performance

Inorganic Conductors & Semi-conductors



Established fabrication methods and industrial processing

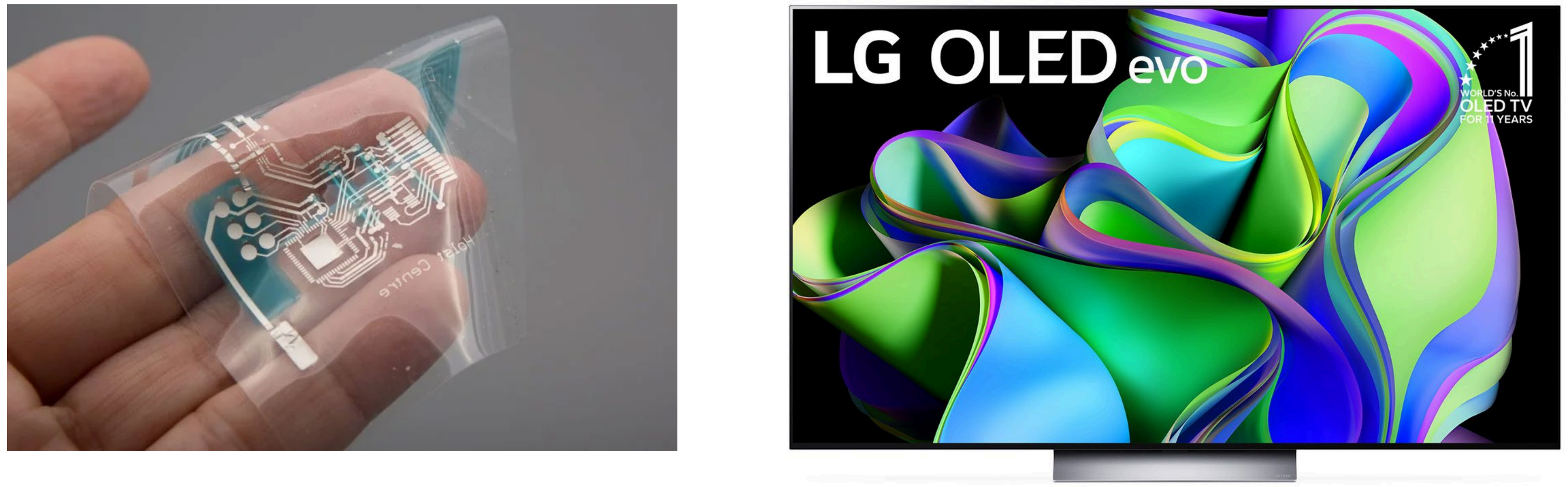
Excellent and stable conductivity

High charge carrier mobility

Rigid materials create mechanical mismatch with biology

Resource constraints

Organic Conductors & Semi-conductors



Flexible and intrinsically stretchable

Solution processable and compatible with additive manufacturing

High conductivity

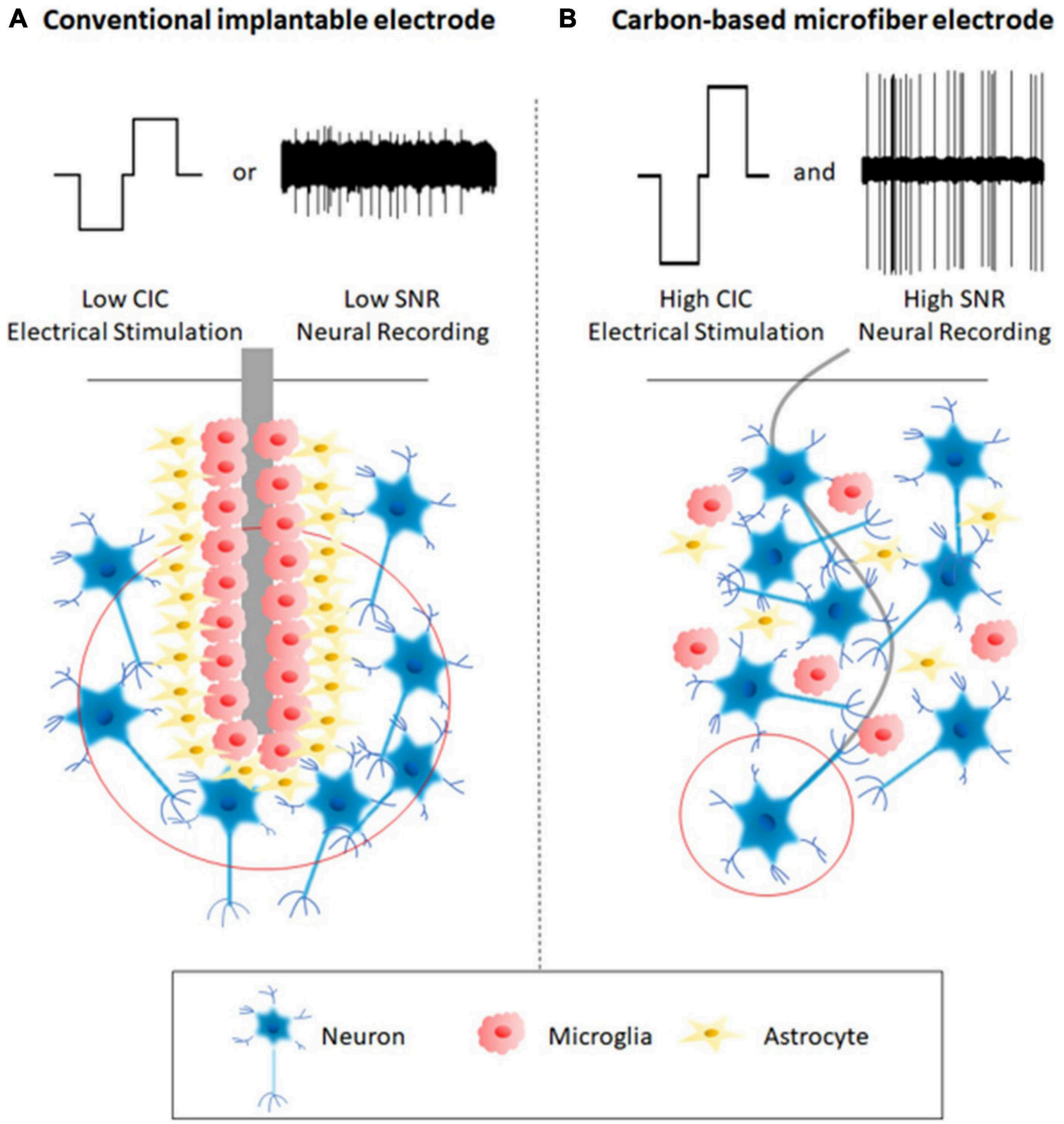
Lower charge carrier mobility

Lower chemical stability

Where do we draw the line between surface and bulk?

One of the key desirable qualities of a bioelectronic interface is its **conductivity** or **impedance**

The lower the impedance of the sensor, the more the original signal of interest is preserved



Low impedance leads to:

Ability to detect smaller biological signals

Reduced noise and higher signal-to-noise ratios (SNR)

Maintenance of high spatial resolution

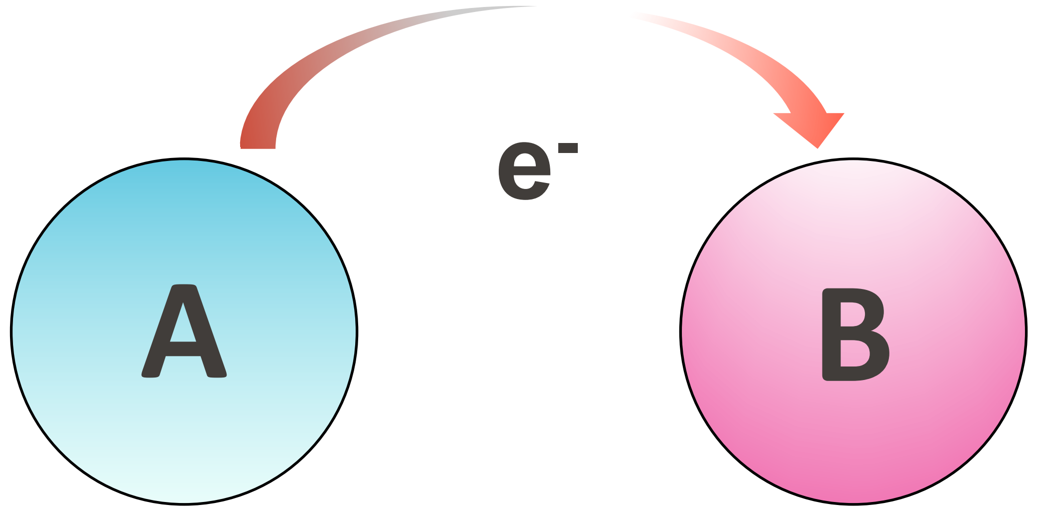
High charge injection capacity for stimulation

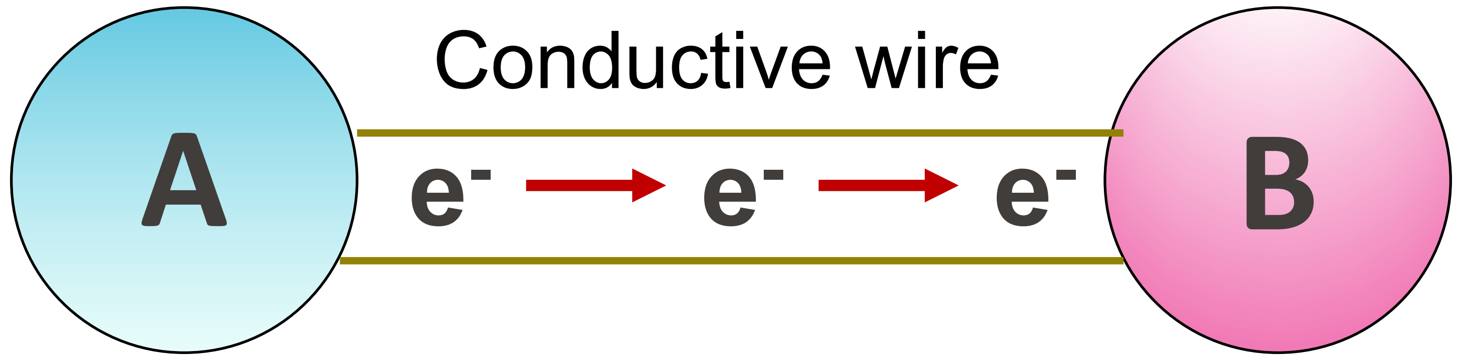
Hejazi, *et al*, *Front Neurosci*, *25*, **2021**

A Reminder on Electrochemistry

Electricity: movement of electrons $e^- \rightarrow e^- \rightarrow e^-$

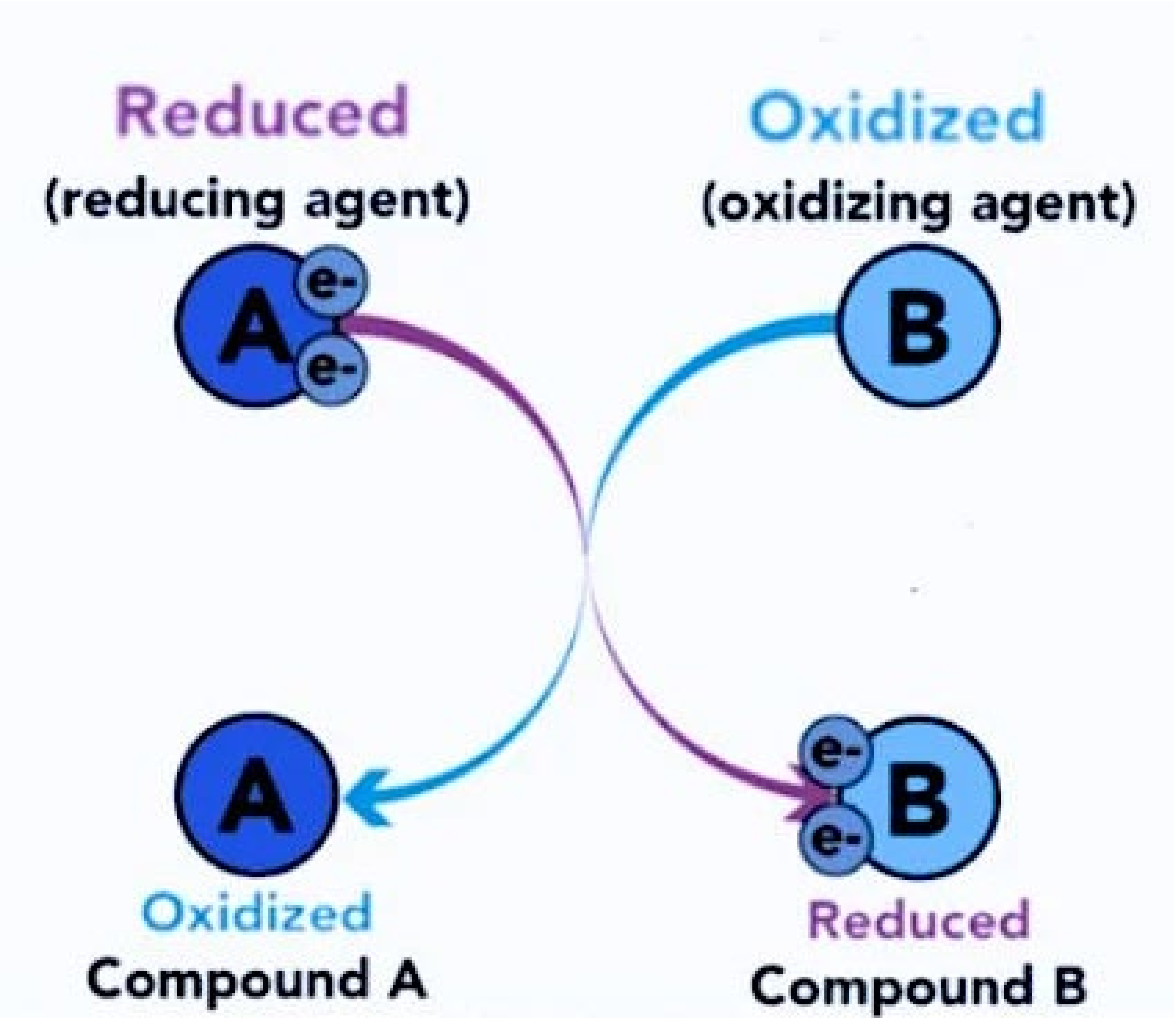
Certain chemical reactions ➔ create electricity



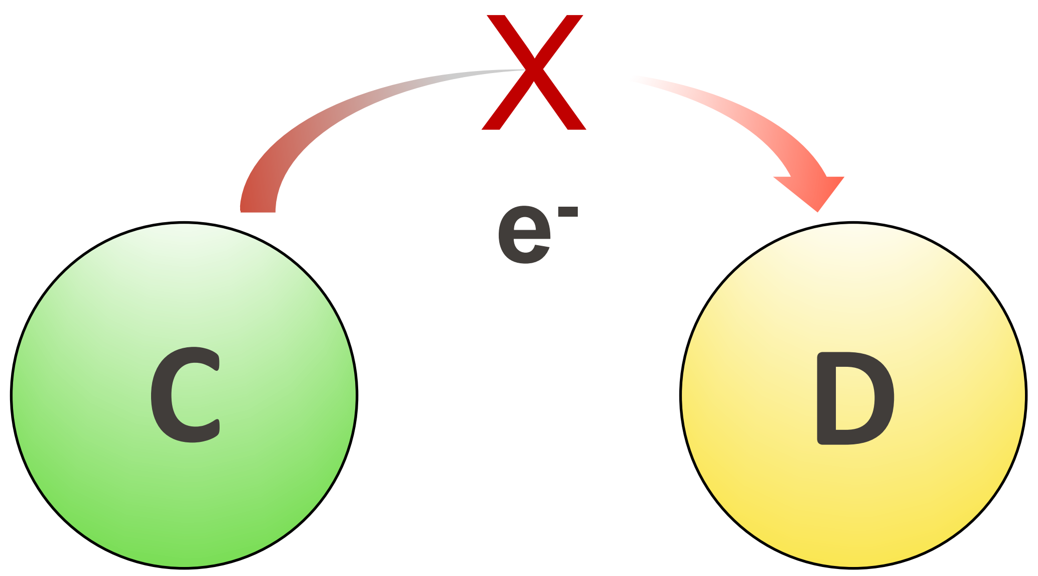


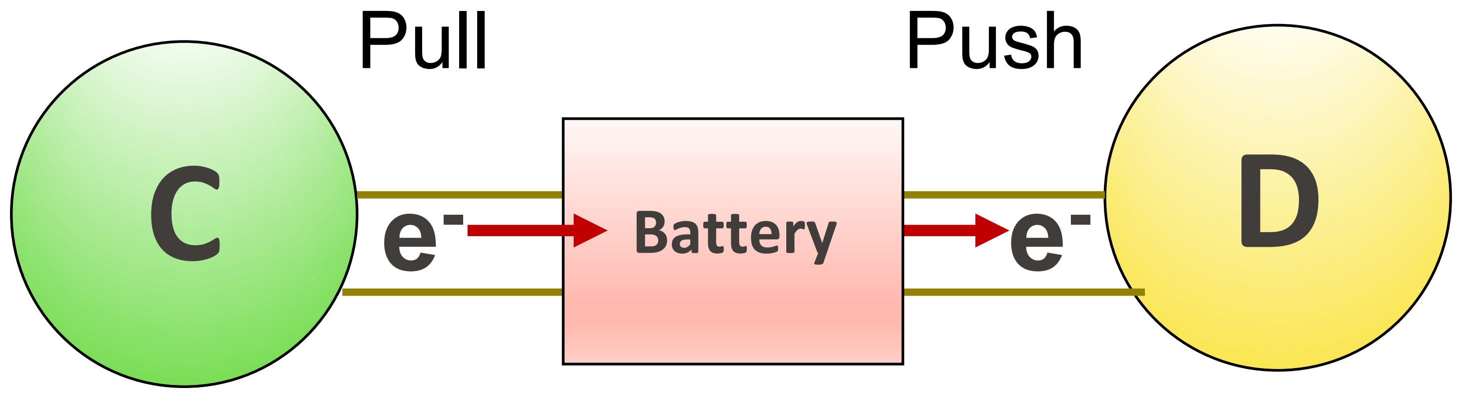
Oxidation & Reduction Reactions

Spontaneous reaction



Electricity ➔ make certain chemical reactions happen

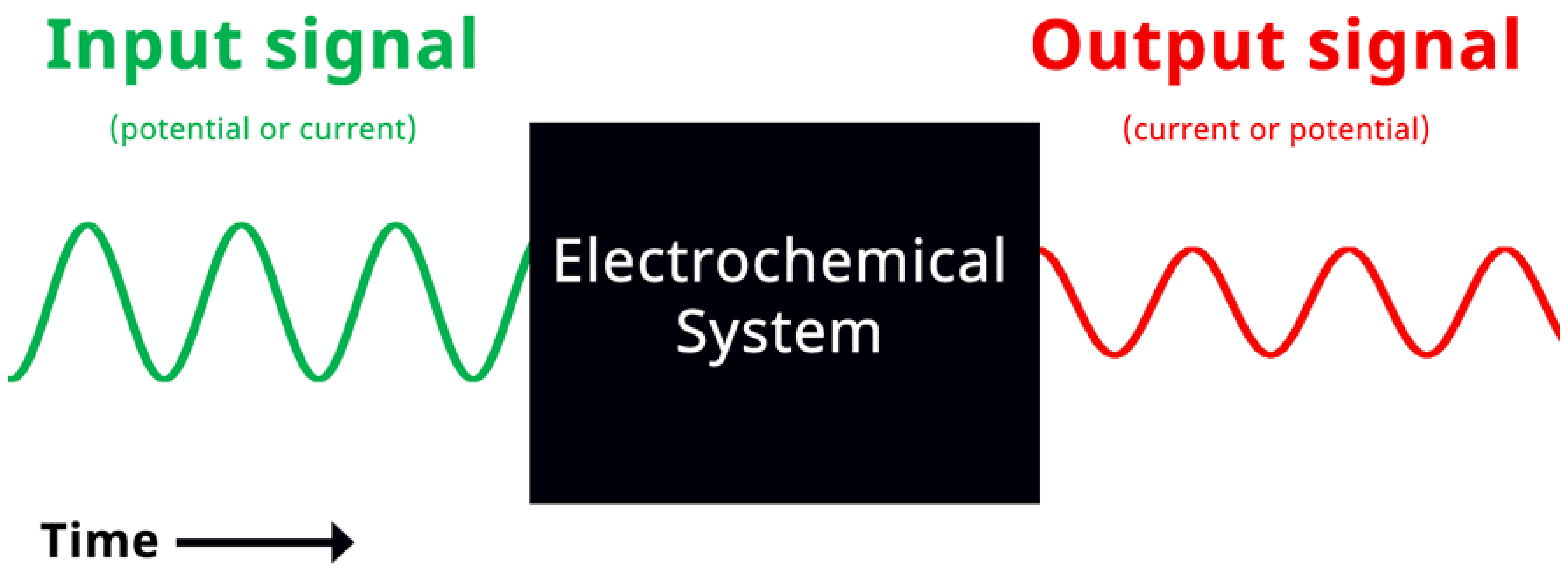


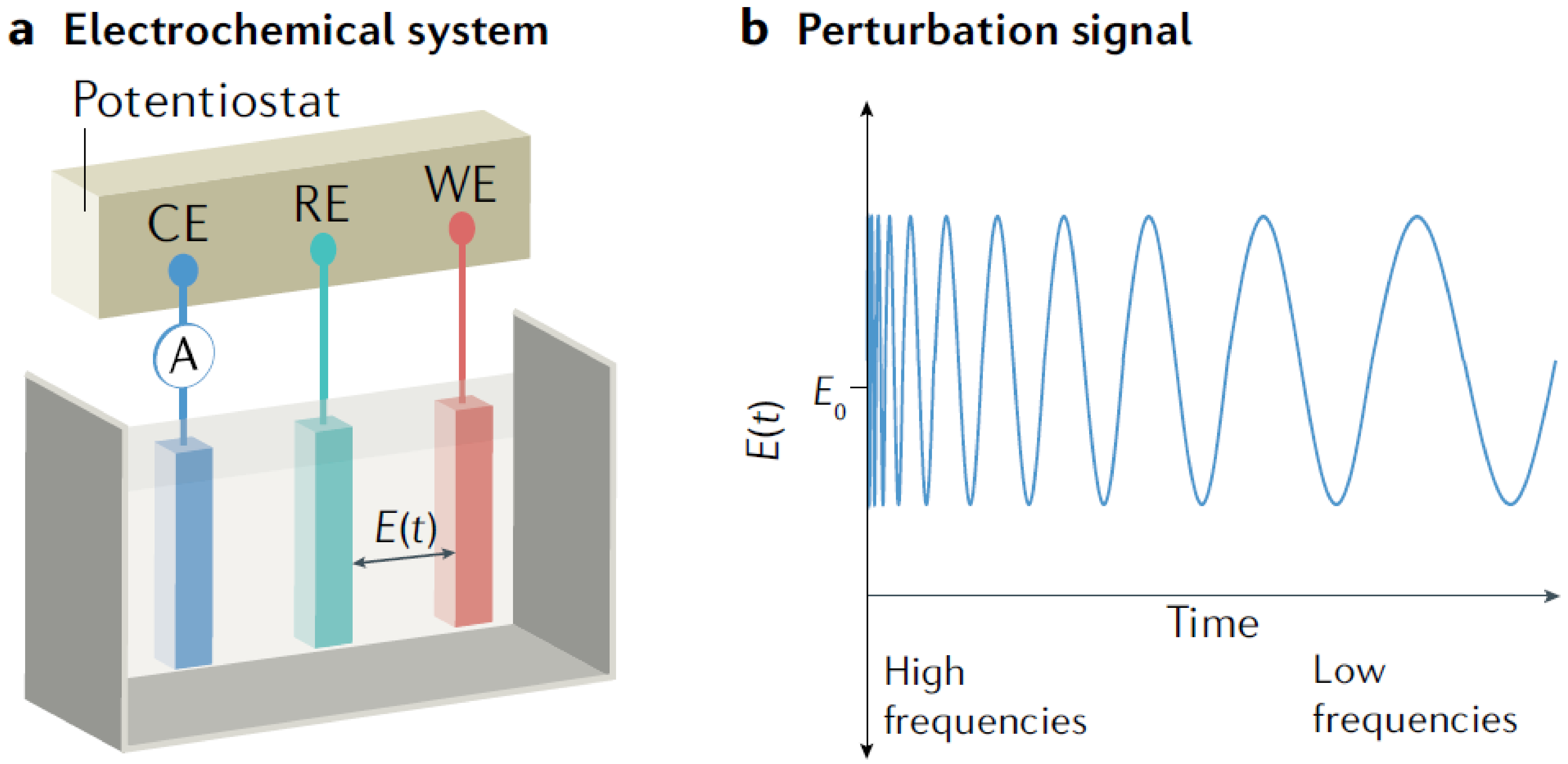


Non spontaneous reaction

Electrochemical Impedance Spectroscopy (EIS)

Non-destructive, small-signal analysis technique to characterize an electrochemical interface





$$Z(\omega) = \frac{\tilde{V}(\omega)}{\tilde{I}(\omega)}$$

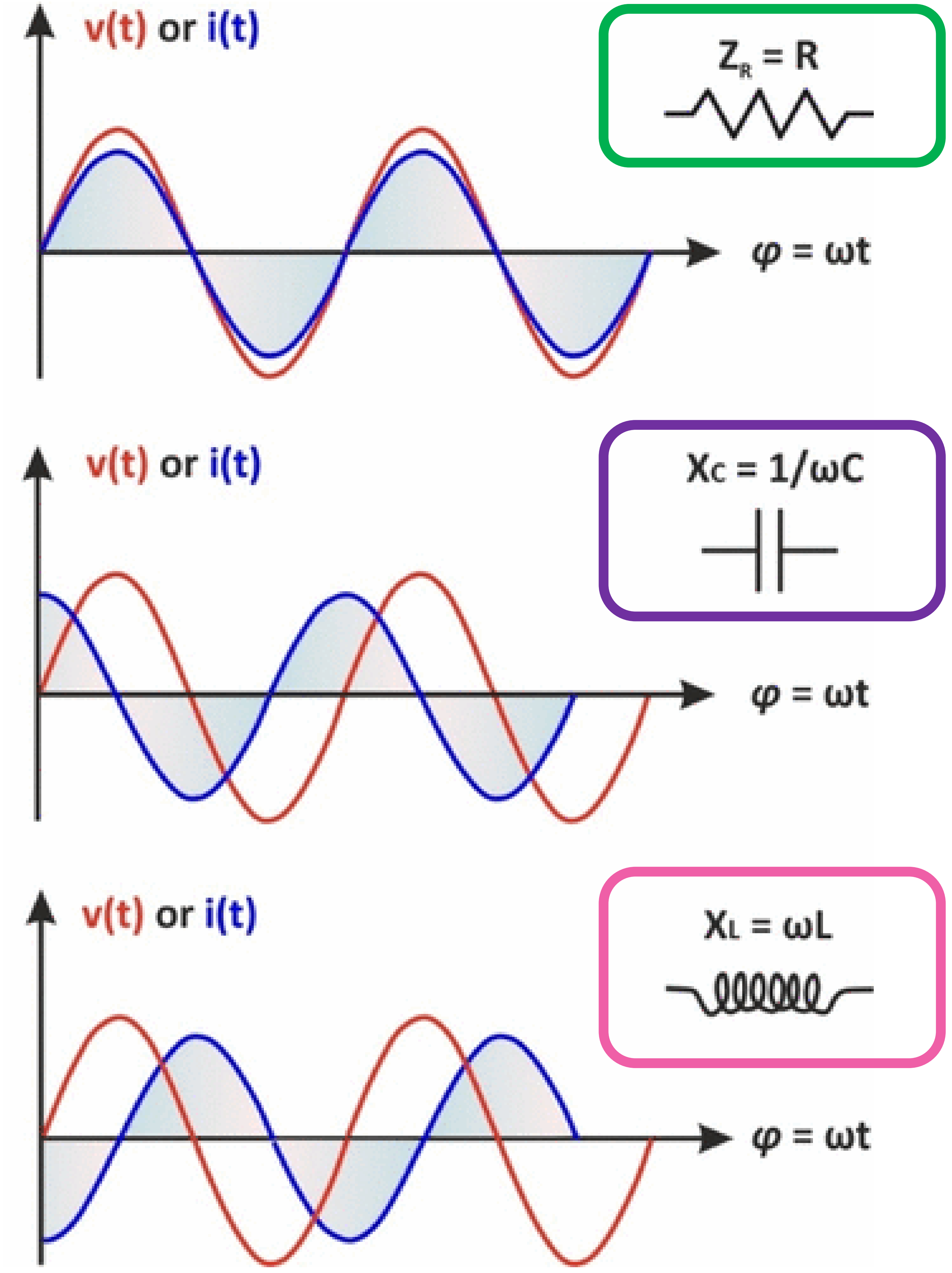
$$= \left|\frac{\tilde{V}(\omega)}{\tilde{I}(\omega)}\right|(\cos\phi(\omega) + \mathrm{j}\sin\phi(\omega))$$

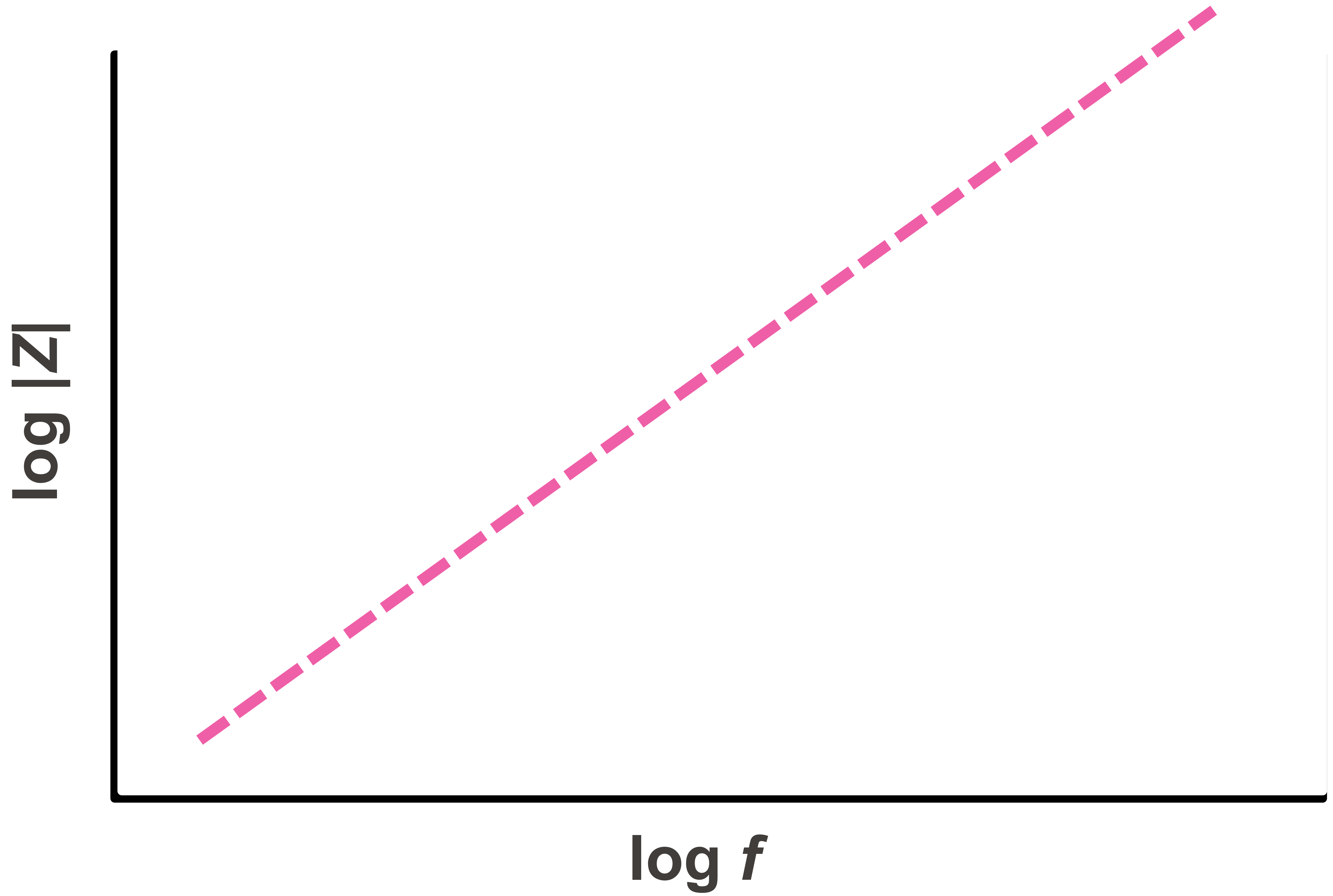
$$= Z_\mathrm{r} + \mathrm{j}Z_\mathrm{j}$$

Wang, *et al*, *Nat Rev Methods Primers*, *41*, **2021**

Electrochemical Impedance Spectroscopy (EIS)

Interfaces can then be modeled as an equivalent circuit:





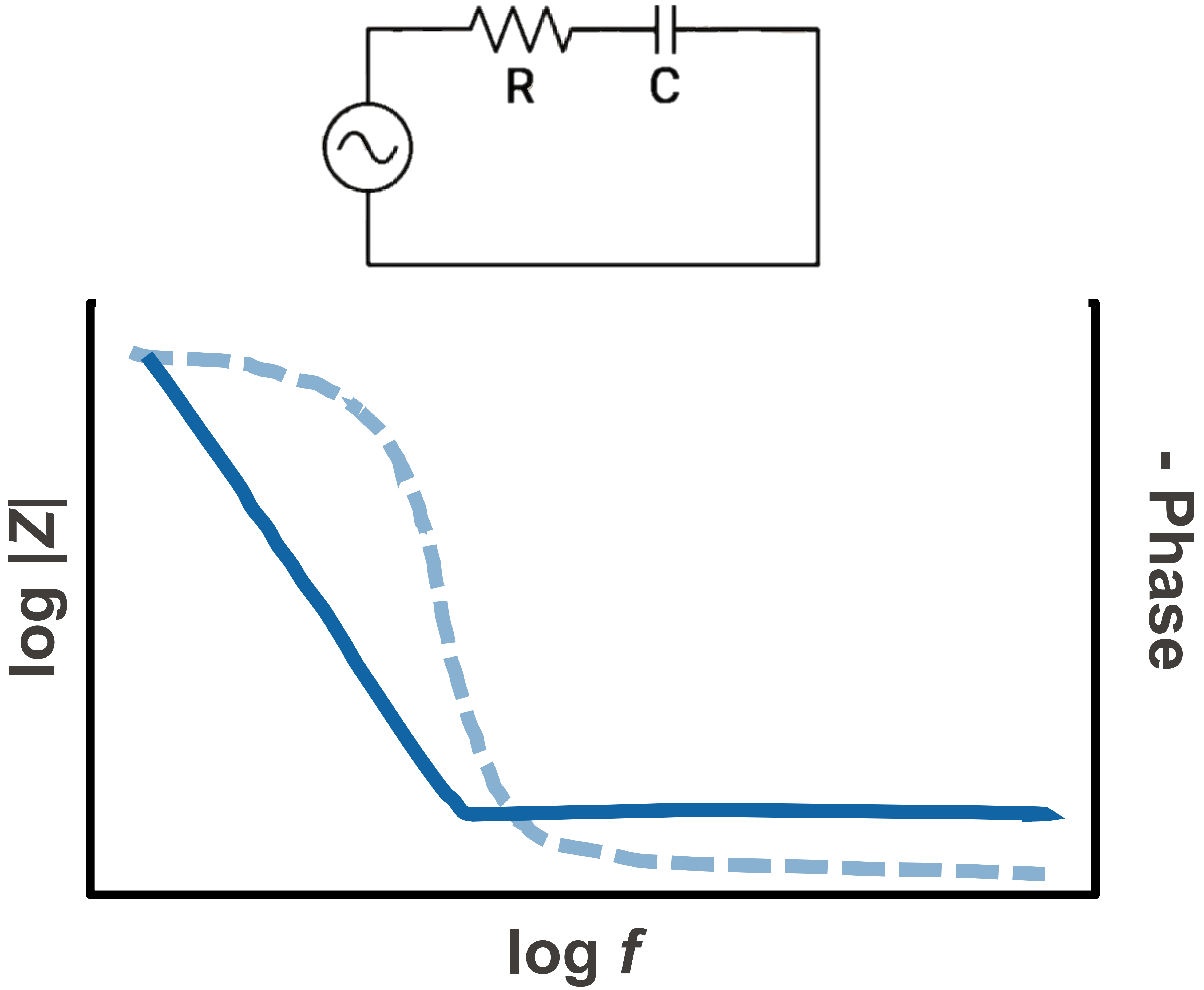
CHEMINA

Electrochemical Impedance Spectroscopy (EIS)

Interfaces can then be modeled as an equivalent circuit:

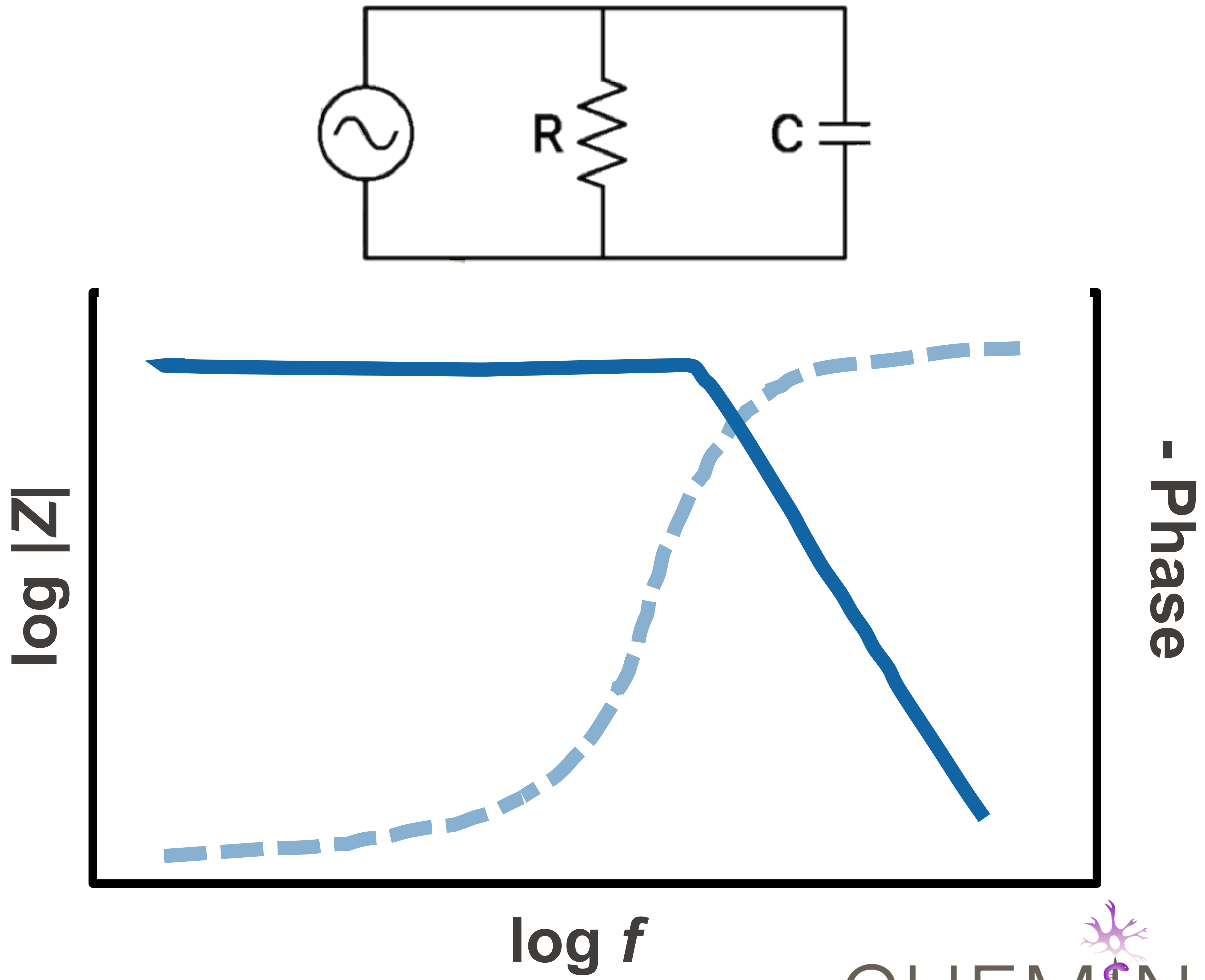
Series R-C circuit

$$Z_{\text{total}} \approx Z_{\text{largest}}$$

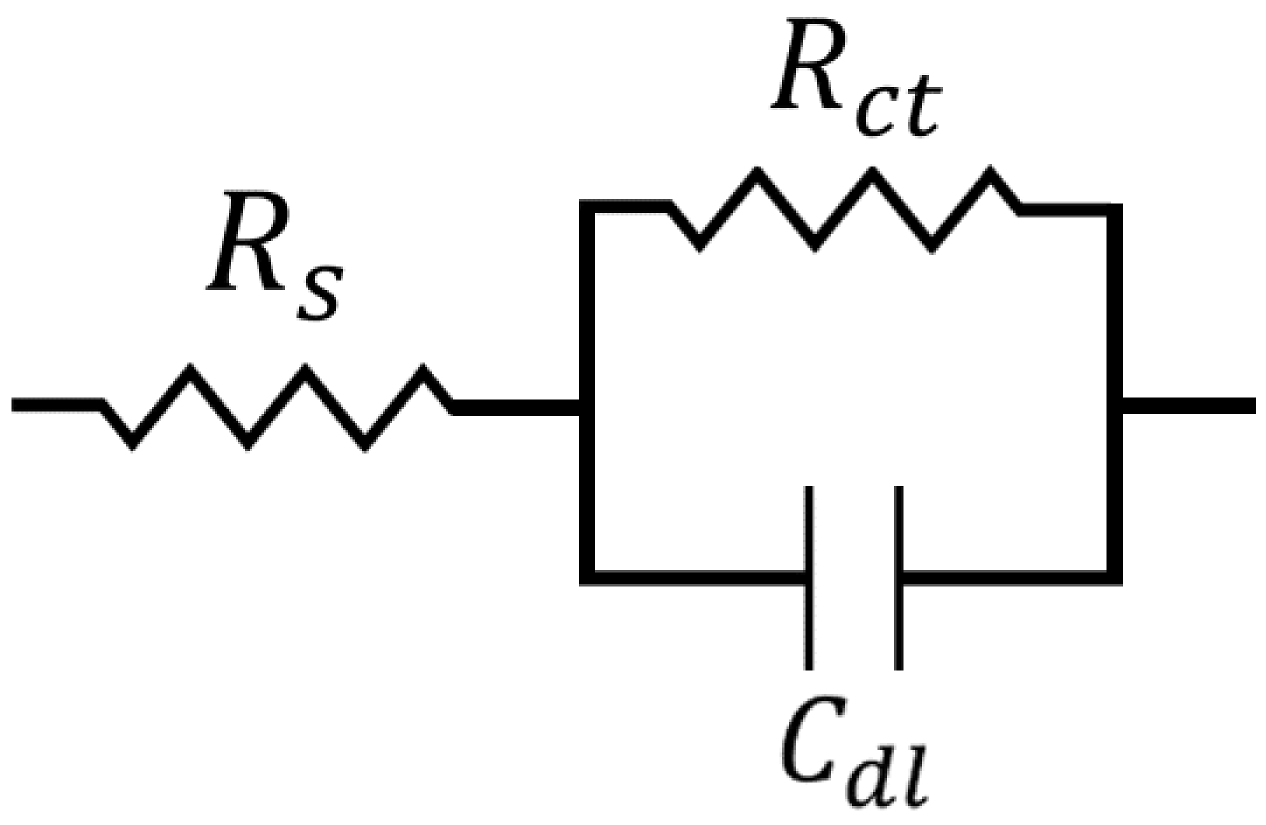


Parallel R-C circuit

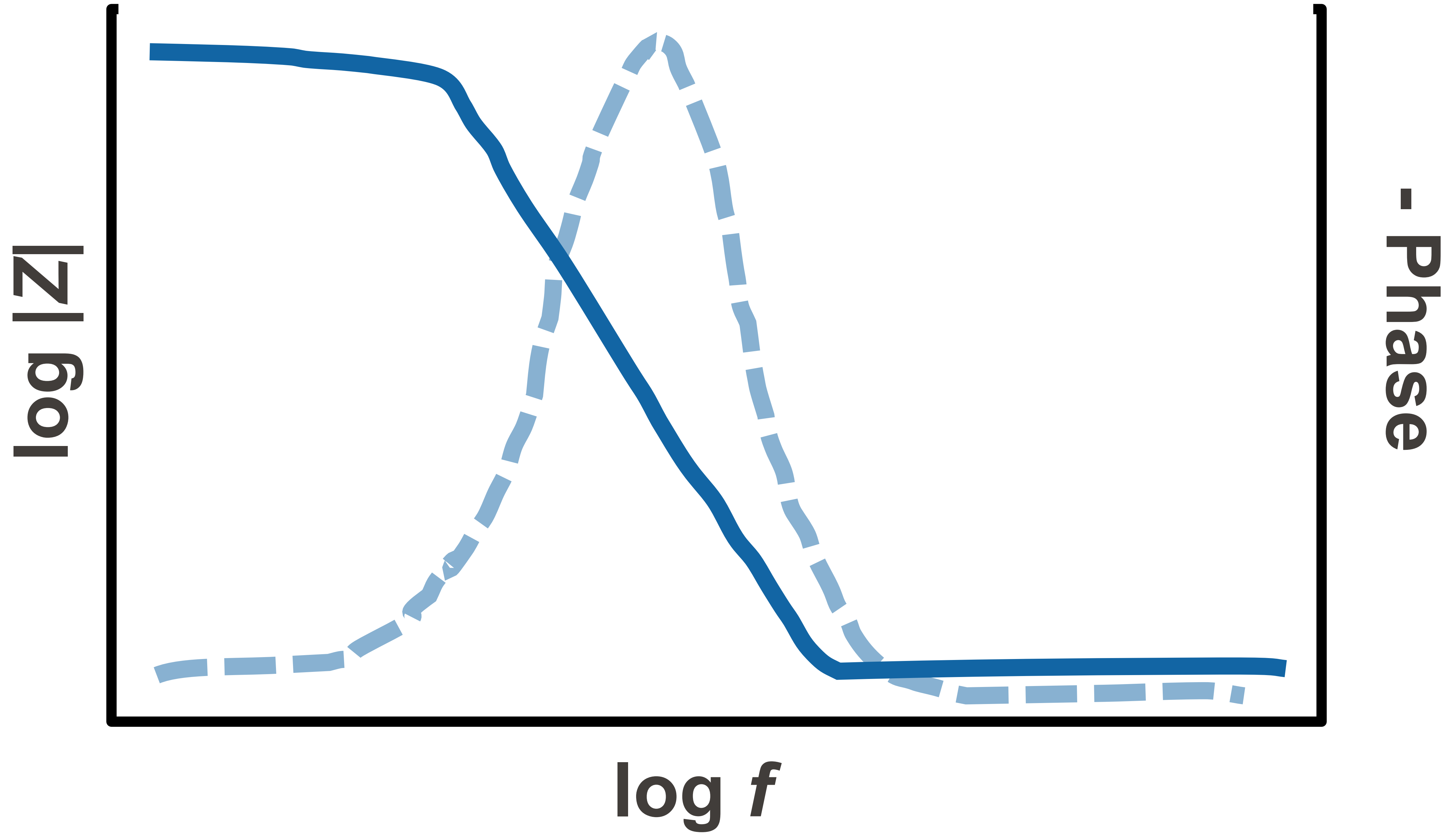
$$Z_{\text{total}} \approx Z_{\text{smallest}}$$



Electrochemical Impedance Spectroscopy (EIS)



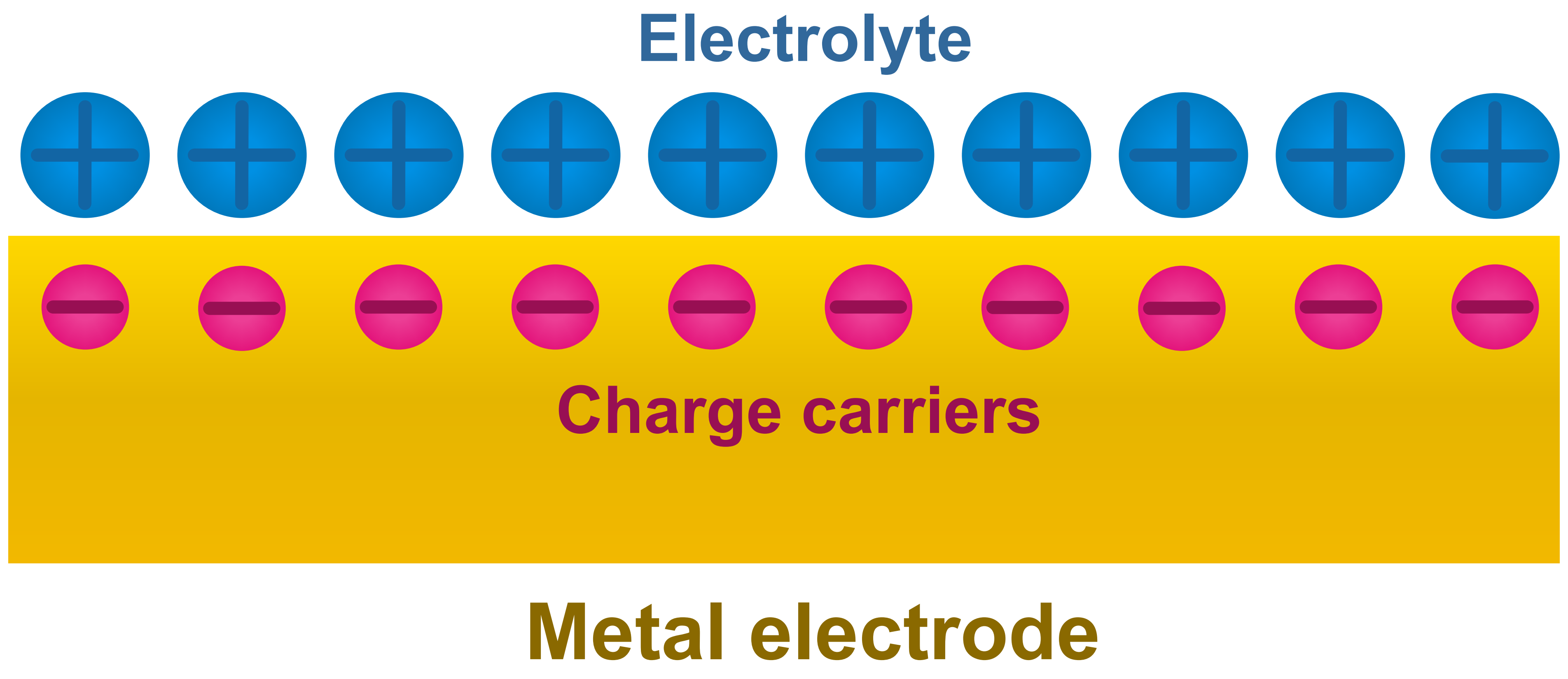
Randles Circuit



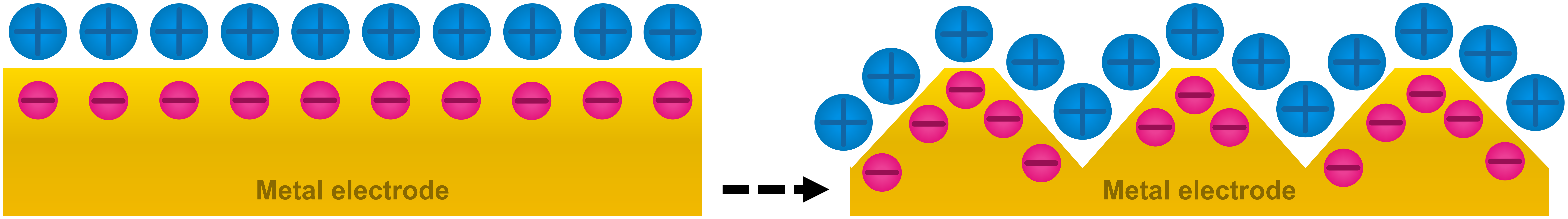
R_s = electrolyte solution resistance

R_{ct} = charge transfer resistance

C_{dl} = double layer capacitance

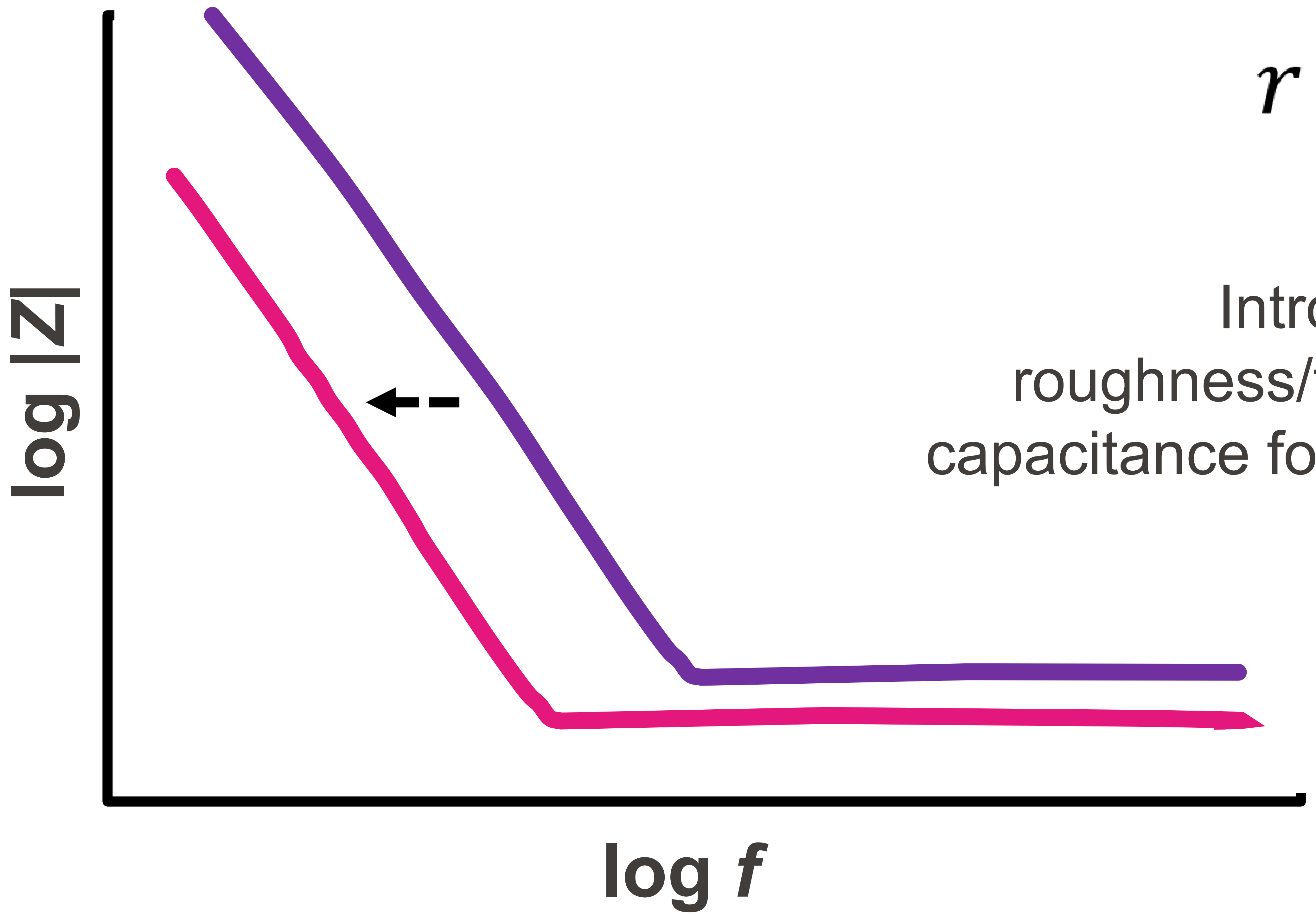


Where do we draw the line between surface and bulk?



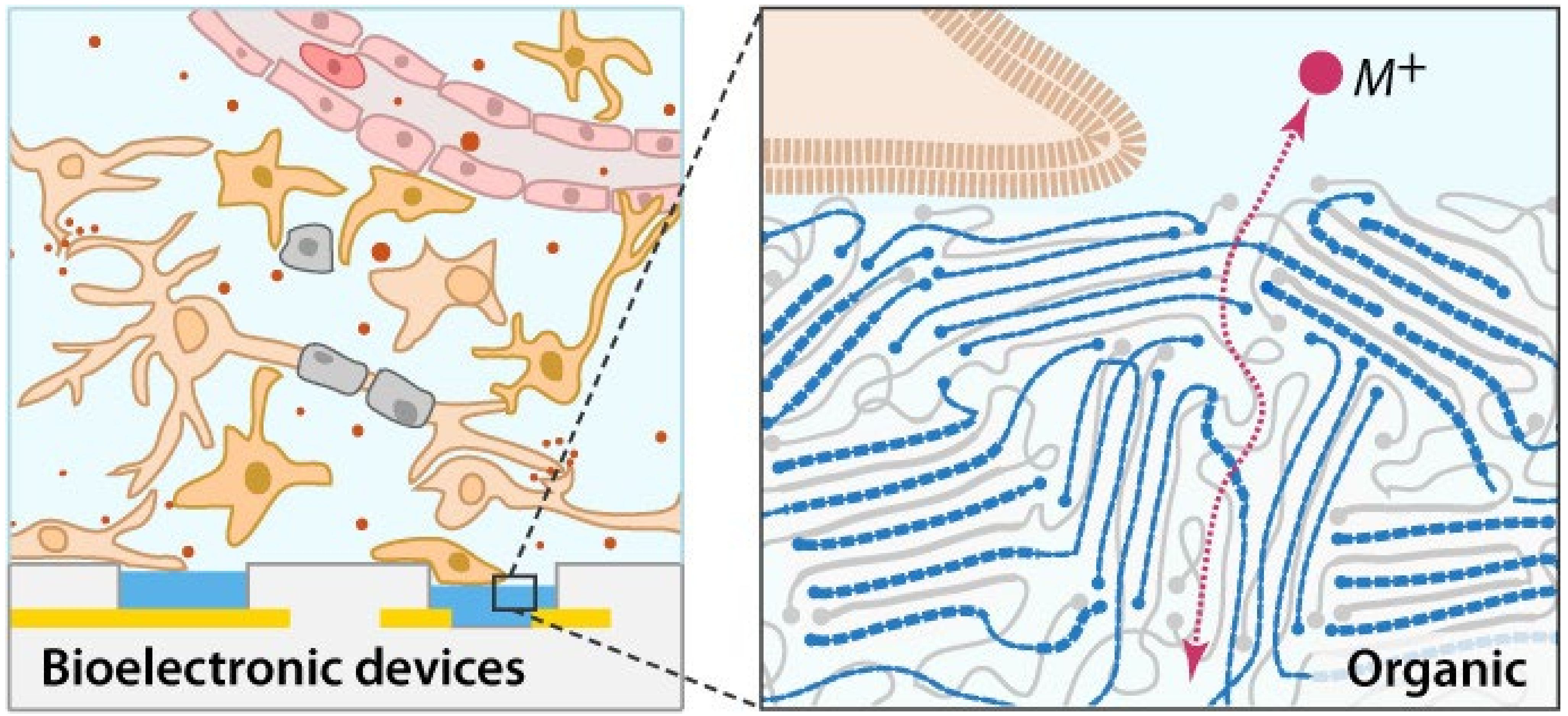
$$r = \frac{A_{real}}{A_{geo}}$$

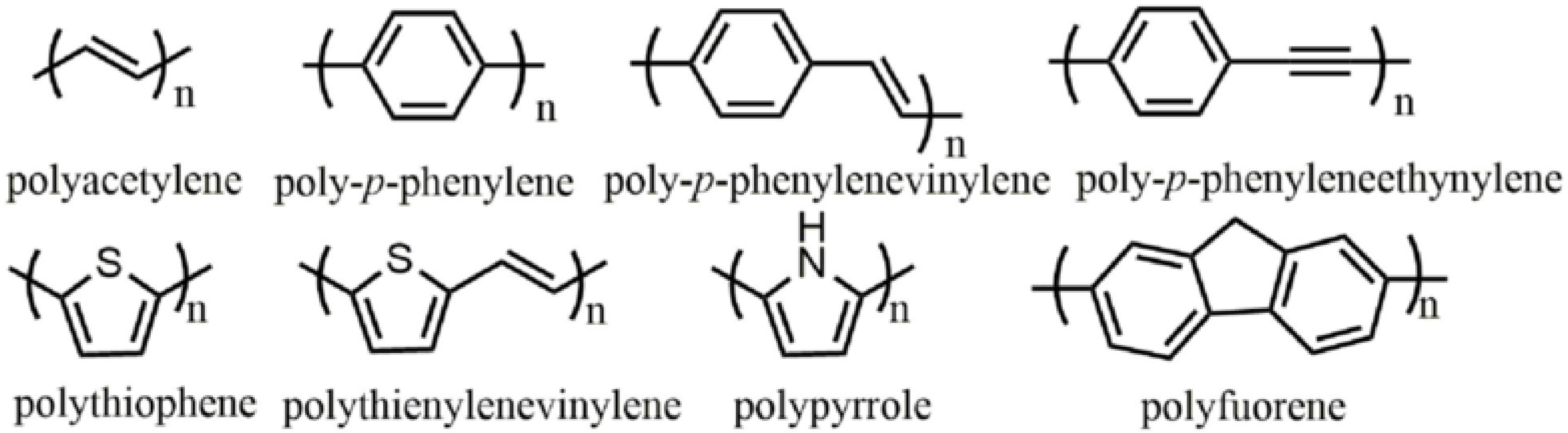
Can we take this to the next level and design semiconductors with three-dimensional interactions with biology?



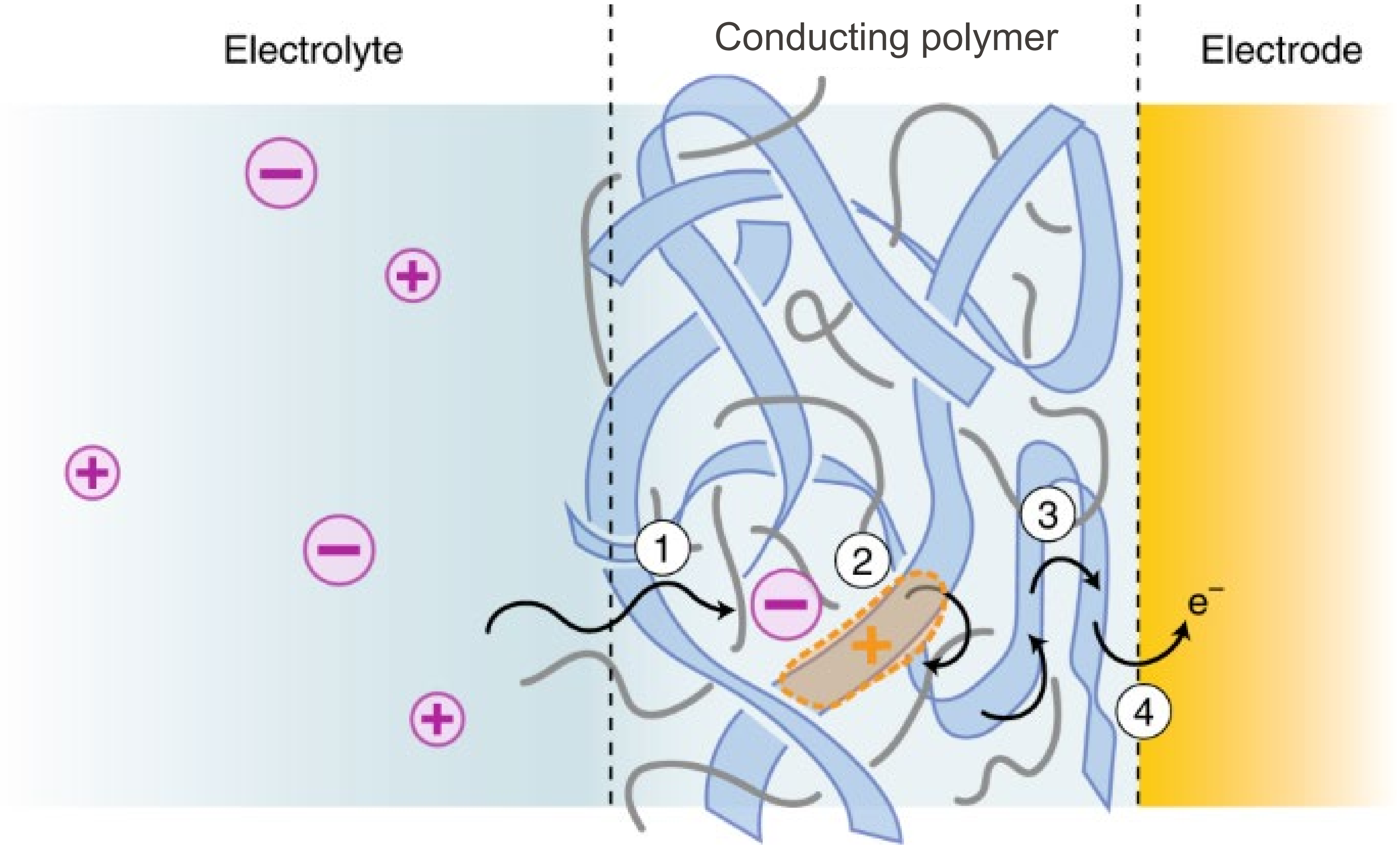
Introducing surface roughness/topographies increases capacitance for the same geometric area

Introduction to Conducting Polymers





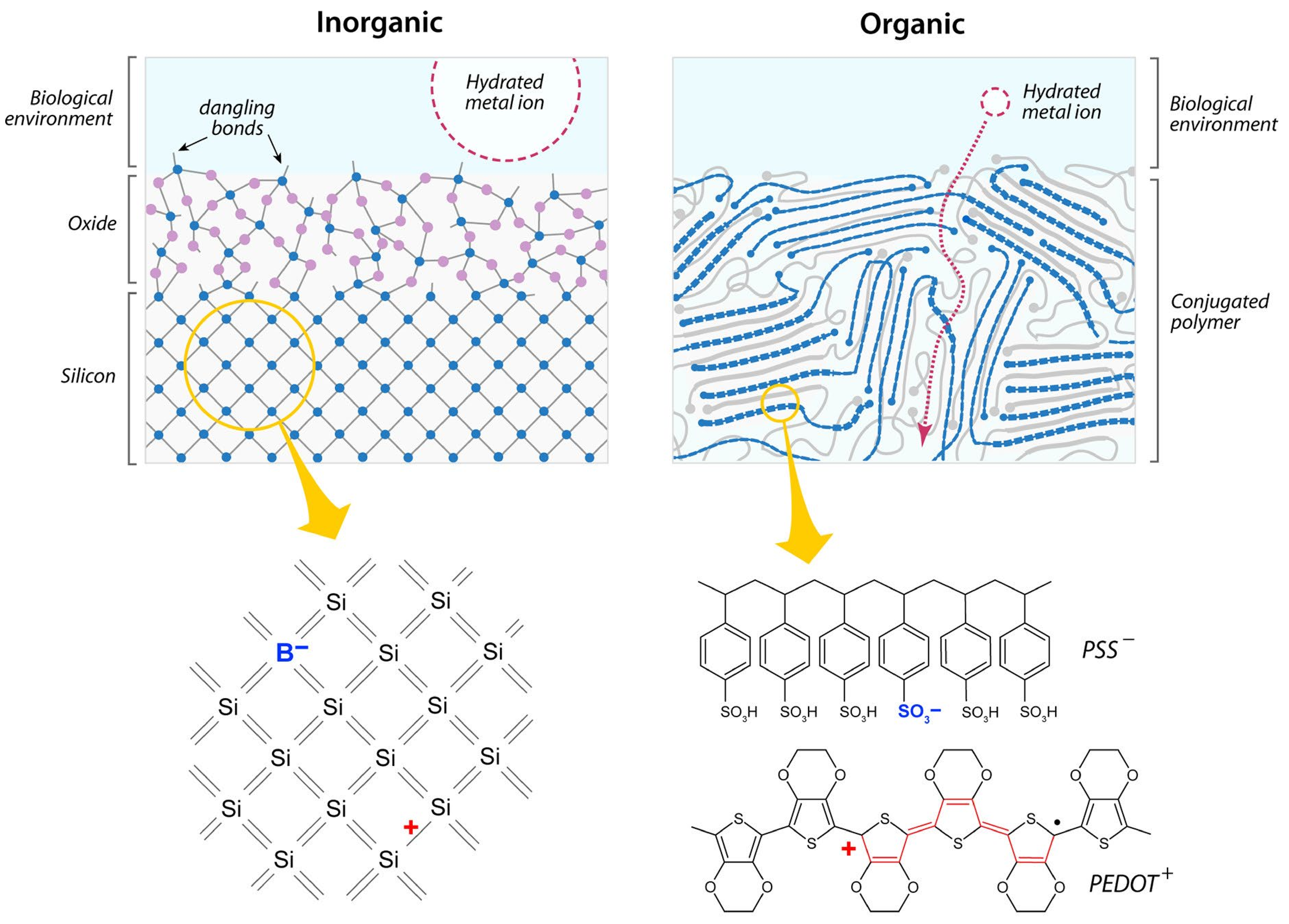
Class of conjugated polymers



Rivnay, Owens & Malliaras, *Chem Mater, 26, 1,* **2013**

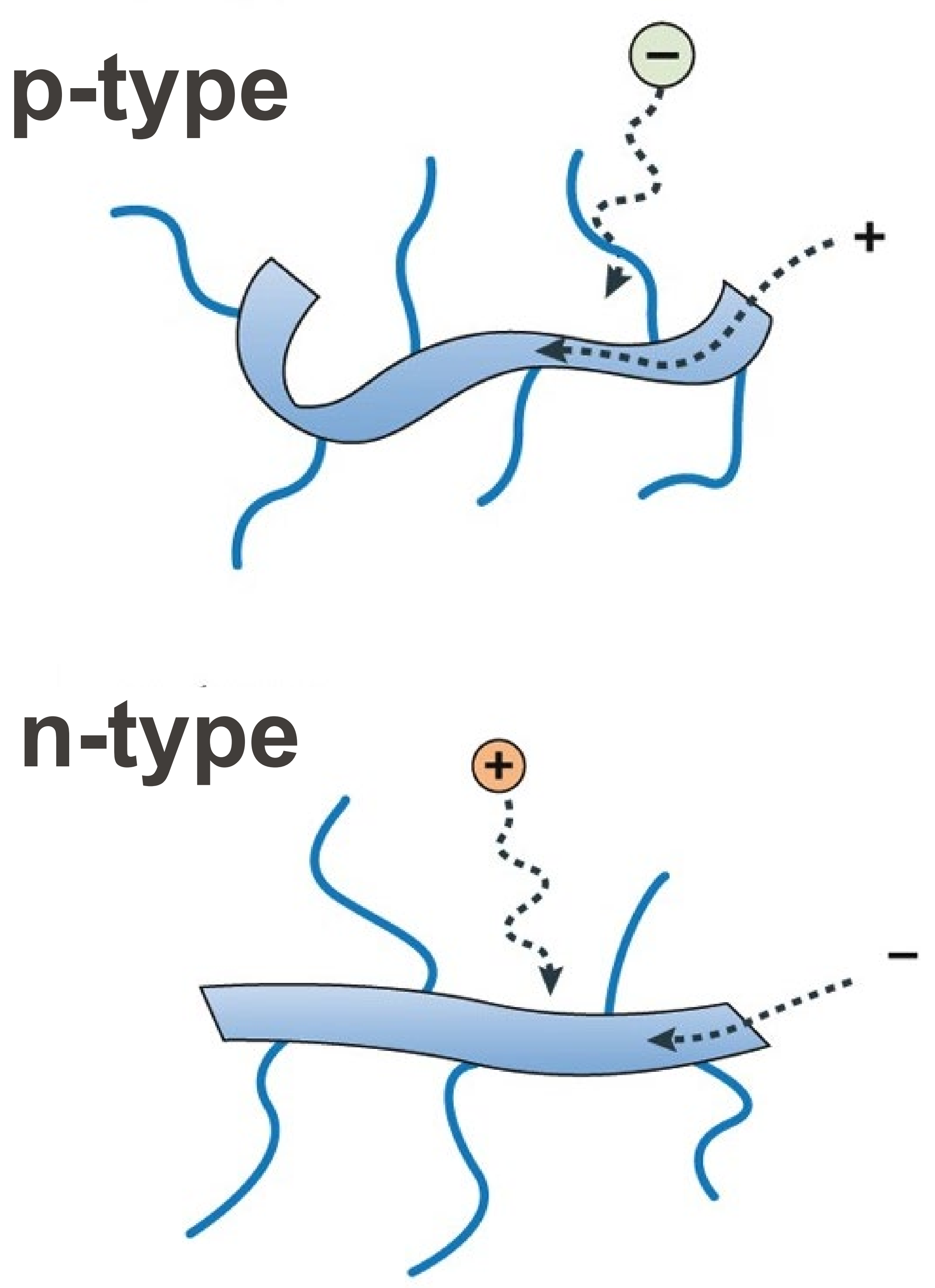
Paulsen, *et al., Nat. Mat., 19,* **2020**

Interfaces of Semiconductors with Biology



p-type silicon

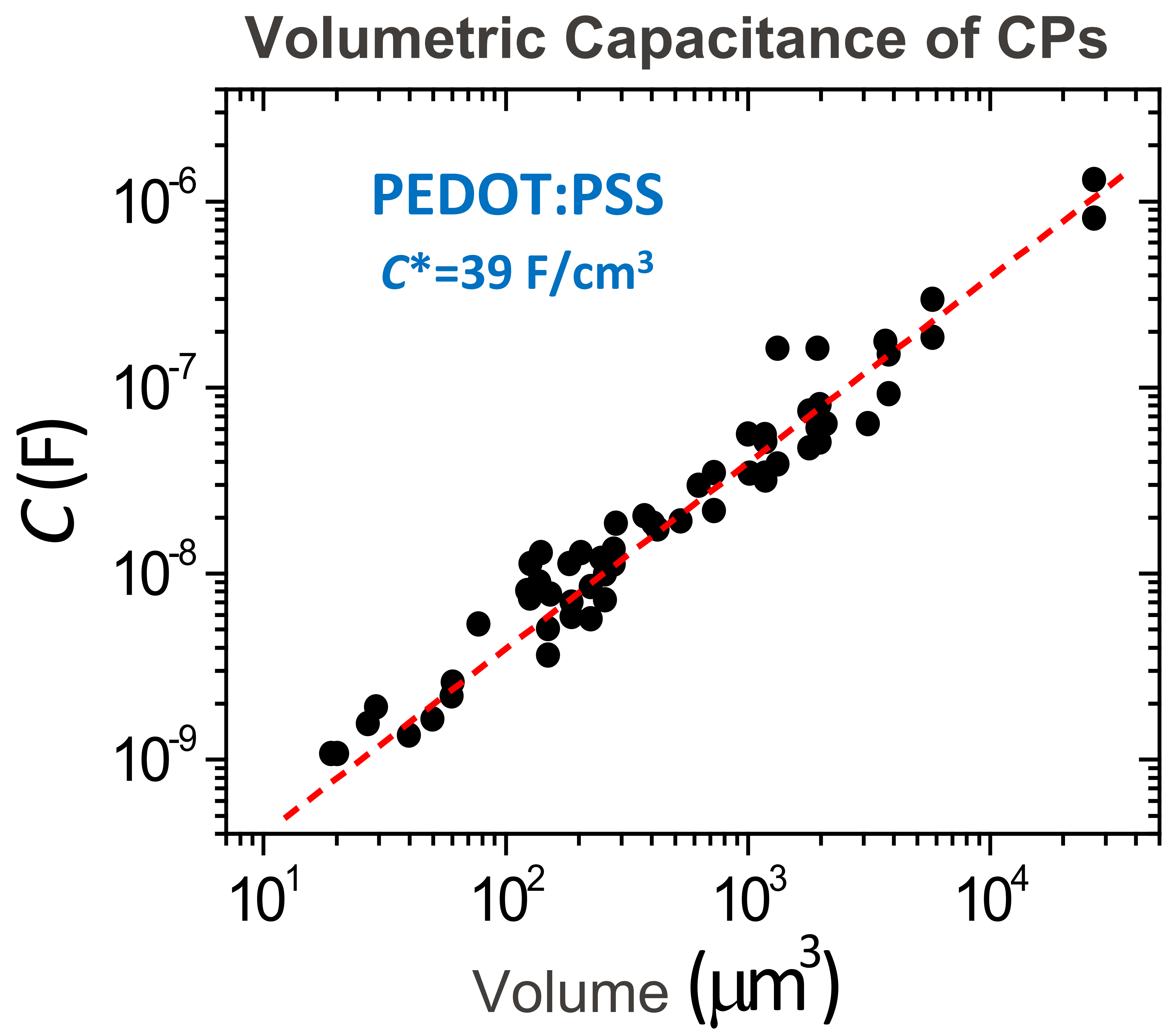
p-type PEDOT

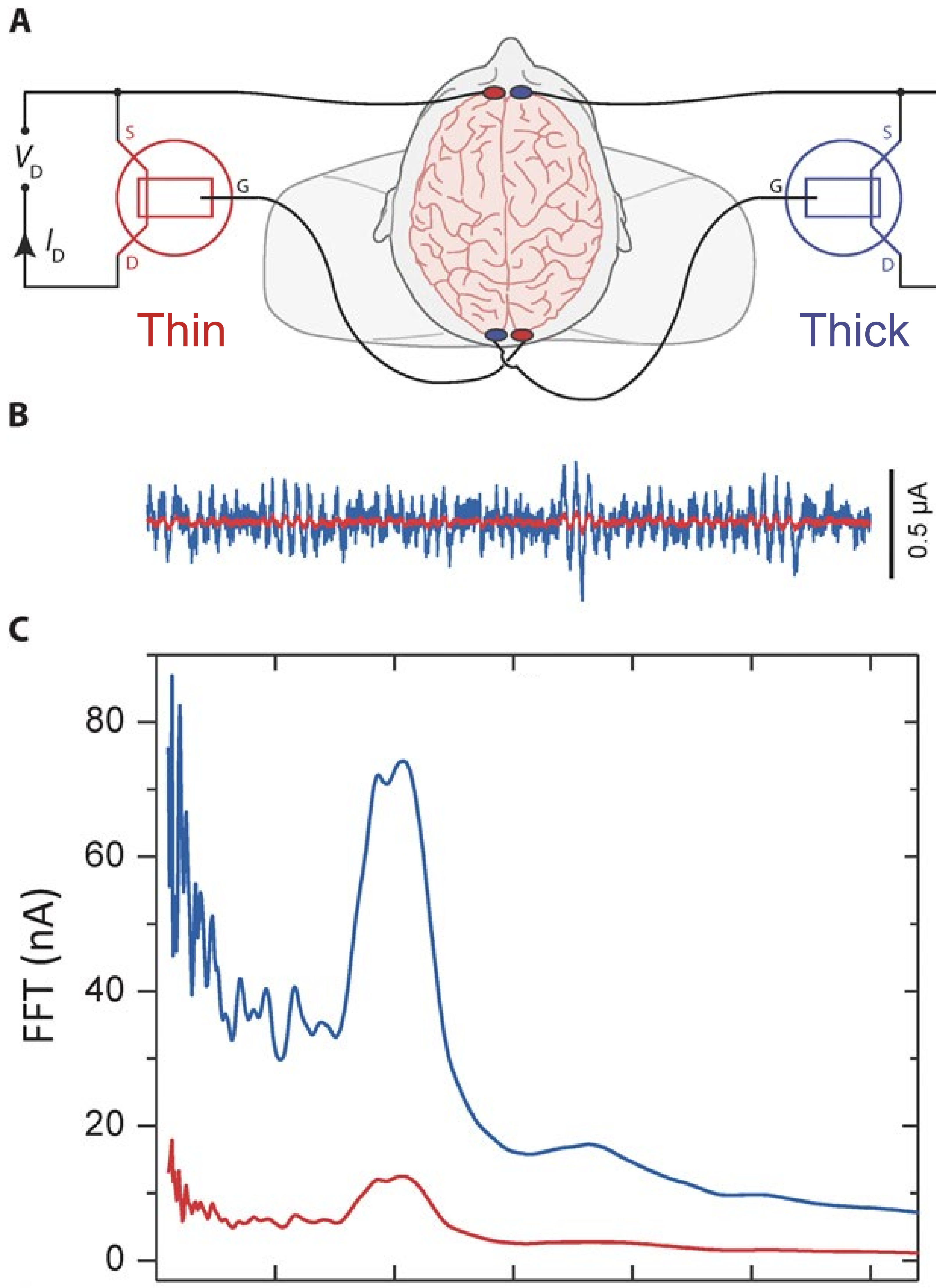


Rivnay, Owens & Malliaras, *Chem Mater, 26, 1,* **2013**

Rivnay, *et al., Nat Rev Mater, 3,* **2018**

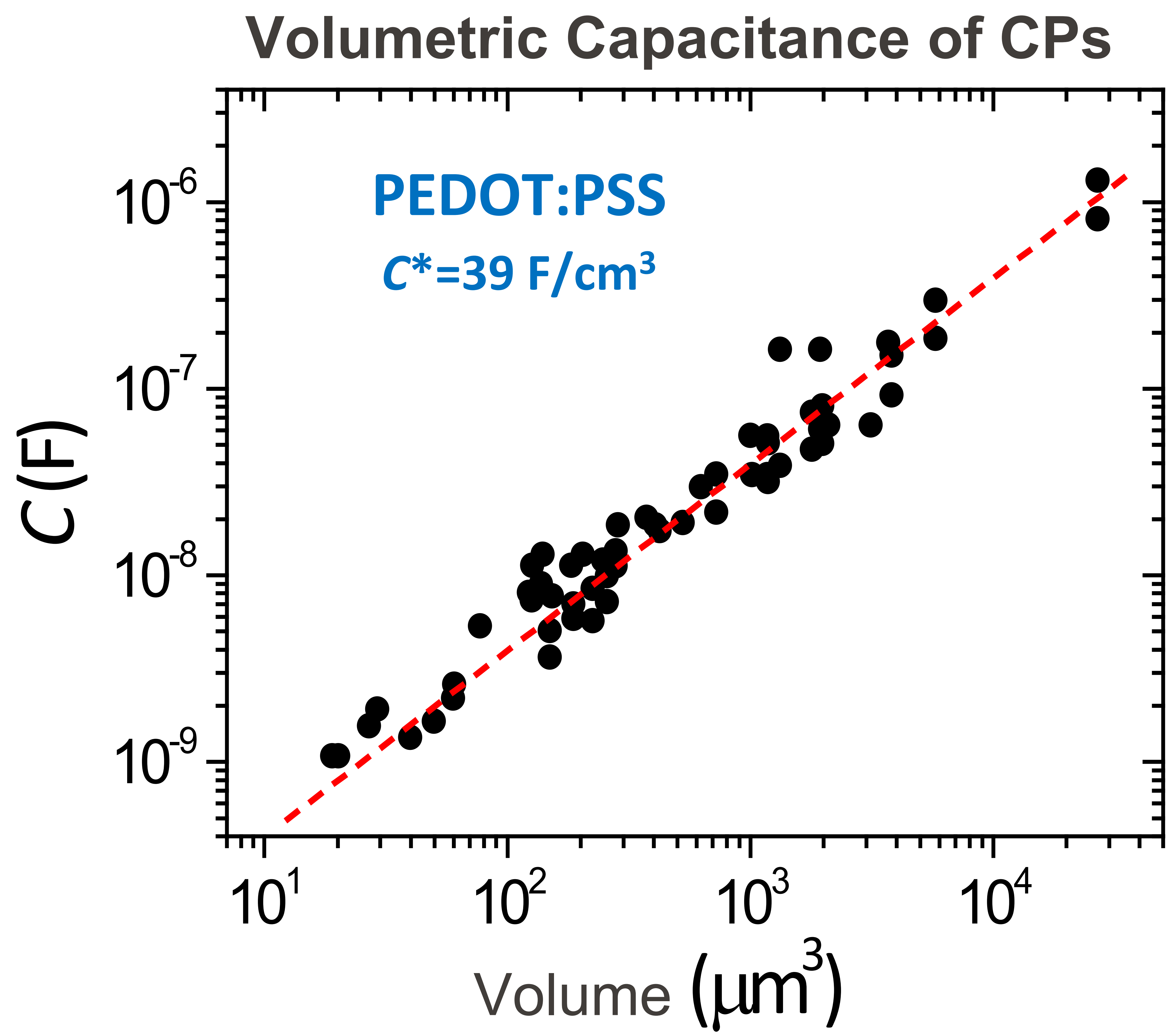
Volumetric Capacitance of Conducting Polymers



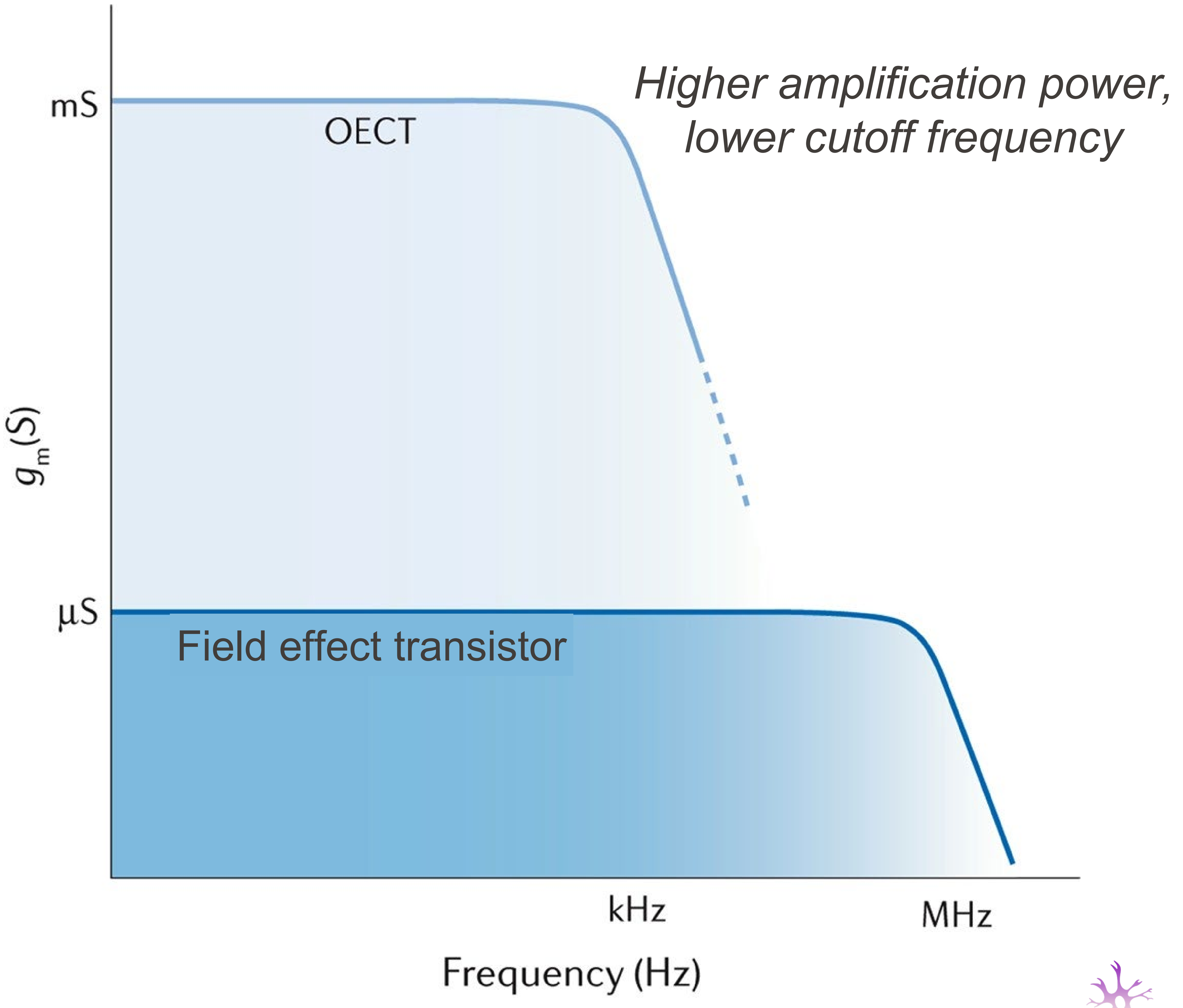


Rivnay, *et al.*, *Sci Adv*, *1*, *4*, **2015**

Volumetric Capacitance of Conducting Polymers



This advantage still presents a tradeoff with time response –



Rivnay, *et al., Sci Adv, 1, 4,* **2015**

Rivnay, *et al., Nat Rev Mat, 3,* **2018**

Advantages of Conducting Polymers in Bioelectronics

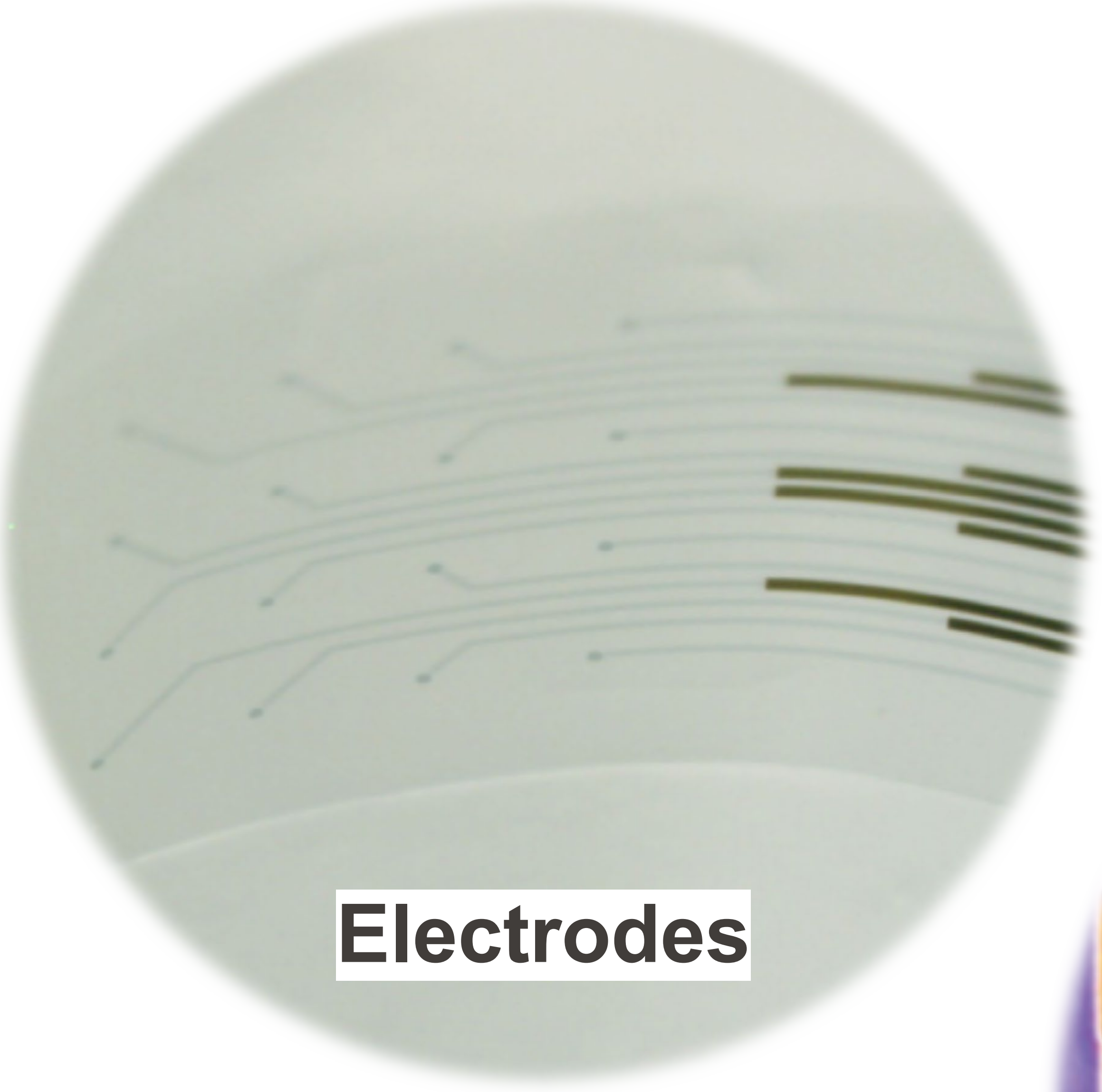
Dijk, *et al.*, *Microsyst Nanoeng, 8,* **2022**

Tyrrell, Boutelle & Campbell, *Adv Func Mat, 31, 1,* **2021**

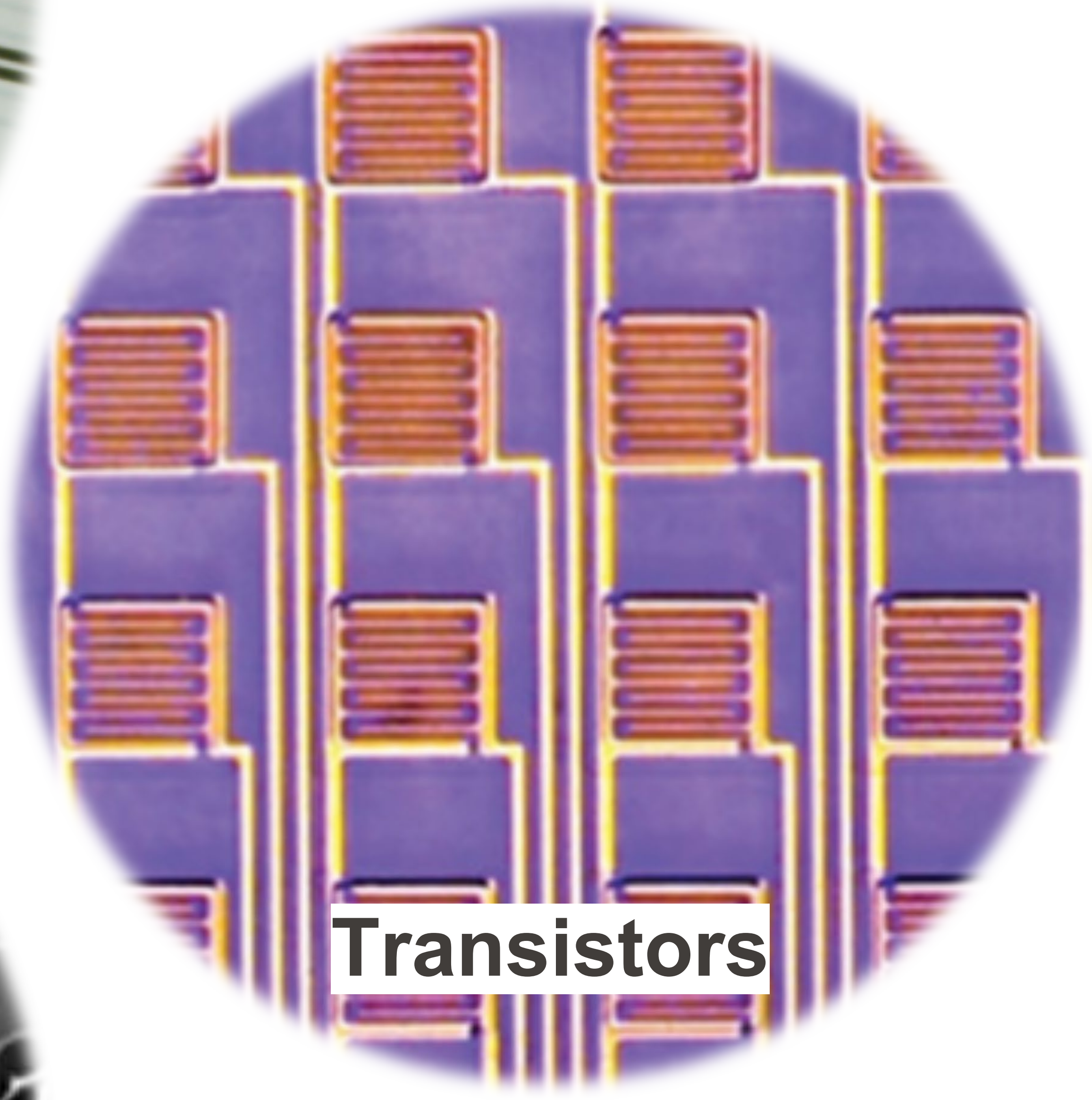
Solazzo & Monaghan, *Synth Metals, 290,* **2022**

- Transducing ionic to electronic signals
- Soft, flexible, and hygroscopic
- Biocompatibility
- Low impedance
- Low voltage operation
- Ease of chemical modification for semiconductor design
- Low temperature processing
- Compatible with additive manufacturing

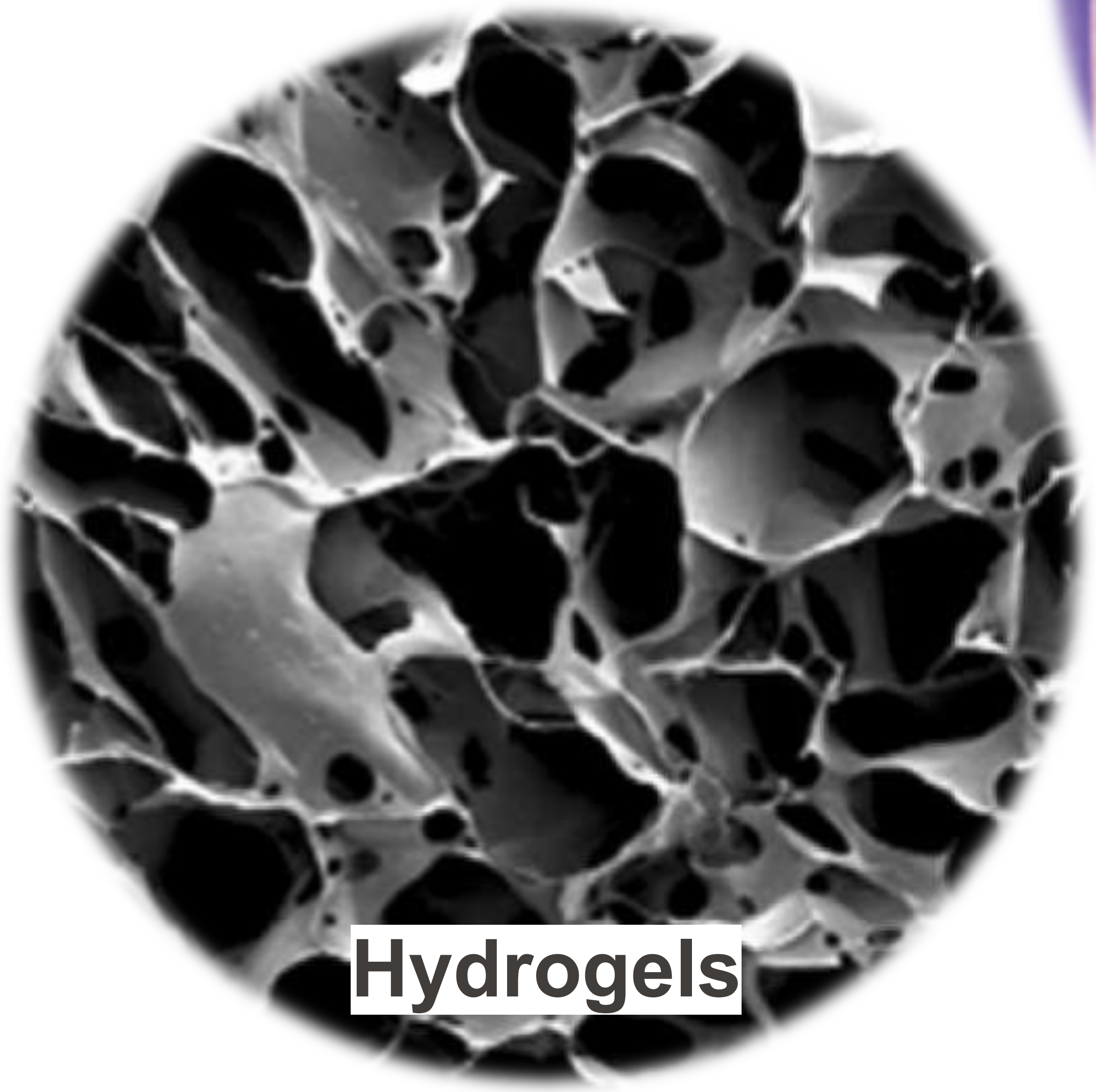
Can be incorporated into: →



Electrodes



Transistors



Hydrogels

Key Takeaways

- Bioelectronic devices cover a wide range of applications, and the interface of the semiconductor and biology greatly dictates its performance
- Electrochemical impedance spectroscopy (EIS) is an important method of characterizing interfaces by quantifying the impedance and capacitance of a system
- Low impedance interfaces can be achieved by not just increasing surface roughness, but by allowing ions to interact with the semiconductor in 3D
- Conducting polymers are promising for their low impedance and high biocompatibility

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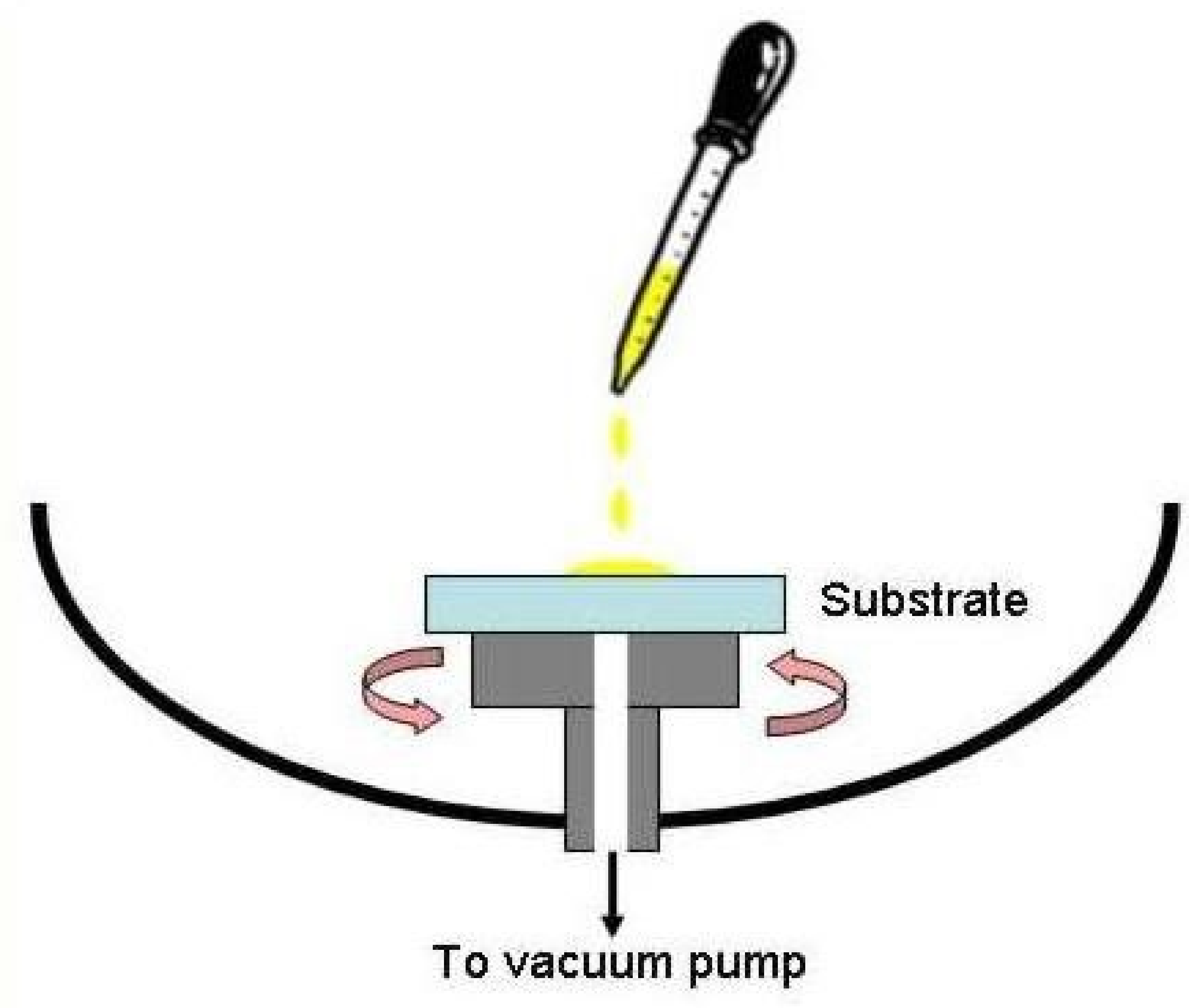
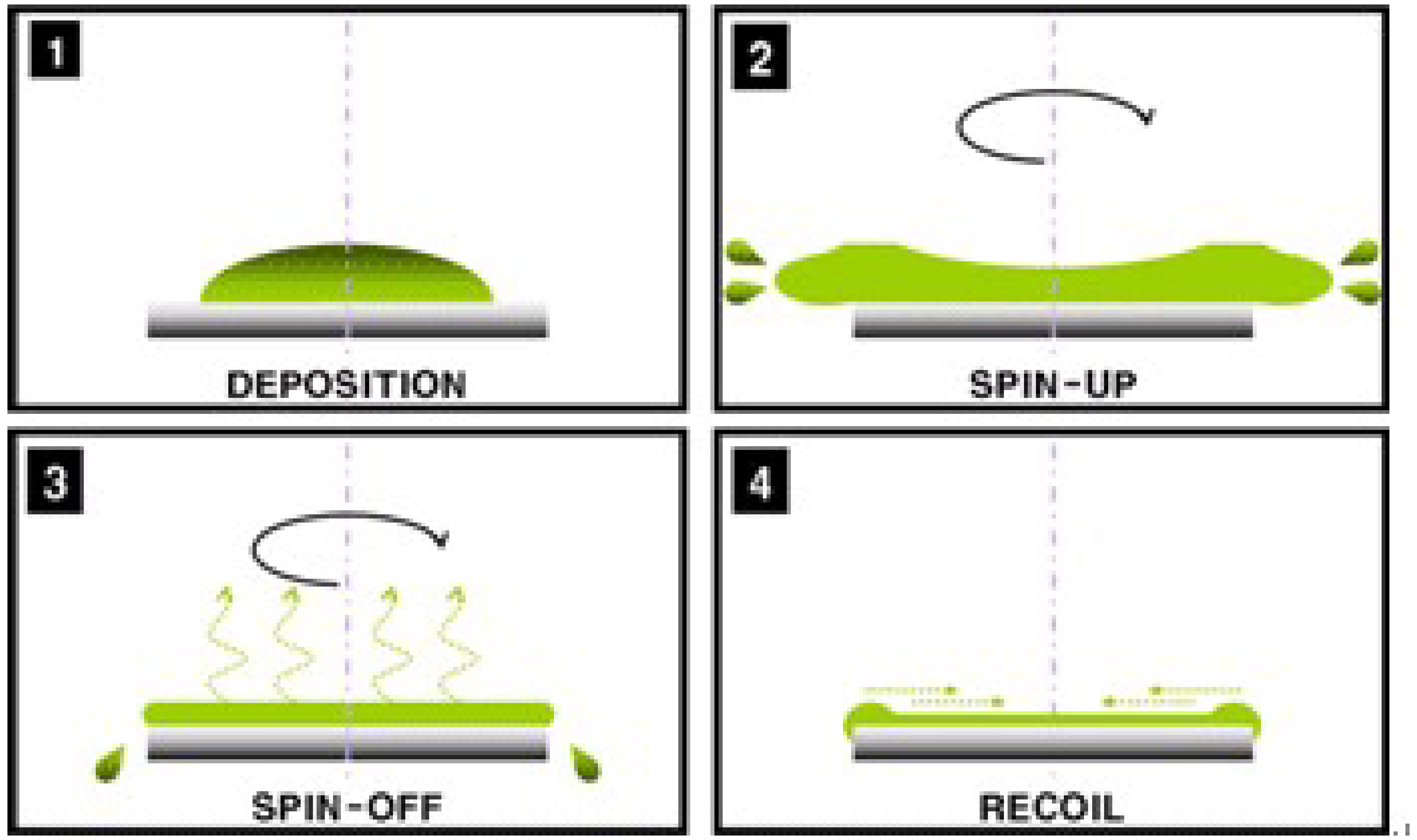
Conducting Polymer Preparation Methods: Spin-Coating

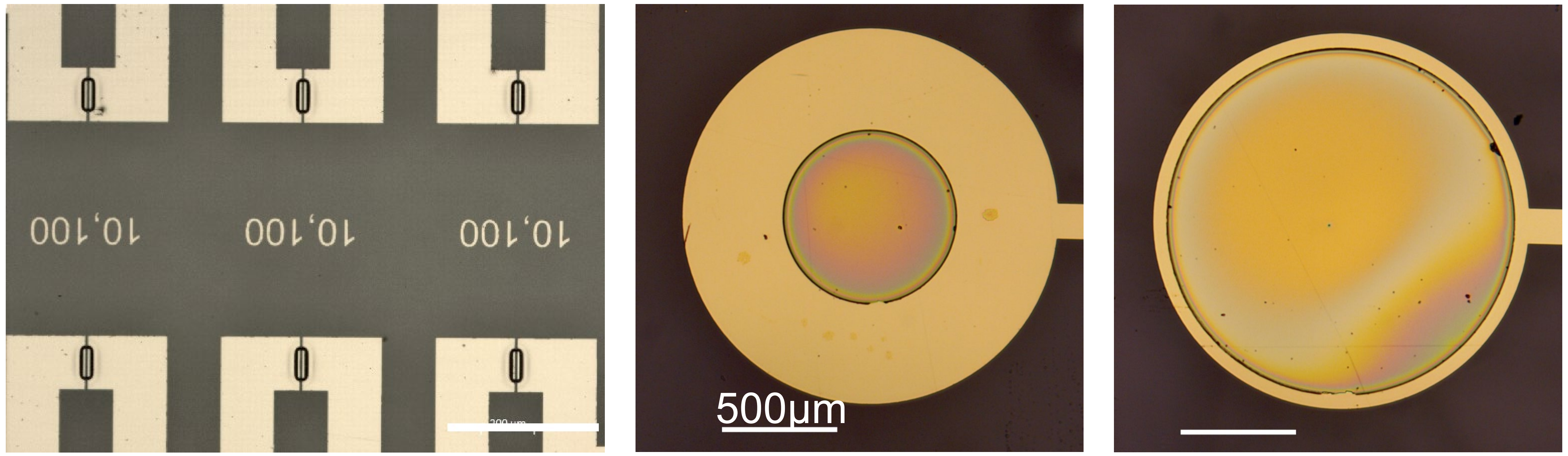
Technique for reproducibly applying nm - µm thin films onto surfaces

- Polymer is dissolved in a solvent and applied to the substrate surface
- Substrate is then spun to spread the solution over the surface
- Cost-effective, widespread, and reproducible

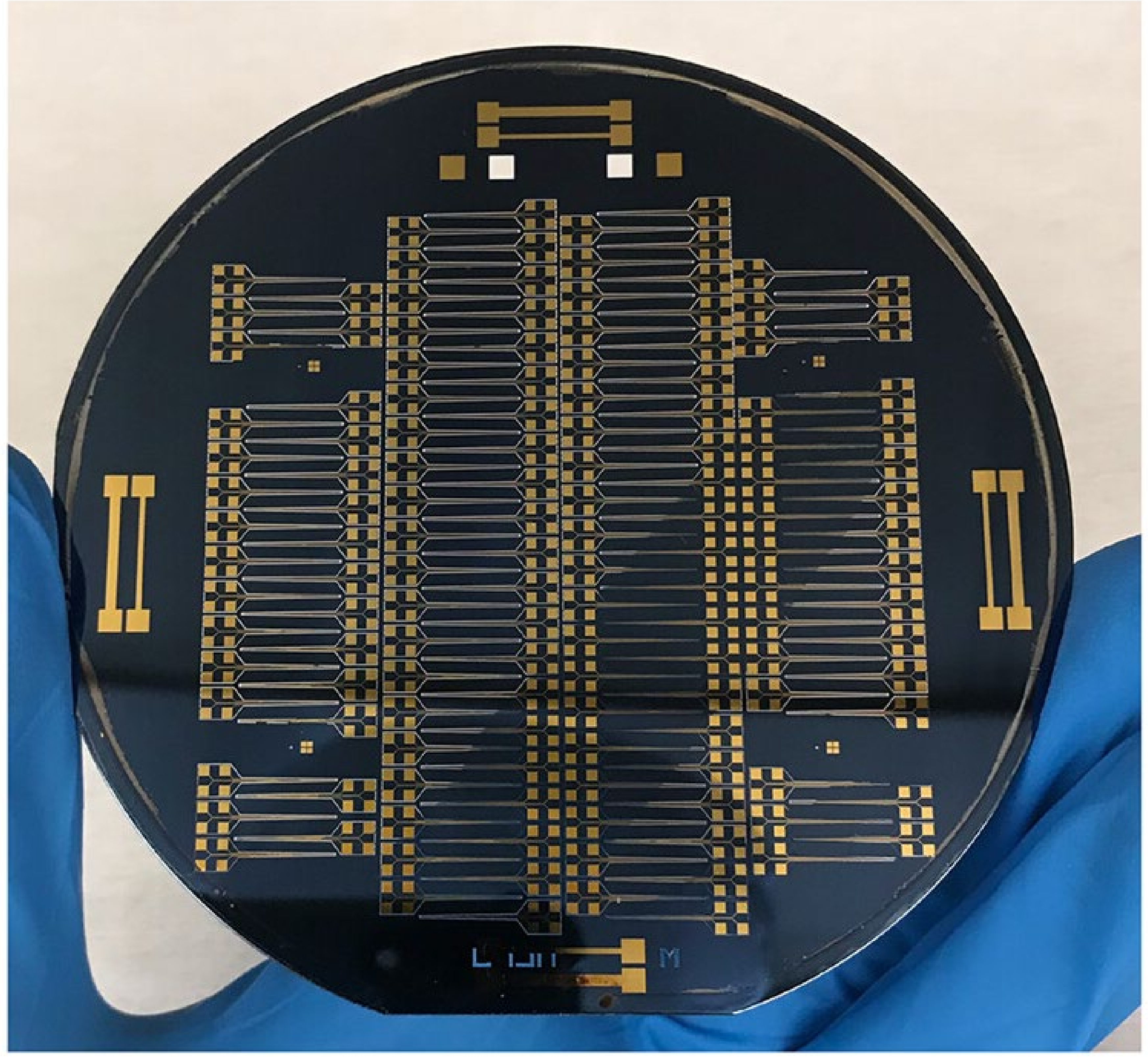




PEDOT:PSS spun-cast on micrometer devices:



Conducting Polymer Compatibility with Microfabrication

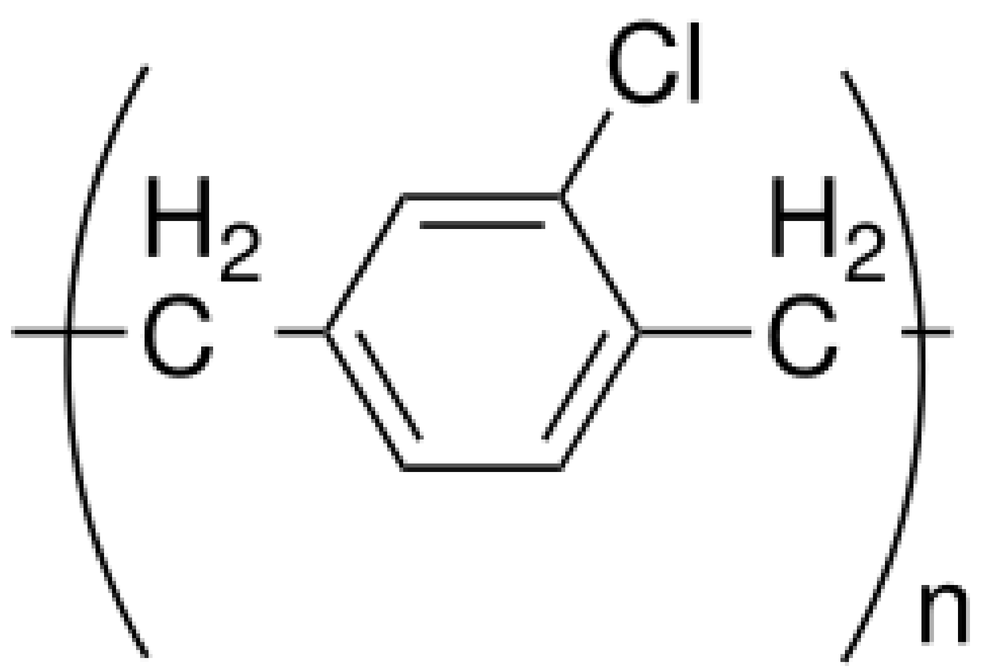


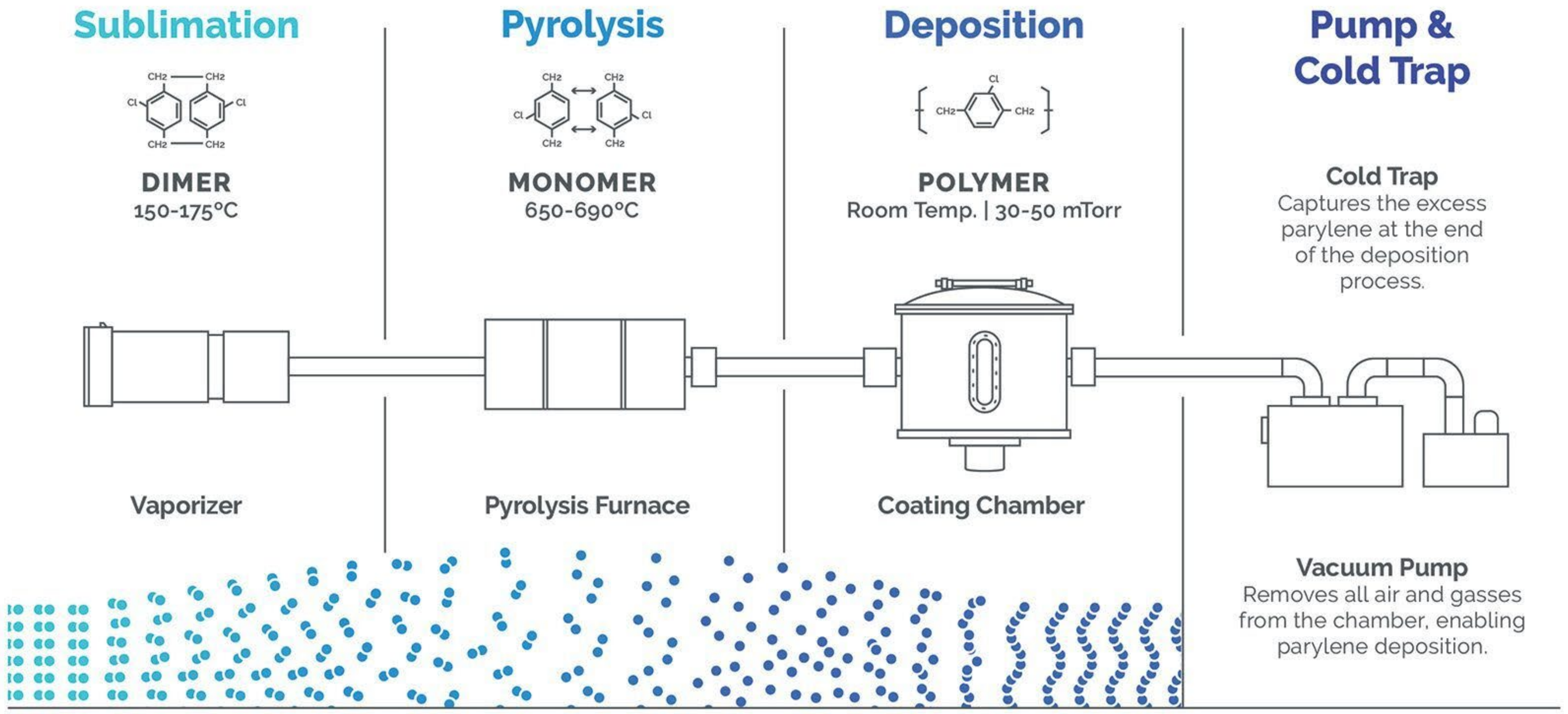
Zhao, *et al.*, *Sci Adv, 7, 48*, **2021**

CMi EPFL Center of MicroNanoTechnology

Conducting Polymer Compatibility with Microfabrication

Parylene-C




Sublimation

DIMER
150-175°C

Pyrolysis

MONOMER
650-690°C

Deposition

POLYMER
Room Temp. | 30-50 mTorr

Pump & Cold Trap

Cold Trap
Captures the excess parylene at the end of the deposition process.

Vaporizer

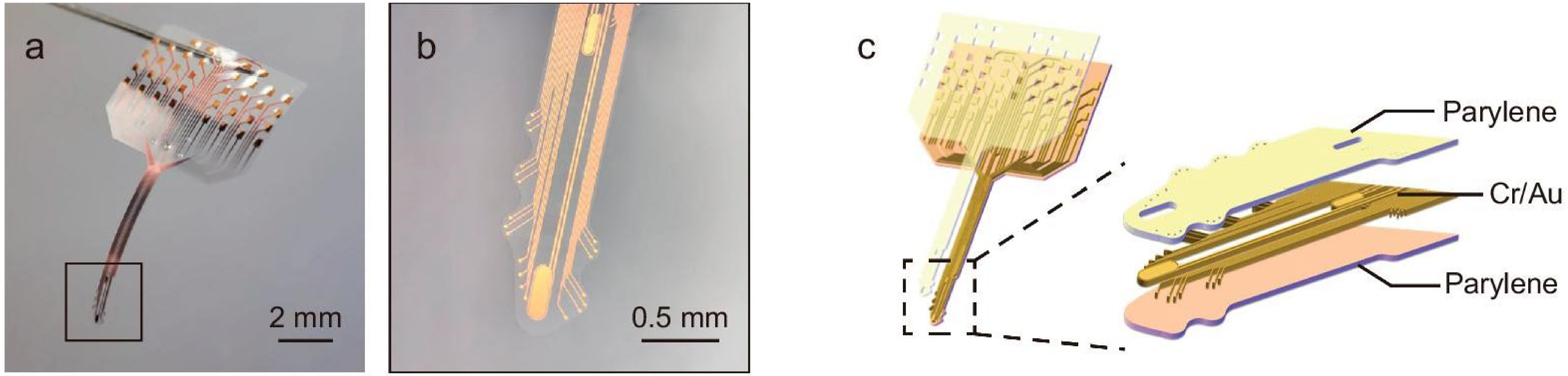
Pyrolysis Furnace

Coating Chamber

Vacuum Pump
Removes all air and gasses from the chamber, enabling parylene deposition.

VSi Parylene

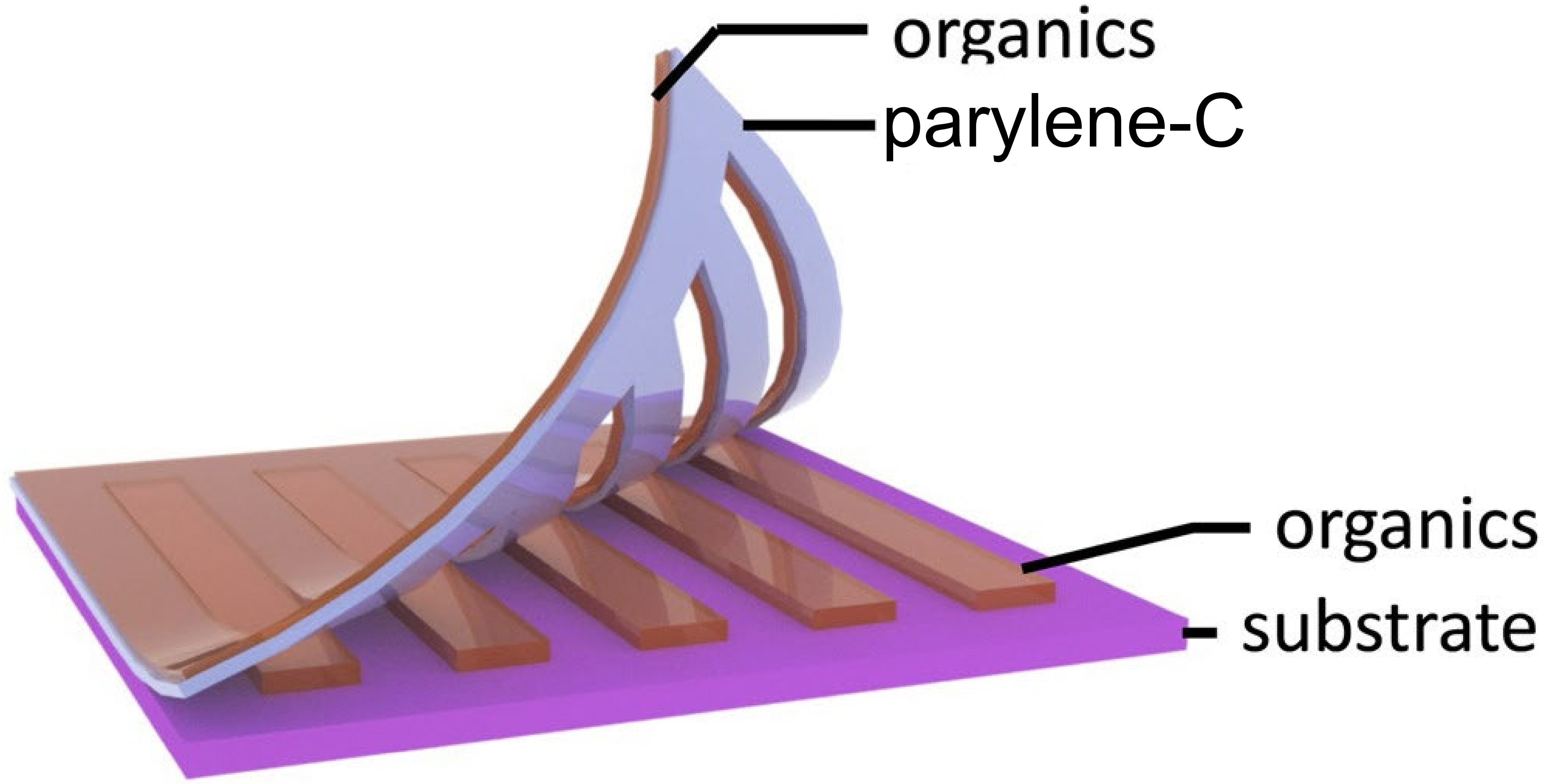
One of the materials of choice for flexible bioelectronics:

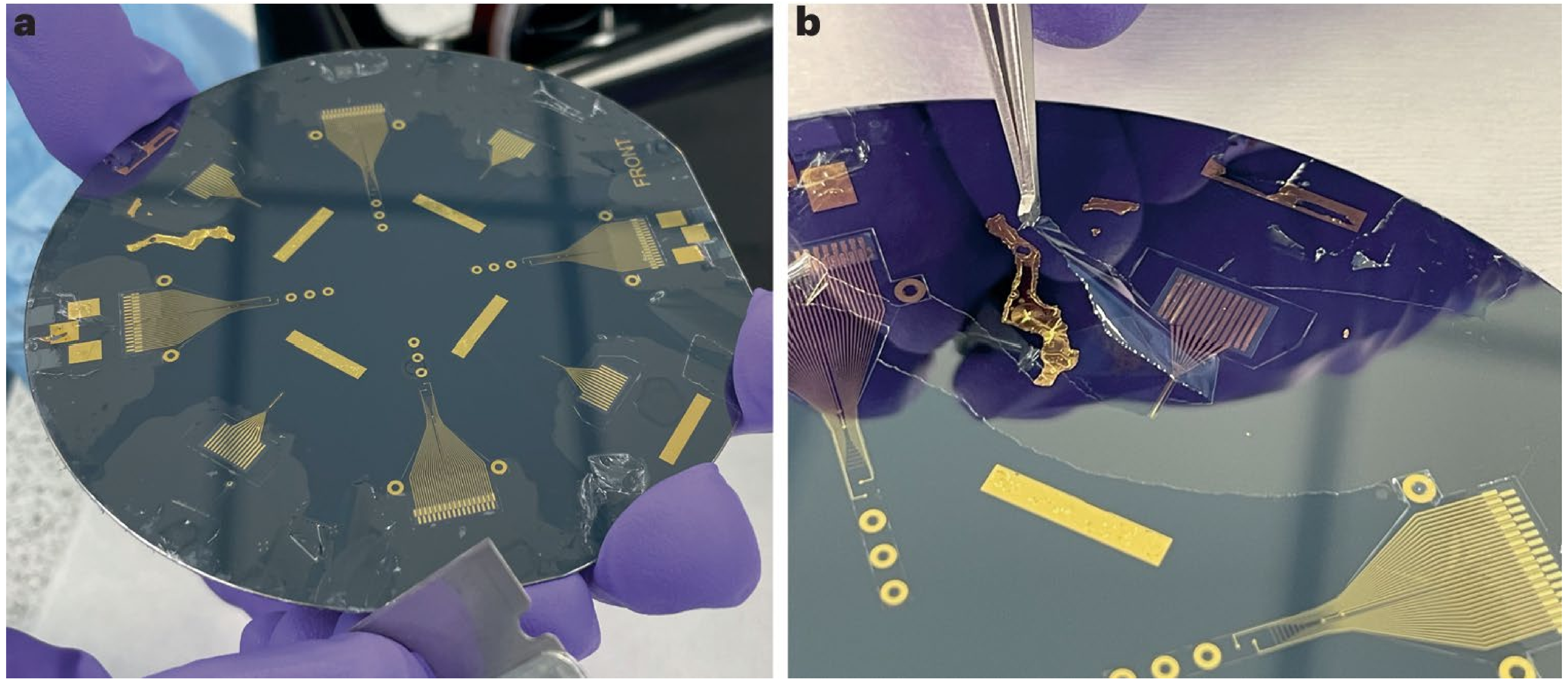


Wang, *et al.*, *Nat Sci Rev*, *12*, *2*, **2025**

Conducting Polymer Compatibility with Microfabrication

Mechanical Peel-Off Method

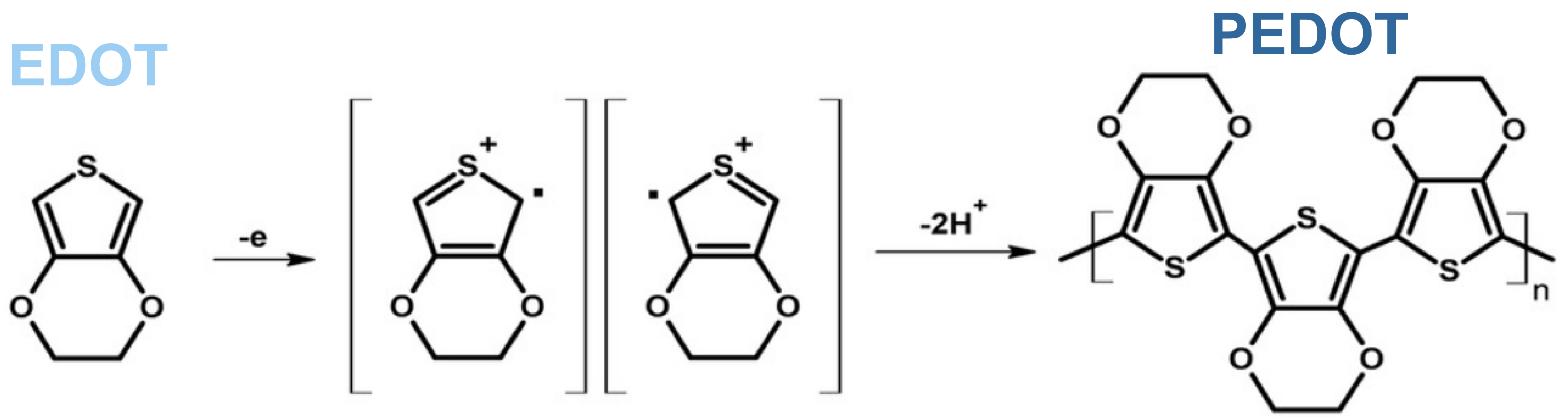


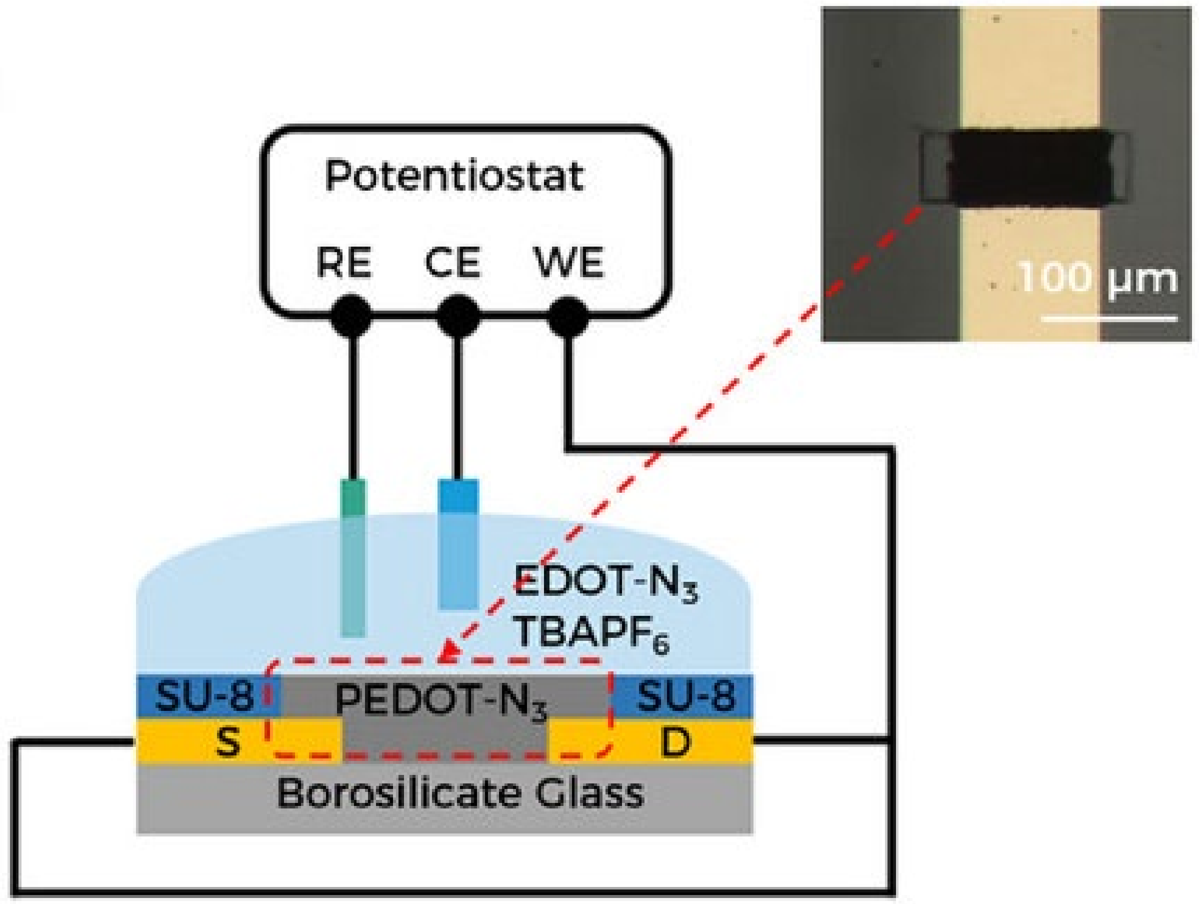


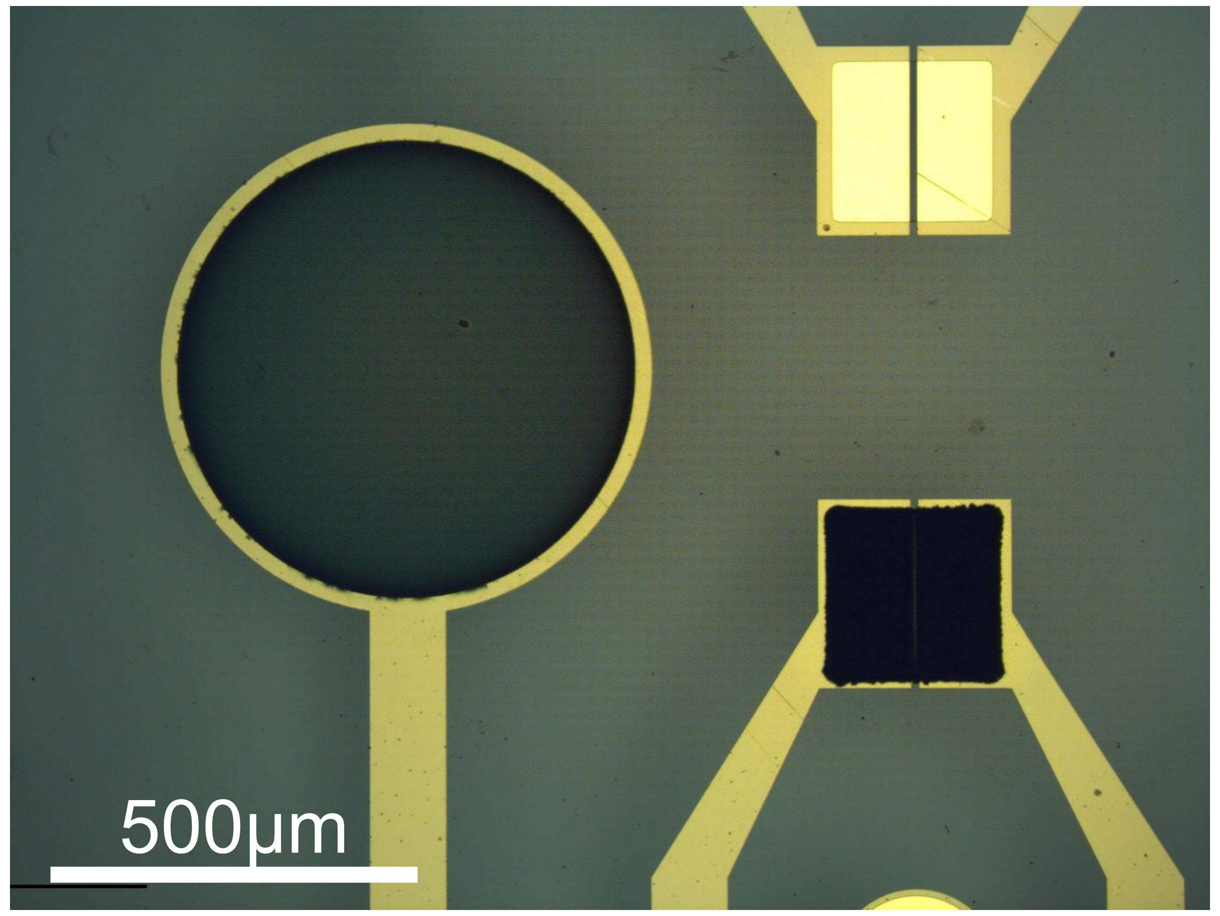
Compatible with polymers dissolved in a variety of solvents

Huang, *et al., Joule, 6, 7,* **2022**
Oldroyd, *et al., Nat Protocols, 20,* **2025**

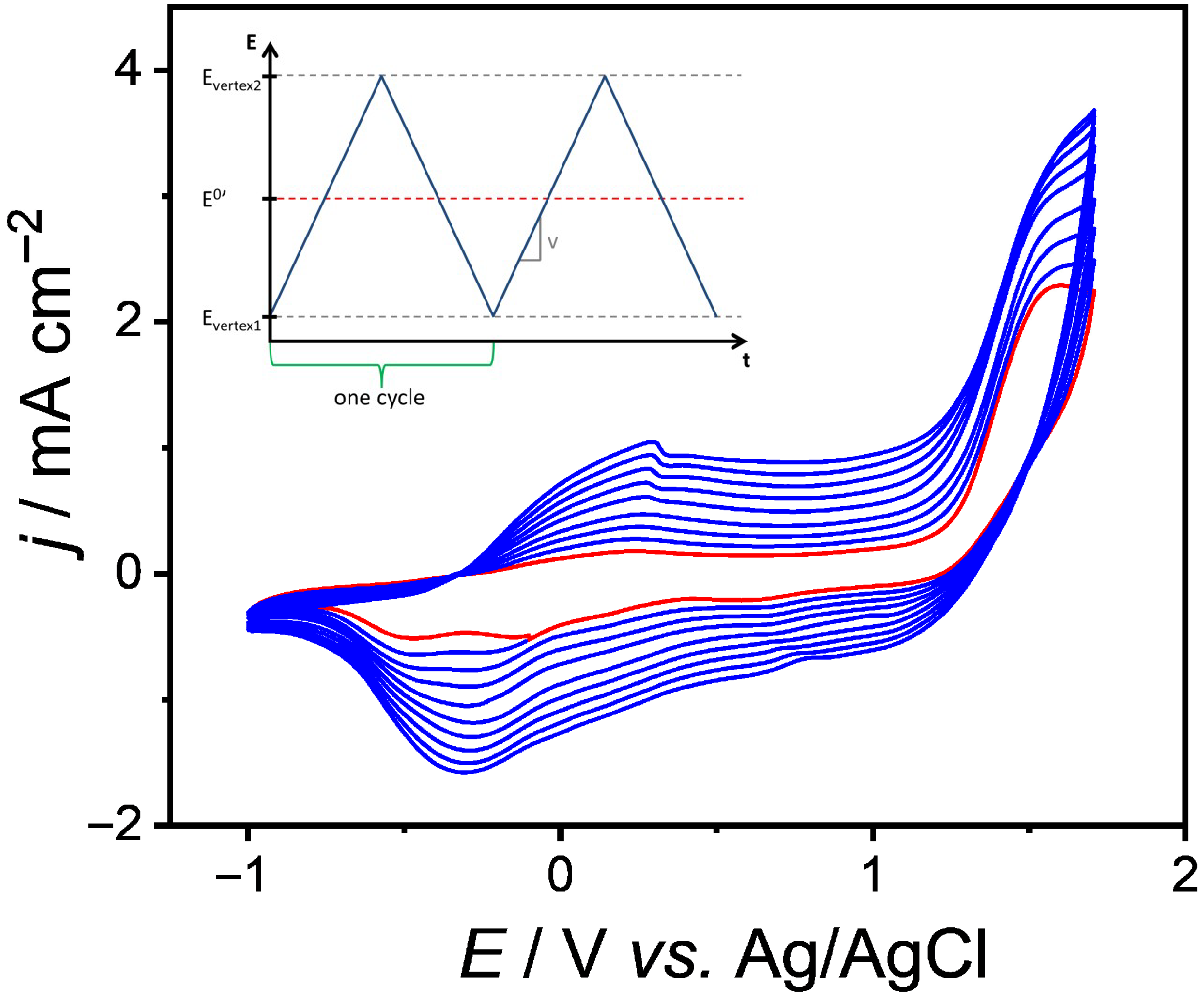
Conducting Polymer Preparation Methods: Electropolymerization







Kassahun, *et al.*, *Adv Elec Mater, e00357*, **2025**

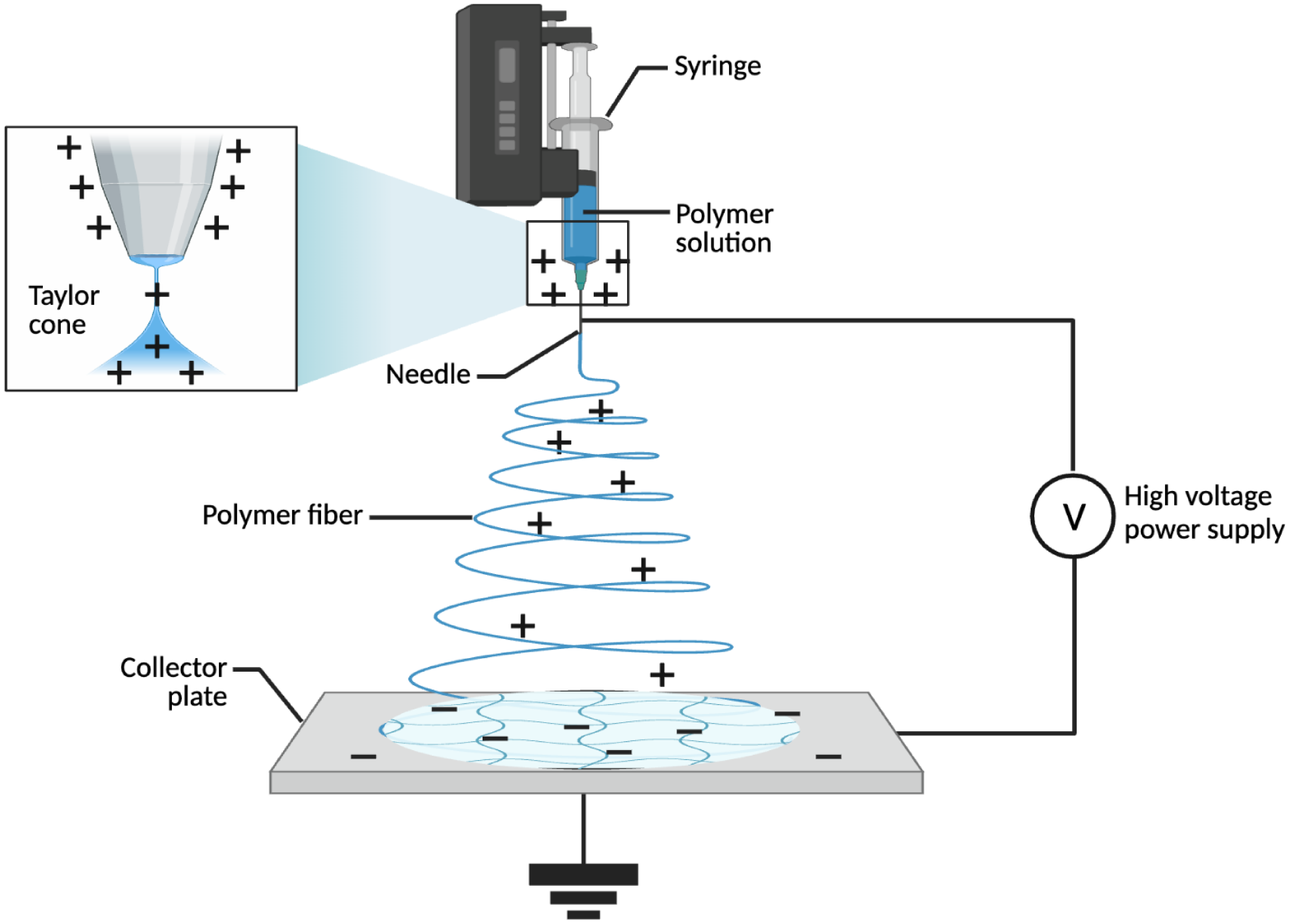


Lin, *et al.*, *Nanomater*, *15*, *21*, **2025**

Monomer is electrochemically polymerized directly onto the substrate of interest

- Applied voltage causes monomers to oxidize and react
- Diverse parameter space to tune film conductivity and morphology, but less control over molecular weight
- Highly localized and able to deposit on diverse substrates
- Ability to produce diverse composite films

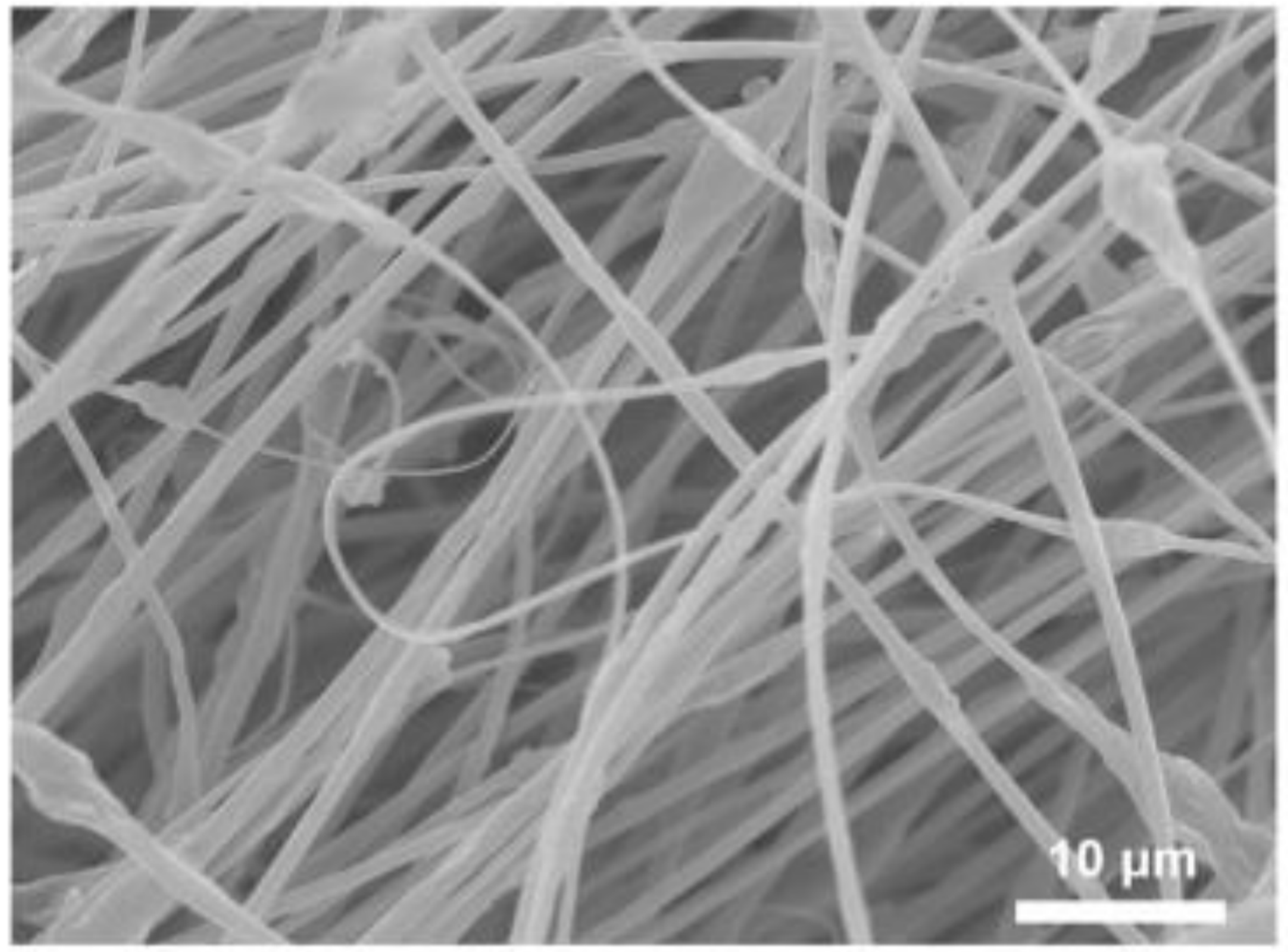
Conducting Polymer Preparation Methods: Electrospinning



Technique to produce conductive nm – µm fibers

- Strong electric field from high applied voltage overcomes surface tension to produce fiber shape
- High surface area and tunable nano-scale morphologies

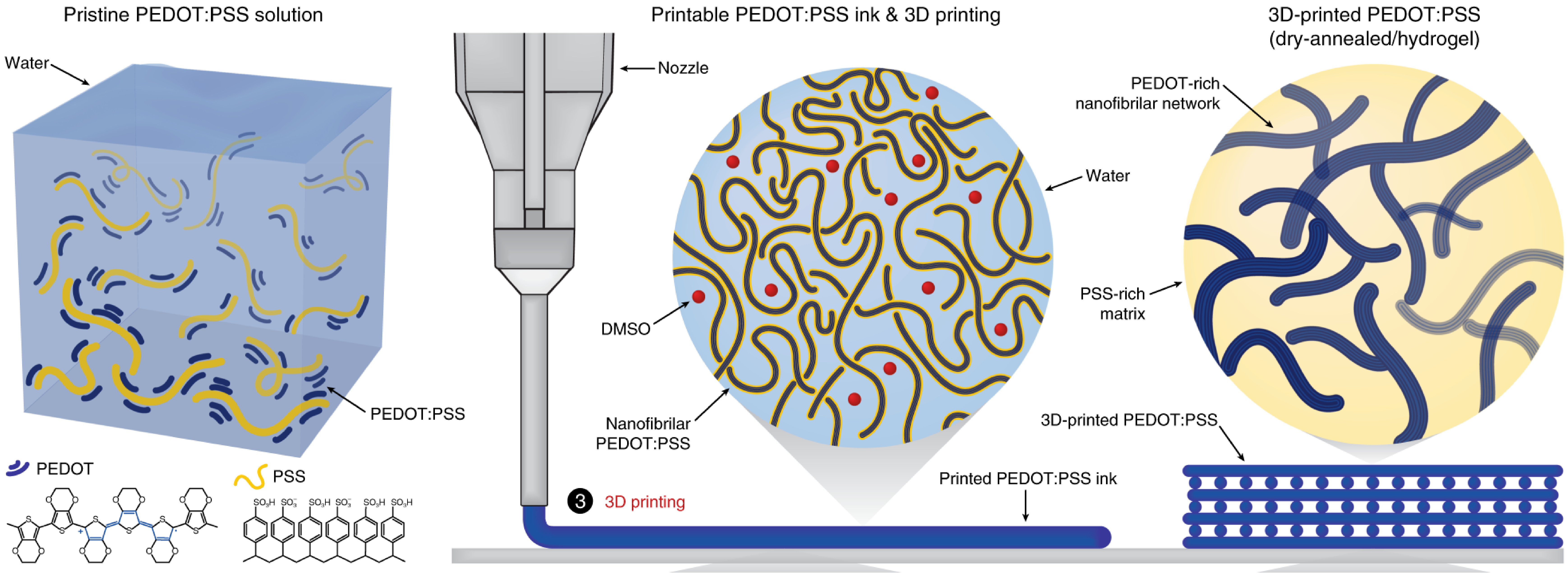
Polyacrylonitrile/PEDOT:PSS fibrils

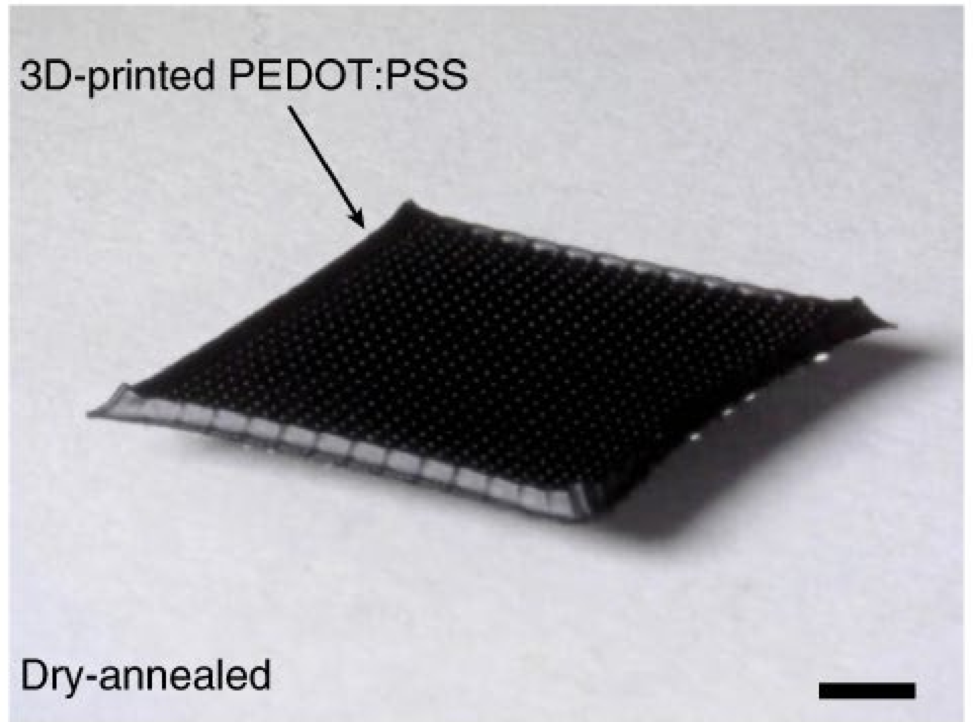


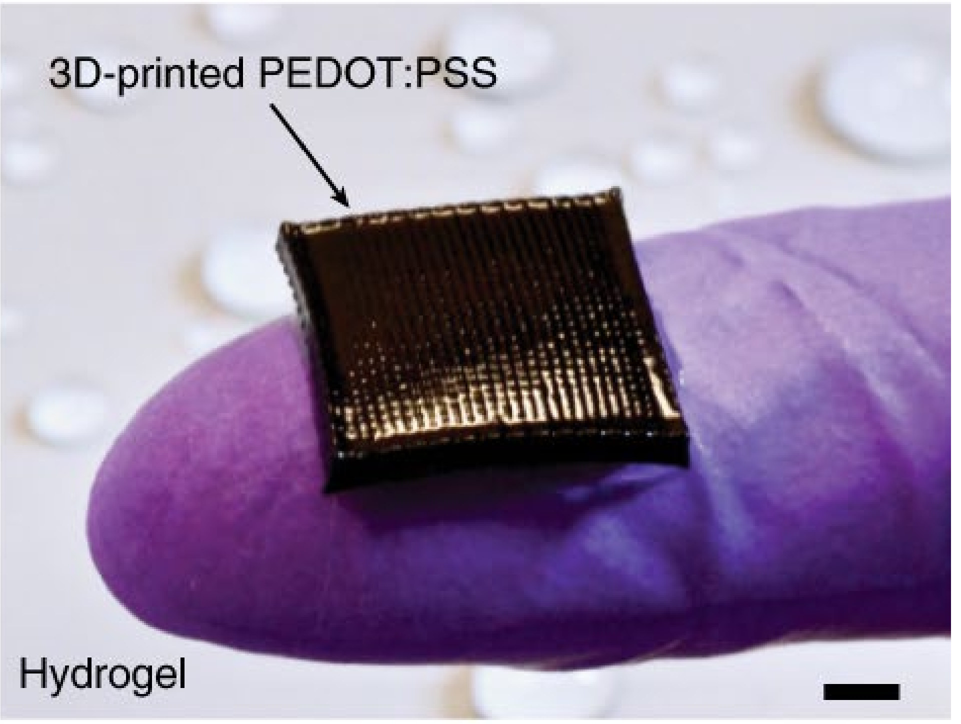
870 ± 240 nm

Barbosa, *et al.*, *Int J Mol Sci, 24, 17,* **2023**

Conducting Polymer Preparation Methods: Printing





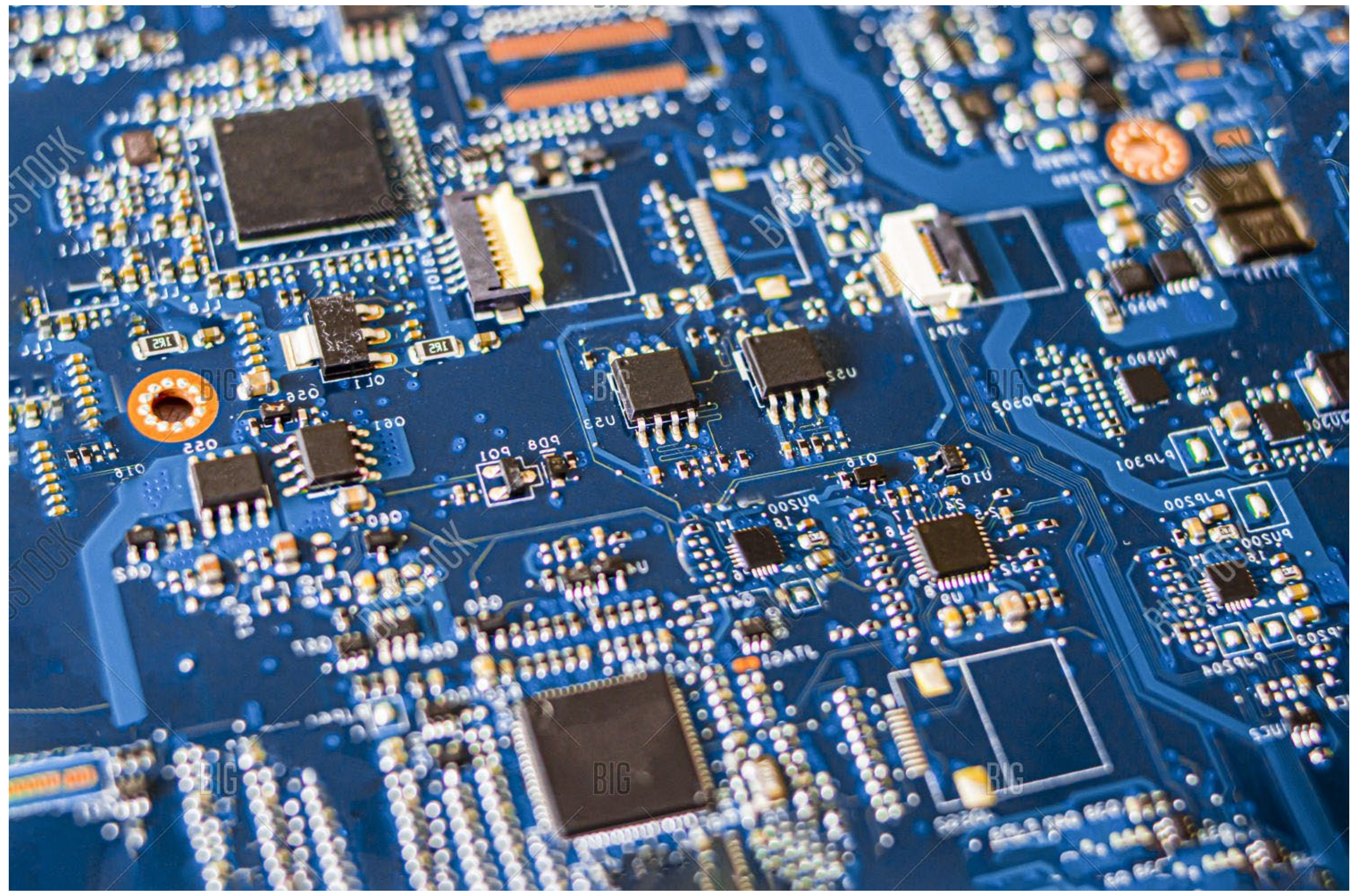


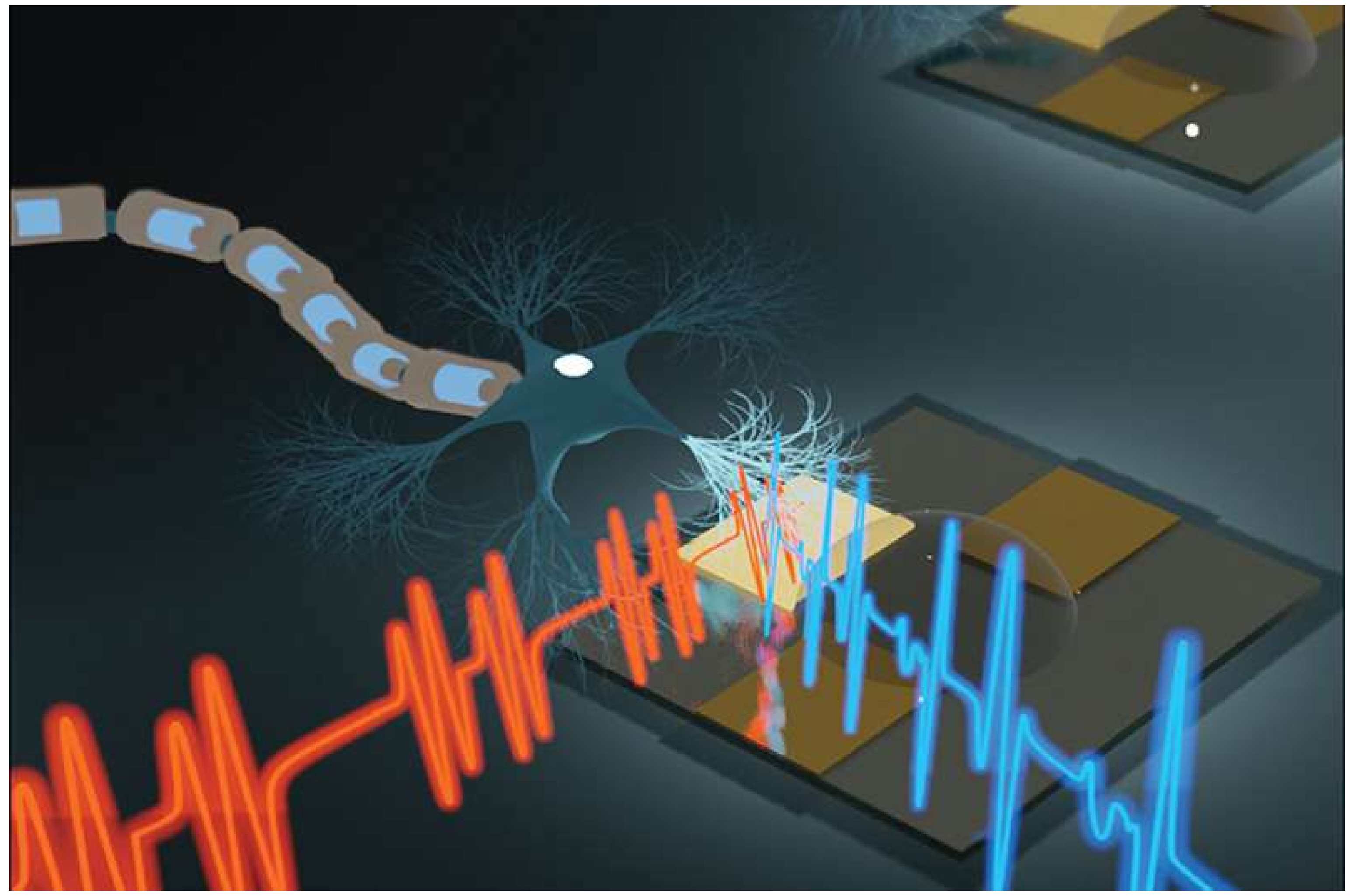
Additive Manufacturing and Printing

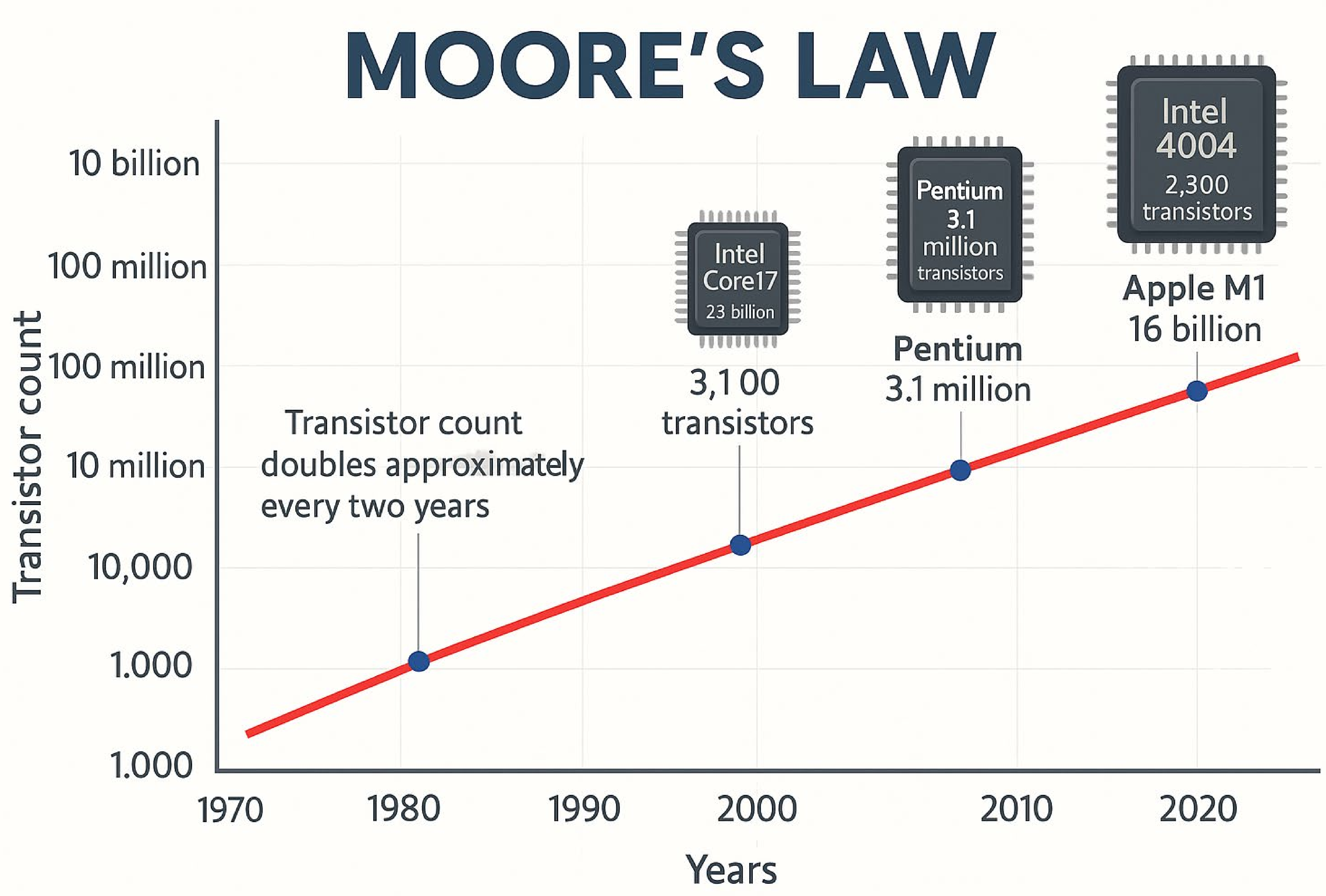
- Polymer solutions can be printed while maintaining high conductivity
- Able to produce high resolution (tens of μms) and high aspect ratio structures
- Less complex process flows

Yuk, et al., Nat Comm, 11, **2020**

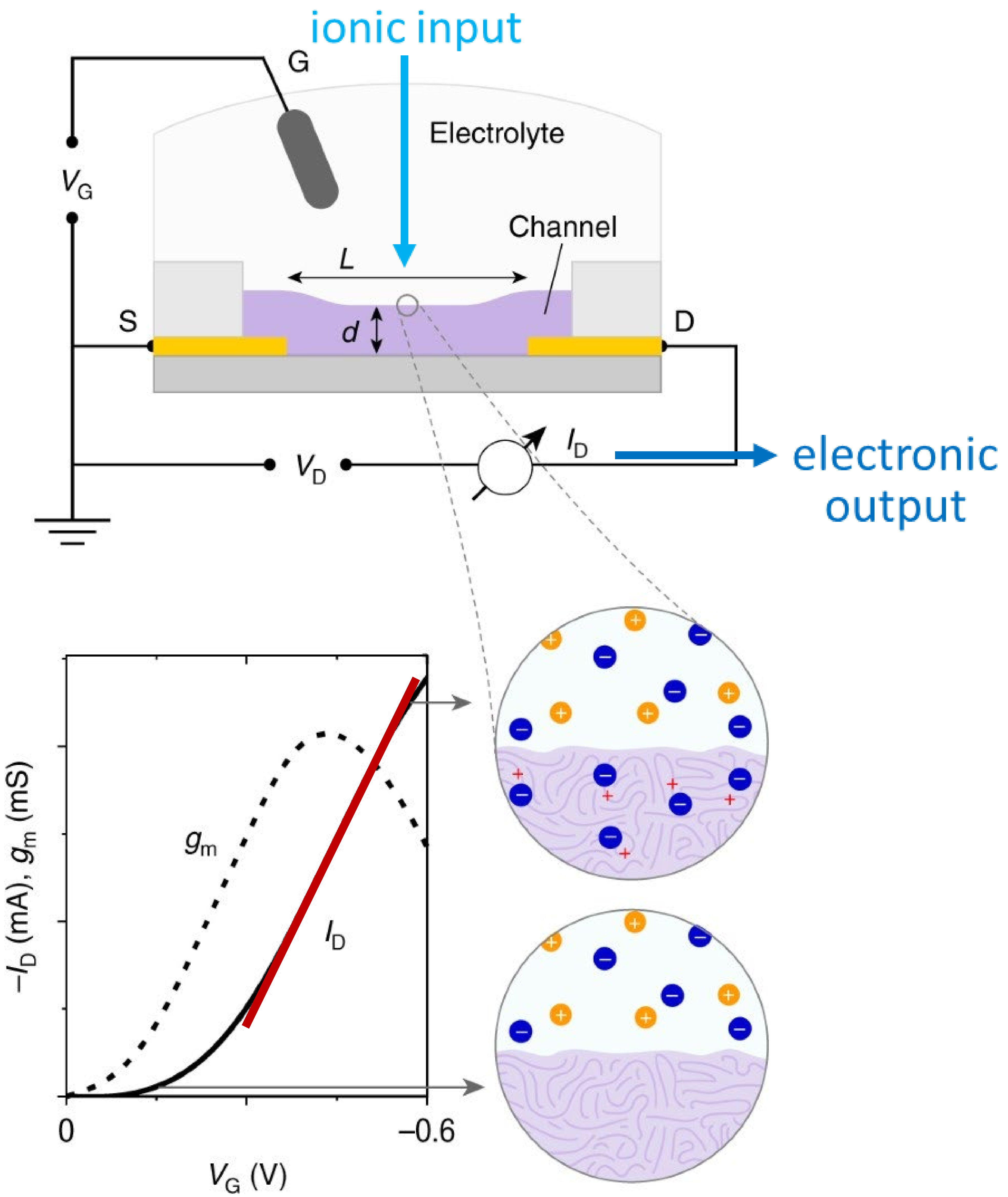
Transistors: Basic Building Blocks of Modern Electronics







Organic Electrochemical Transistors (OECTs)



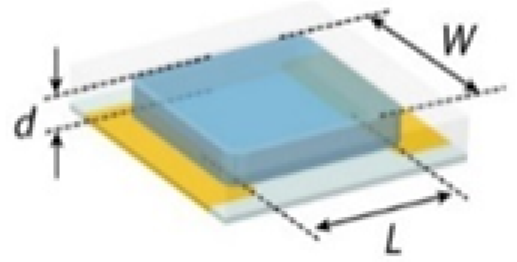
Transfer curves quantify the **amplification power** of a device (g_m):

$$g_m = \frac{\partial I_D}{\partial V_G}$$

Thickness plays a critical role in g_m because of C*

$$g_m = \frac{Wd}{L} \cdot \mu \cdot C^* \cdot (V_{th} - V_G)$$

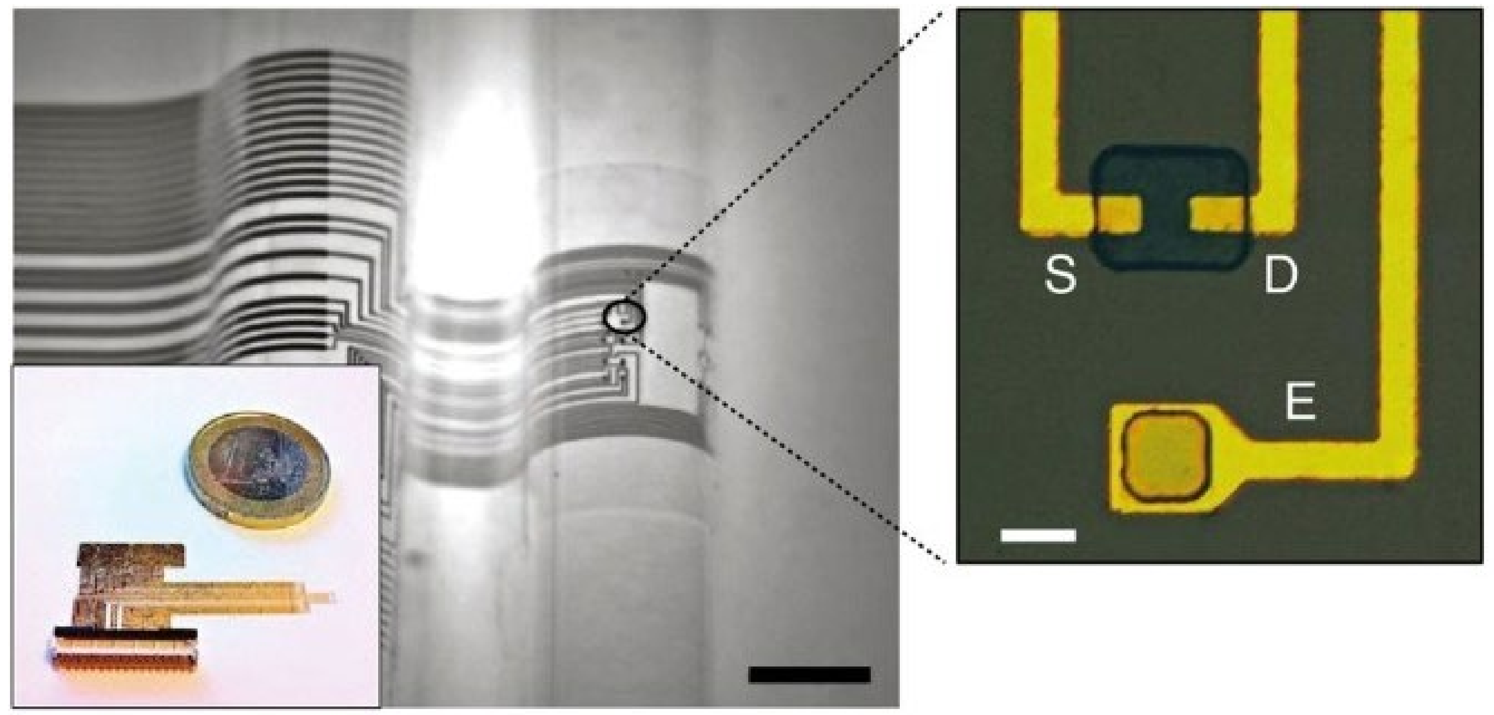
Geometry



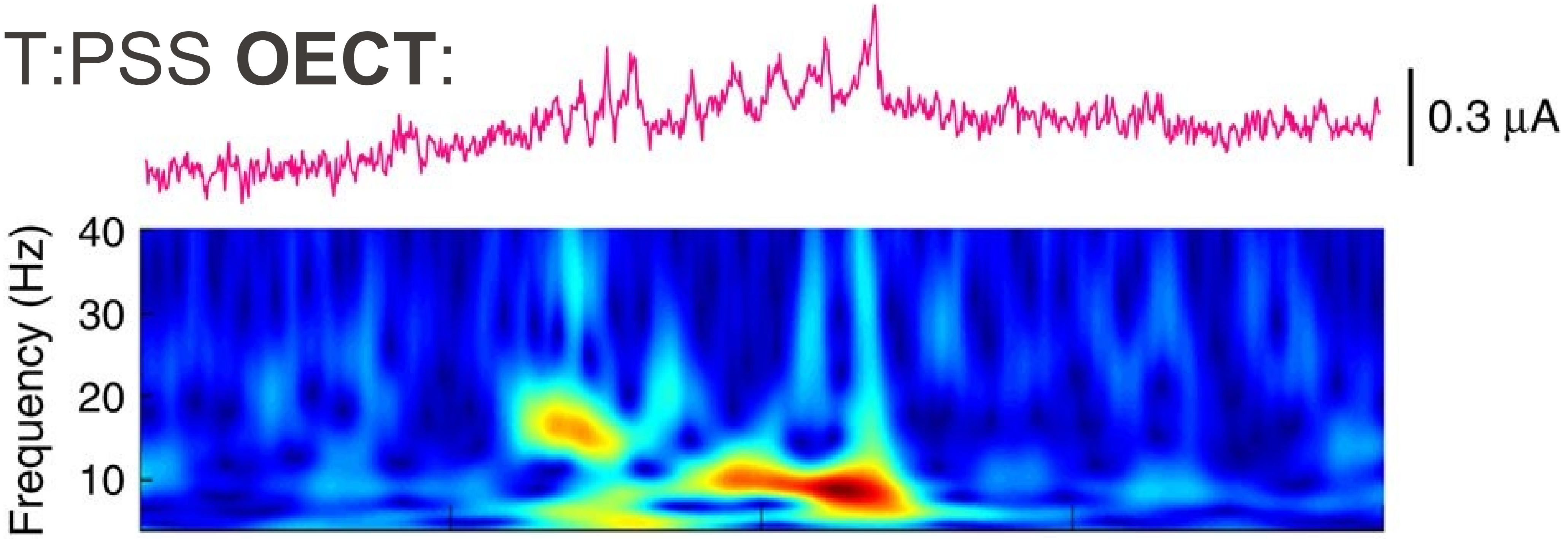
Bias

Materials figure of merit *(for transconductance)*

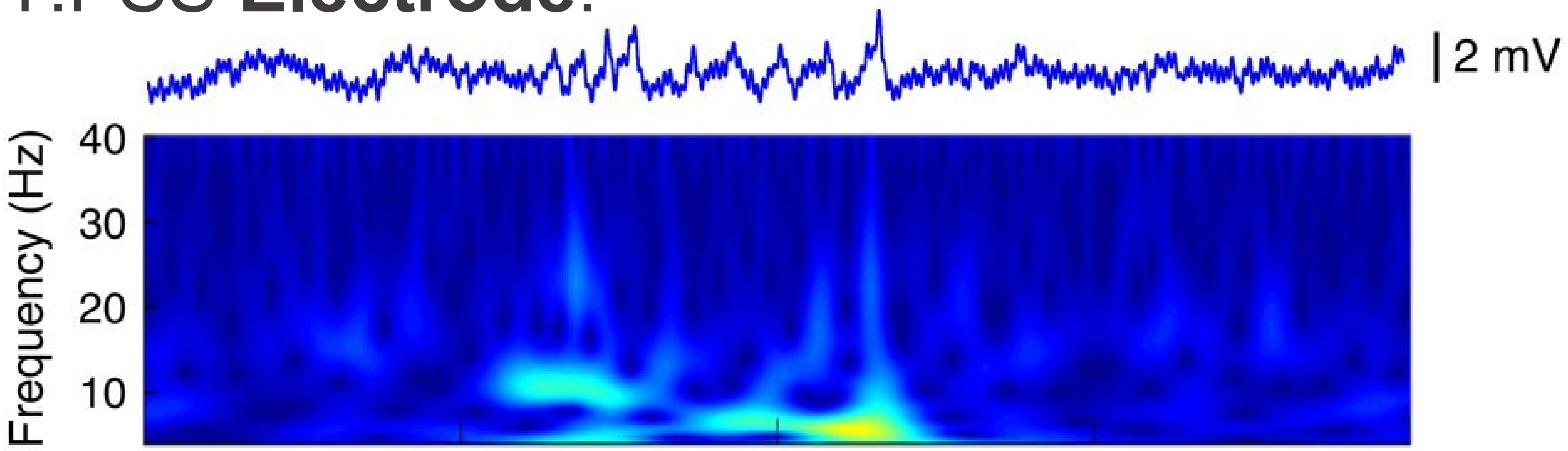
Signal Acquisition is Improved using OECTs



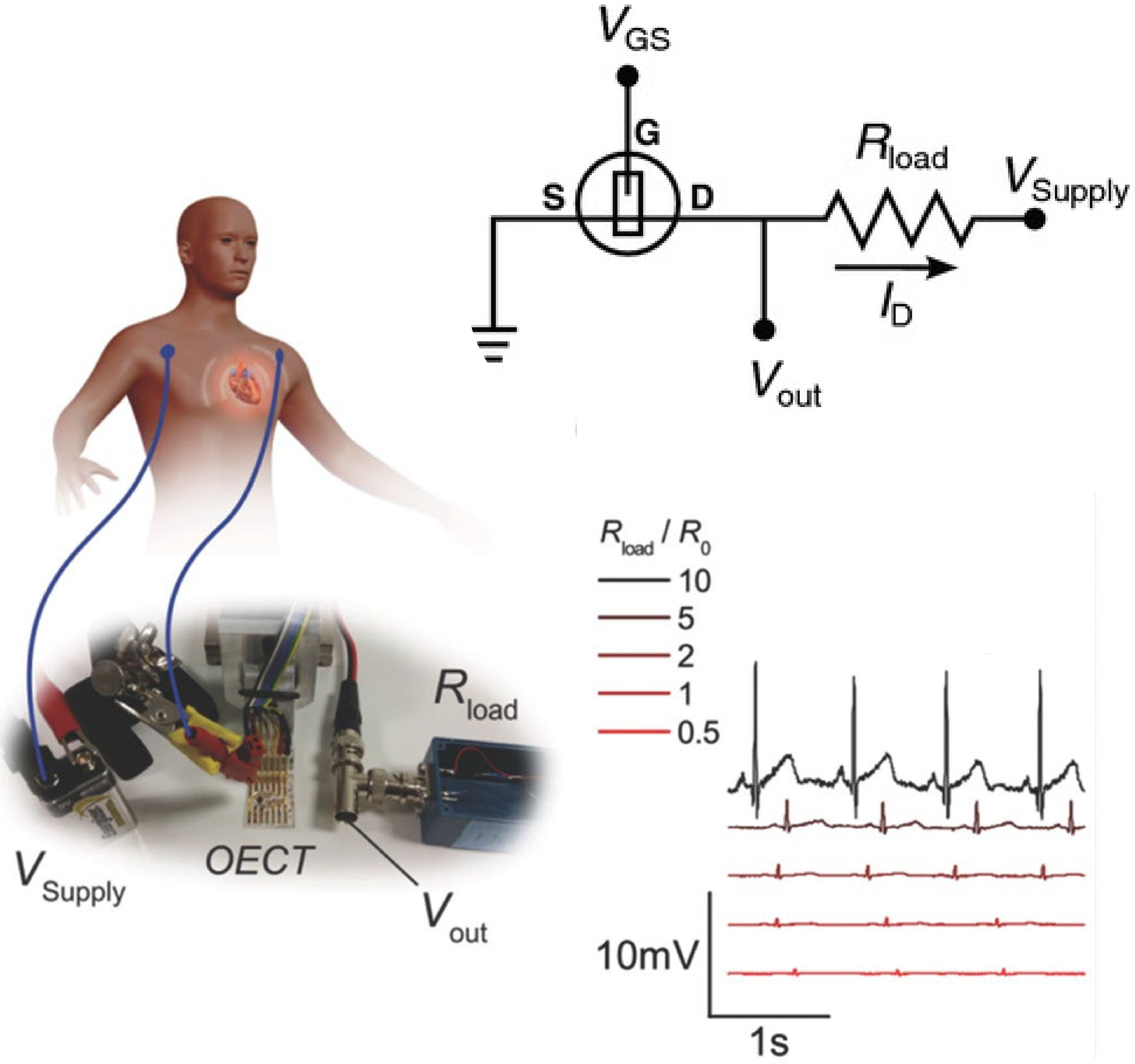
PEDOT:PSS **OECT**:



PEDOT:PSS **Electrode**:



Khodagoly, *et al., Nat Comm, 4,* **2013**

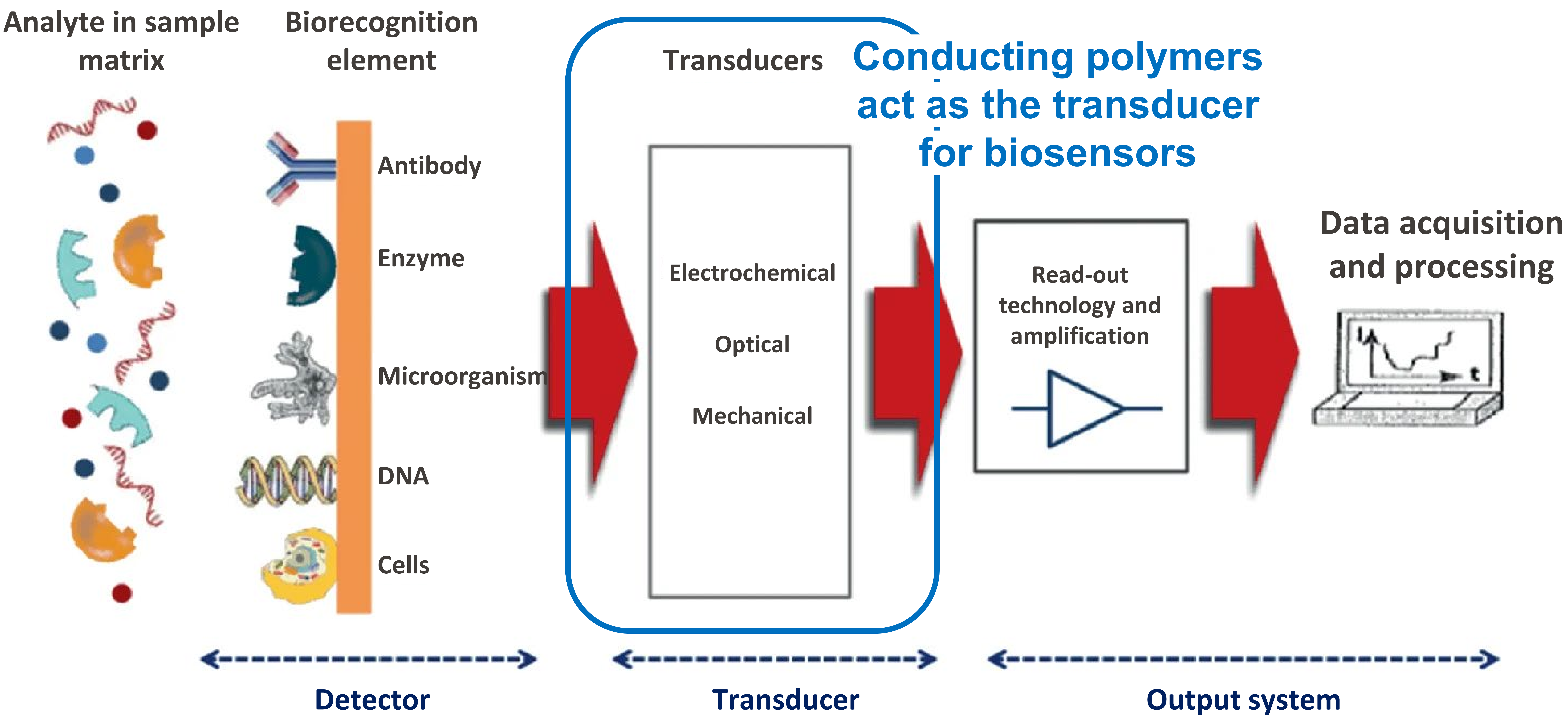


Brandlein, *et al., Adv Sci, 4, 1,* **2016**

Key Takeaways

- Organic conducting polymers have diverse applications and methods of preparation to be useful in these applications
- Conducting polymers can be made compatible with traditional microfabrication (with some creativity!)
- Organic electrochemical transistors (OECTs) offer high amplification power to measure small biological signals

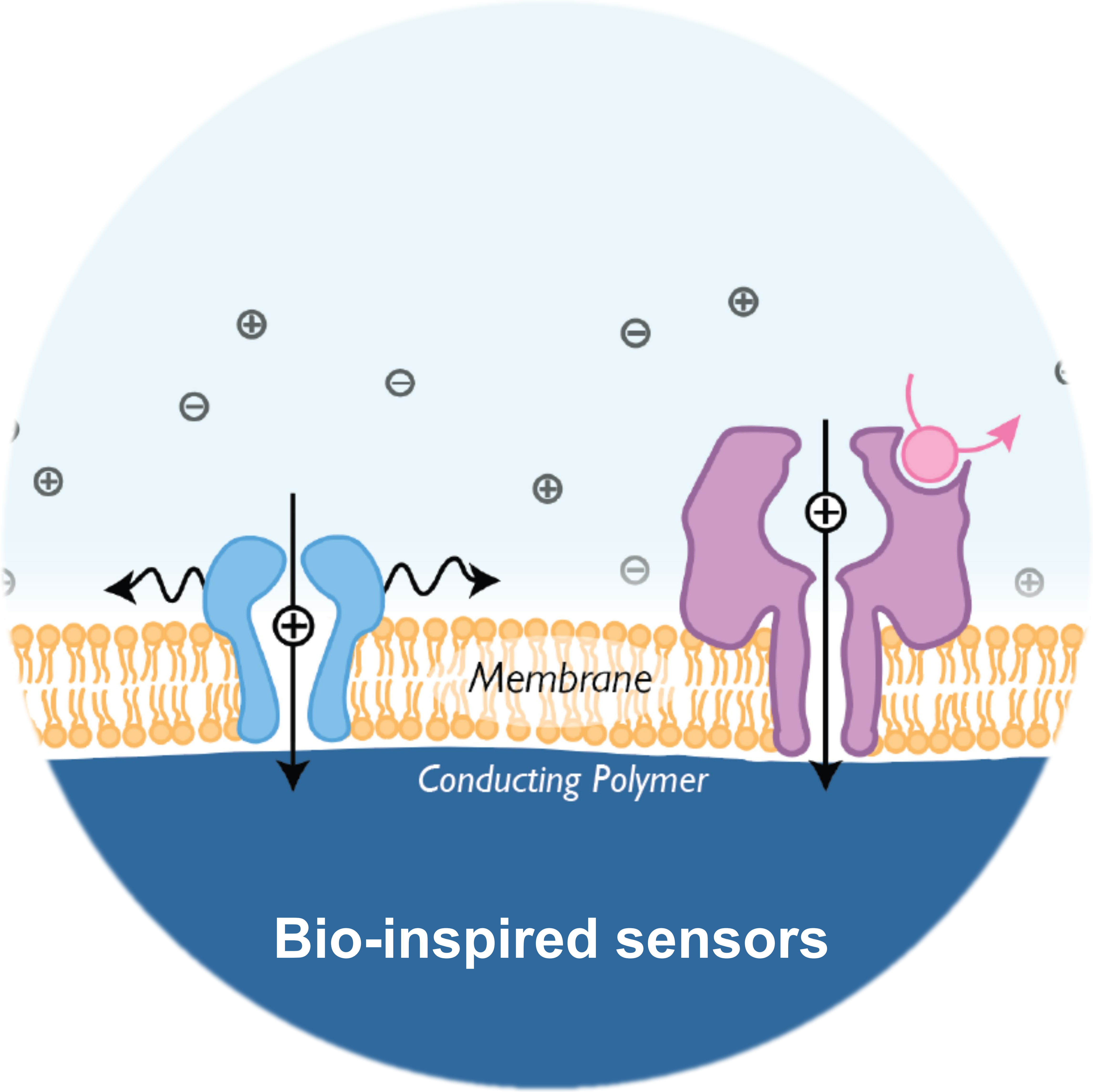
Organic Conducting Polymers in Biosensing



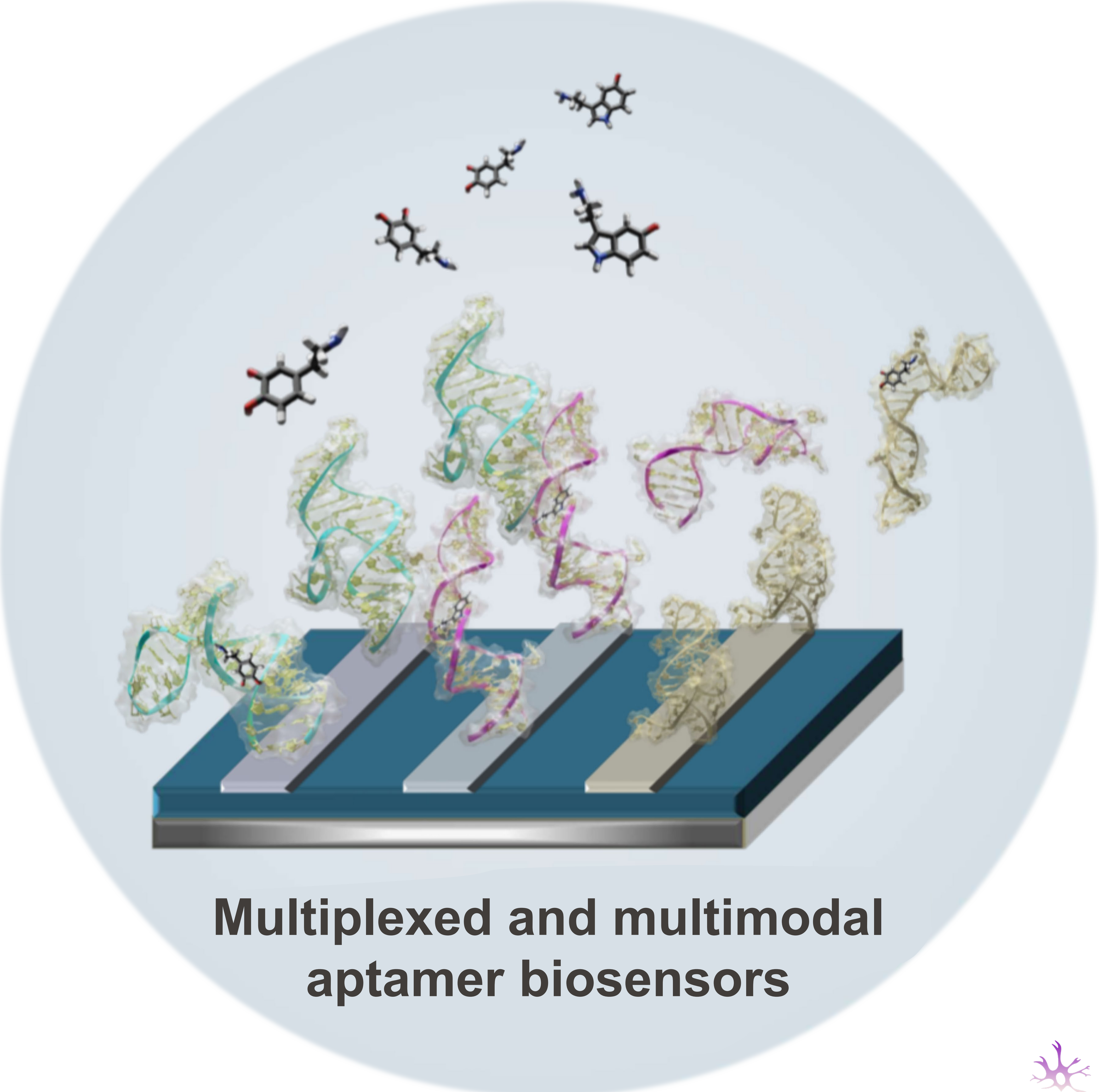
Conducting polymers act as the transducer for biosensors

Bag & Mandal, *Smart Innovation, Systems, Technologies, 322*, **2023**

Organic Conducting Polymers in Biosensing

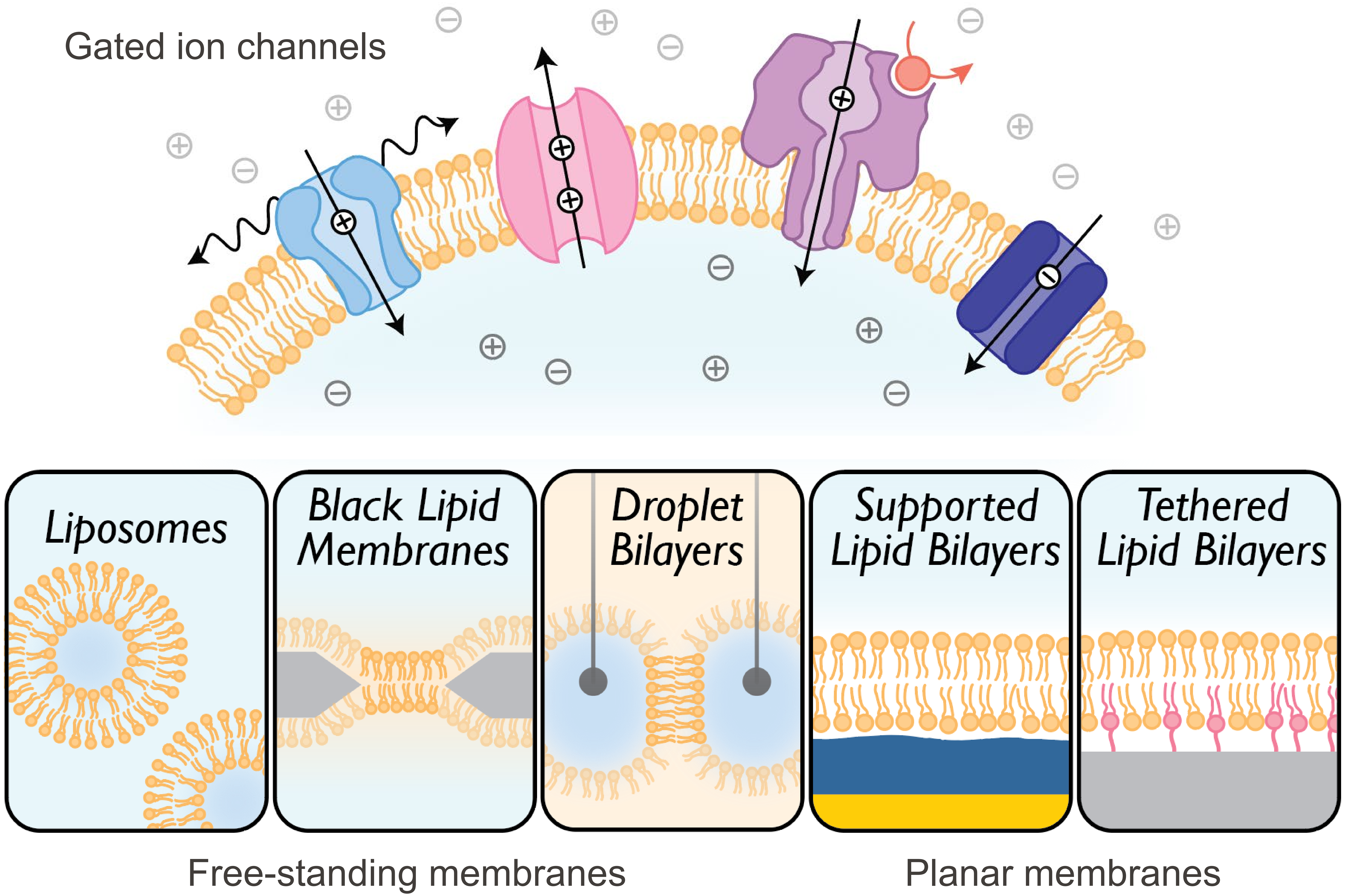


Bio-inspired sensors

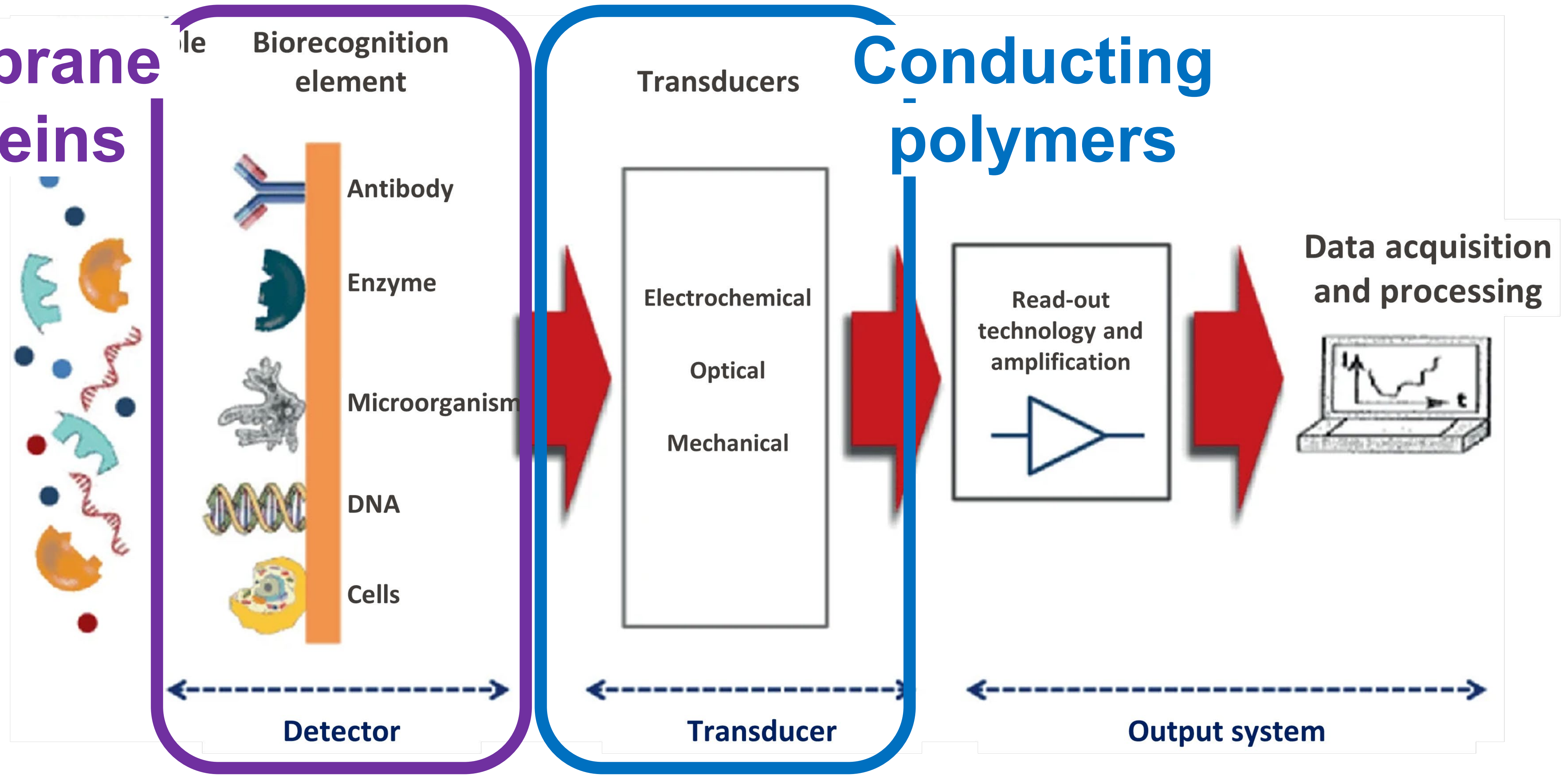


Multiplexed and multimodal aptamer biosensors

Living Cells are the Ultimate Biosensors



Membrane Proteins Can Drive Sensor Response



Membrane proteins

Conducting polymers

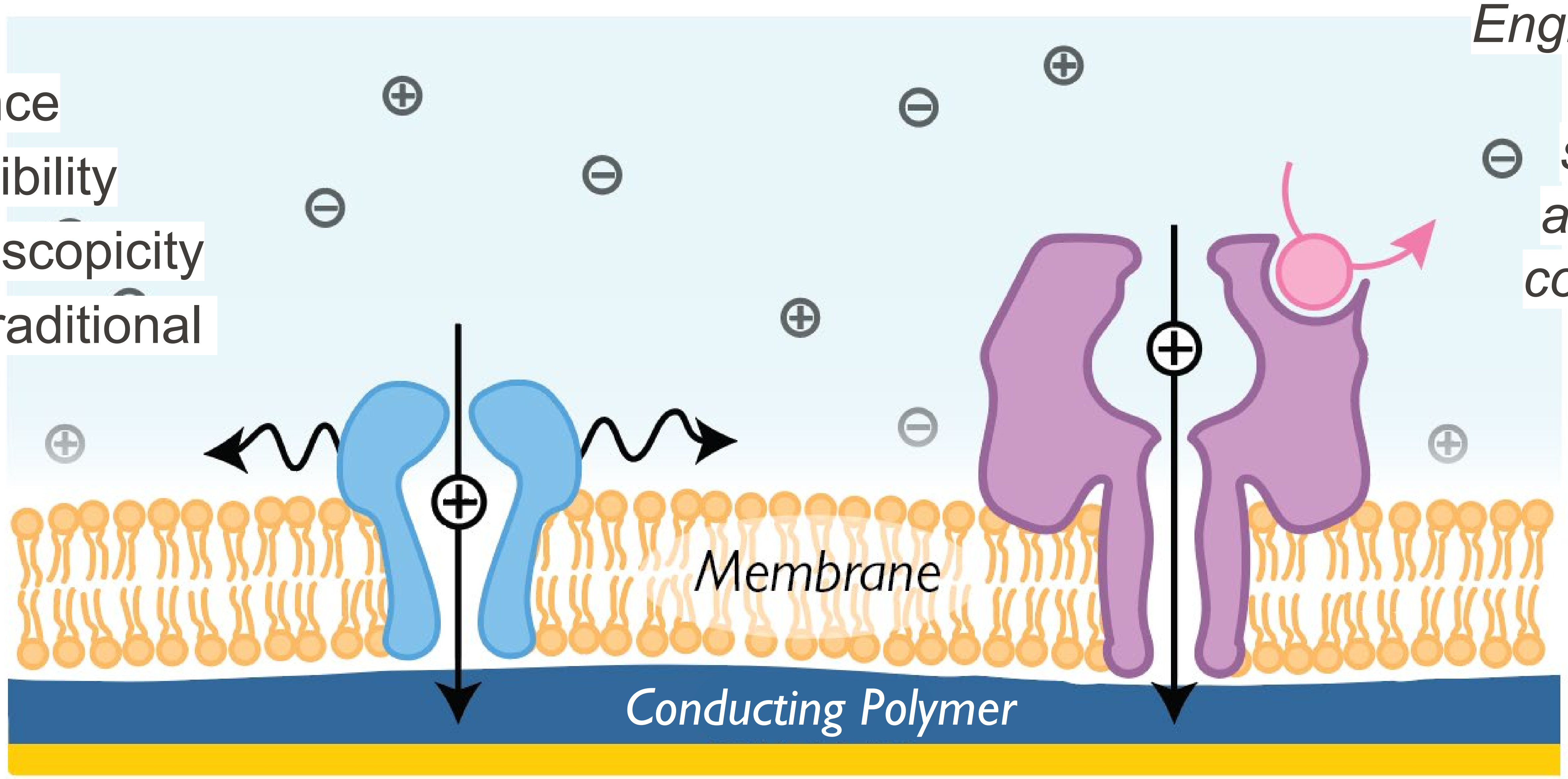
Why put these pieces together?

Low impedance

High biocompatibility

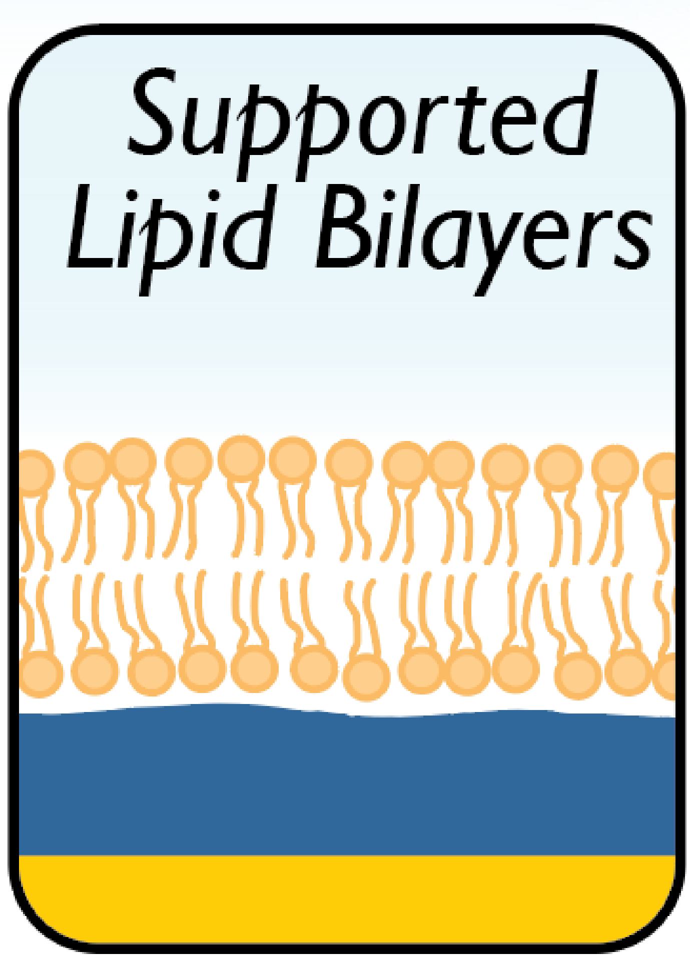
Softness and hygroscopicity

Compatibility with traditional methods



Engineering the interface between sensing elements and organic mixed-conducting polymers

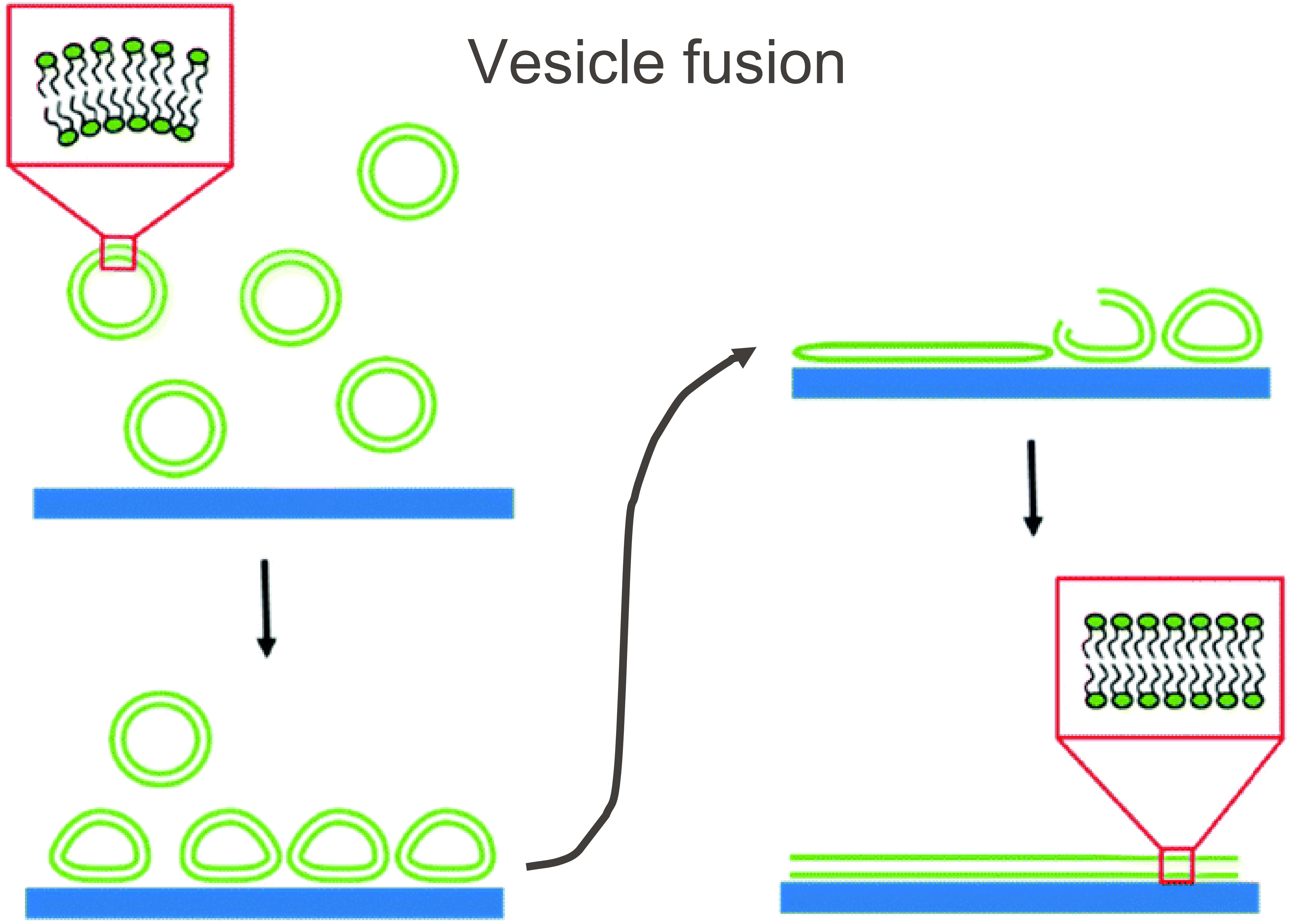
Supported Lipid Bilayers (SLBs) on Conducting Polymers



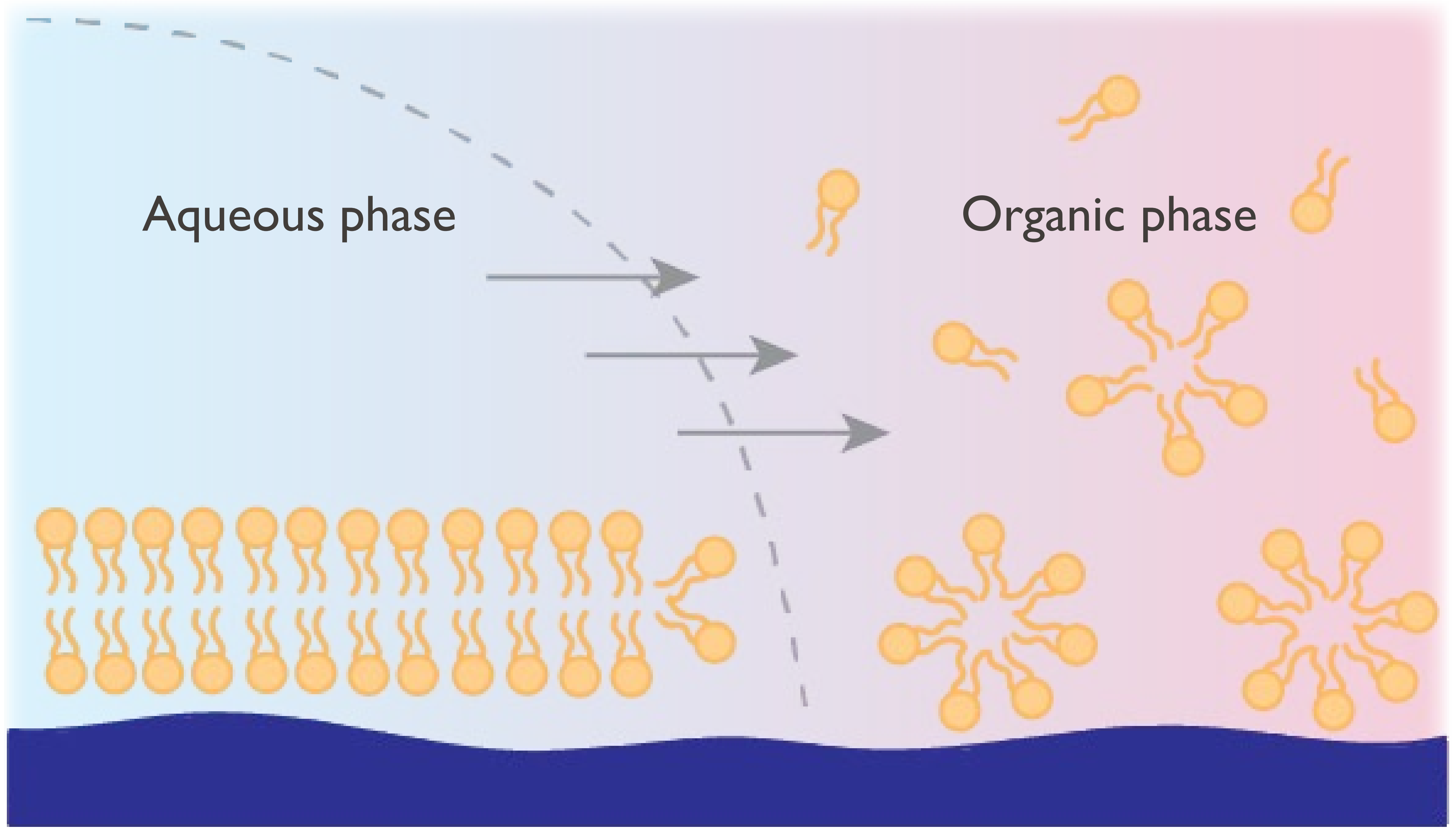
Factors that determine successful bilayer formation:

- Hydrophilicity
- Hygroscopicity
- Surface roughness
- Surface planarity
- Deposition technique

Vesicle fusion

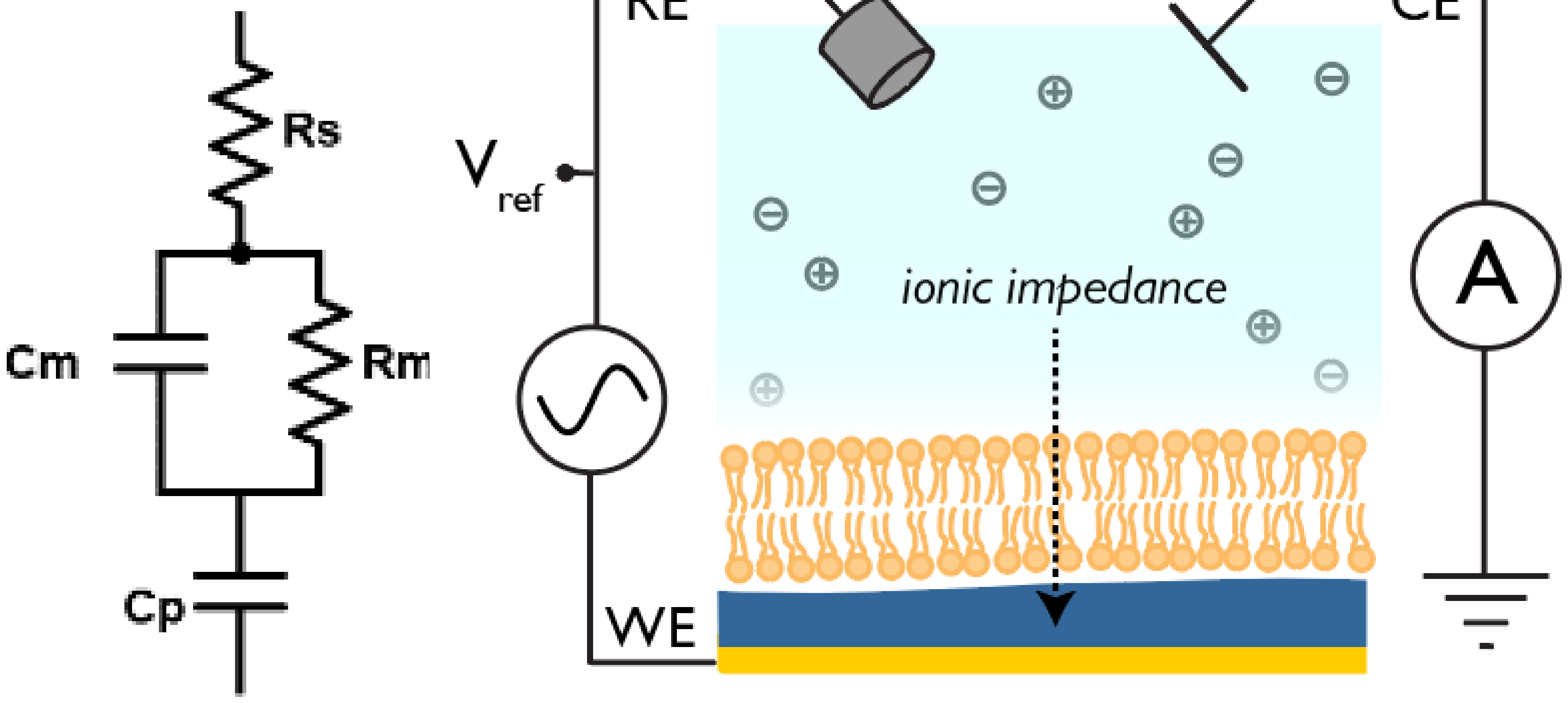


Solvent-assisted bilayer formation



Schafer, *et al., ACS Appl Mat & Inter, 15, 20,* **2023**

Impedance of SLBs as a Measure of Bilayer Integrity

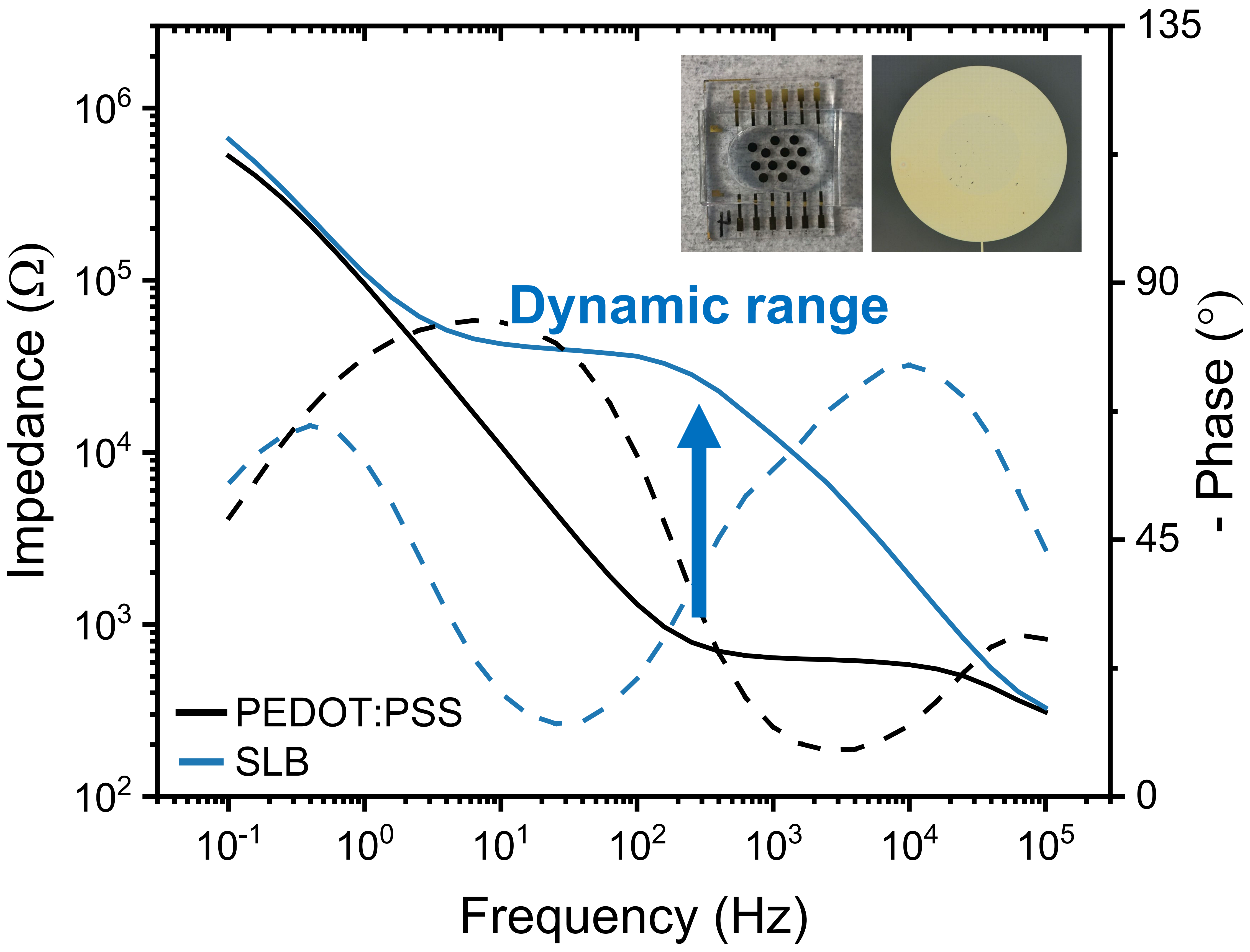


R_s = electrolyte solution resistance

C_p = double layer capacitance

R_m = membrane resistance

C_m = membrane capacitance

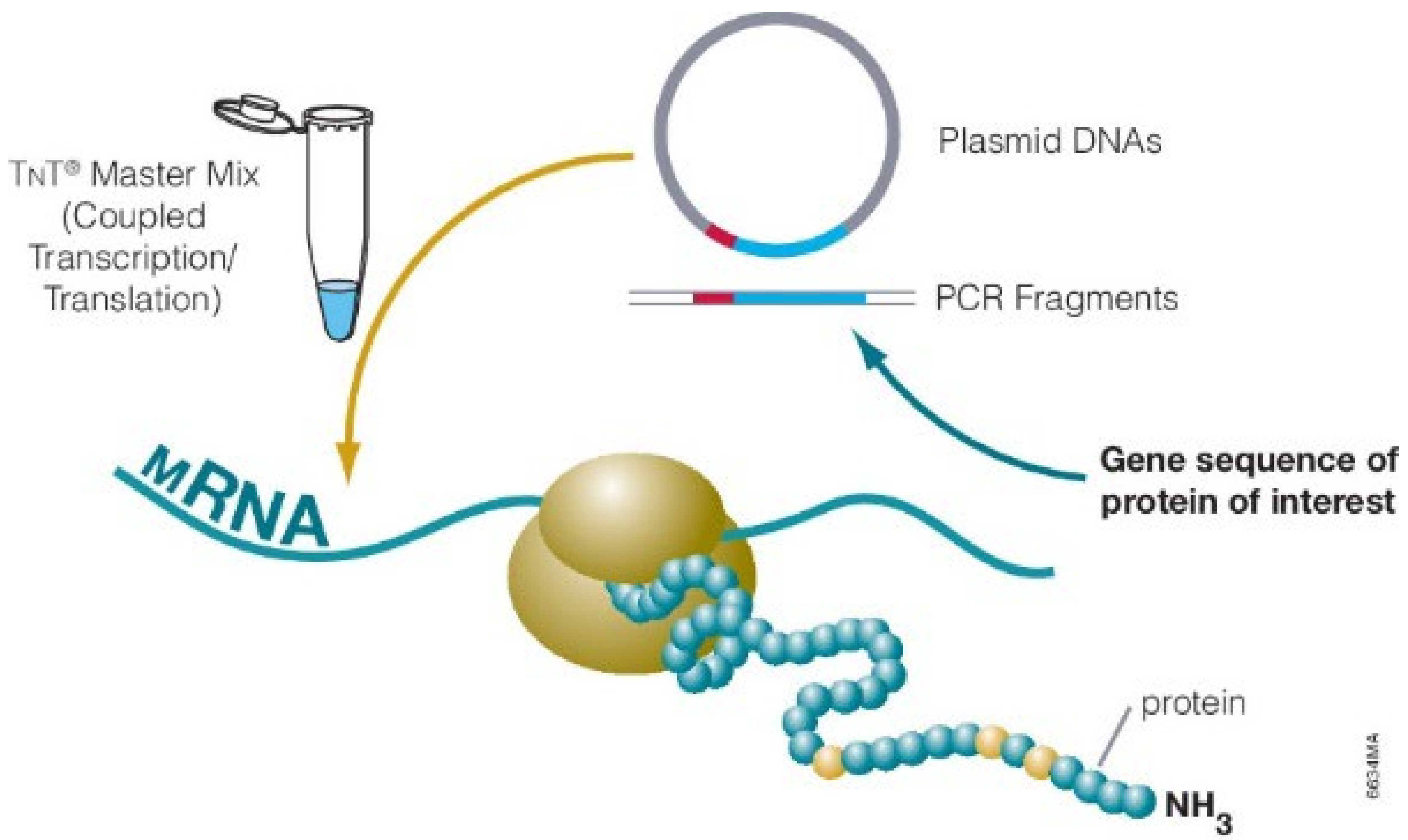


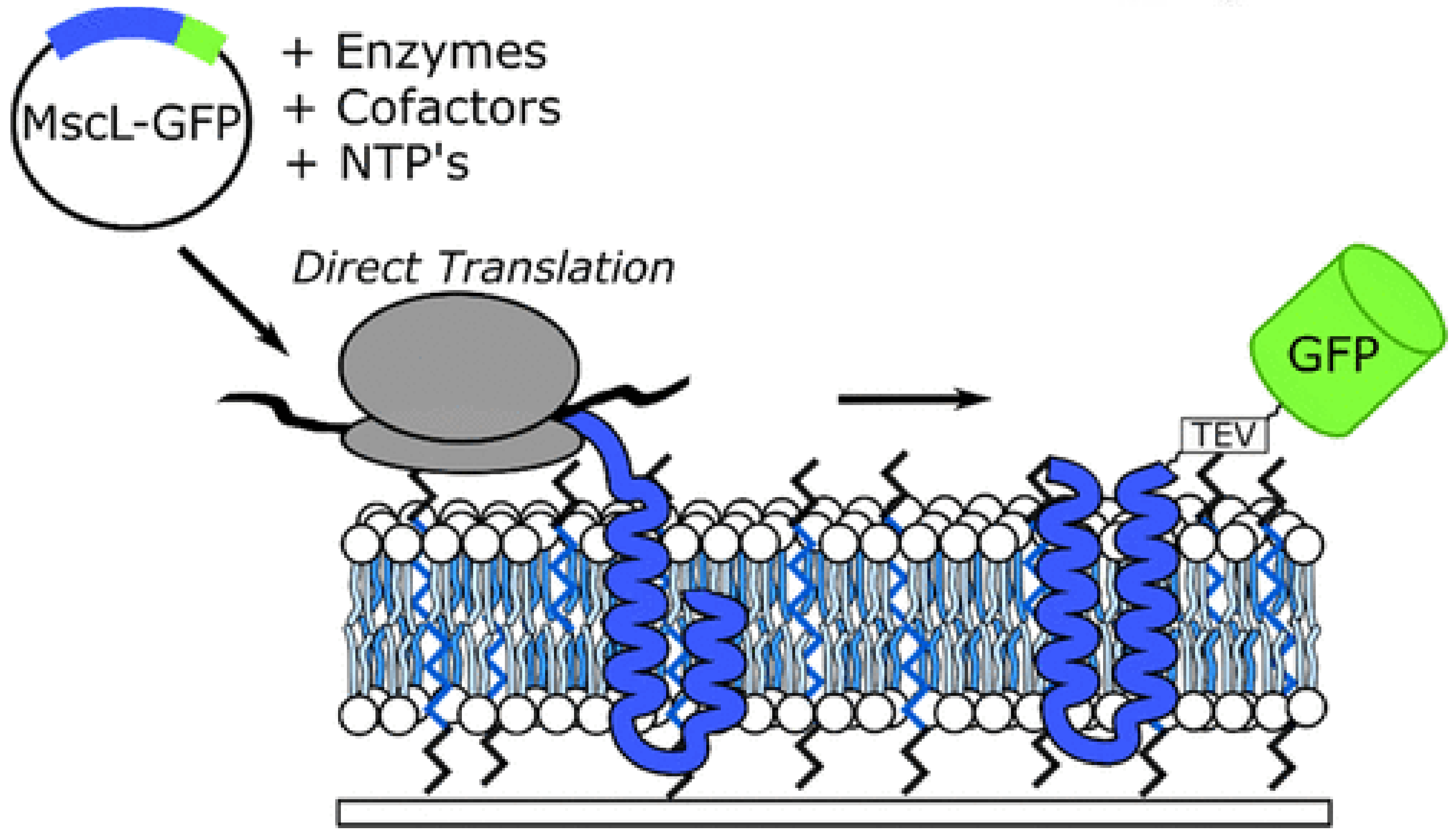
Membrane electrical sealing determines dynamic range and sensing performance

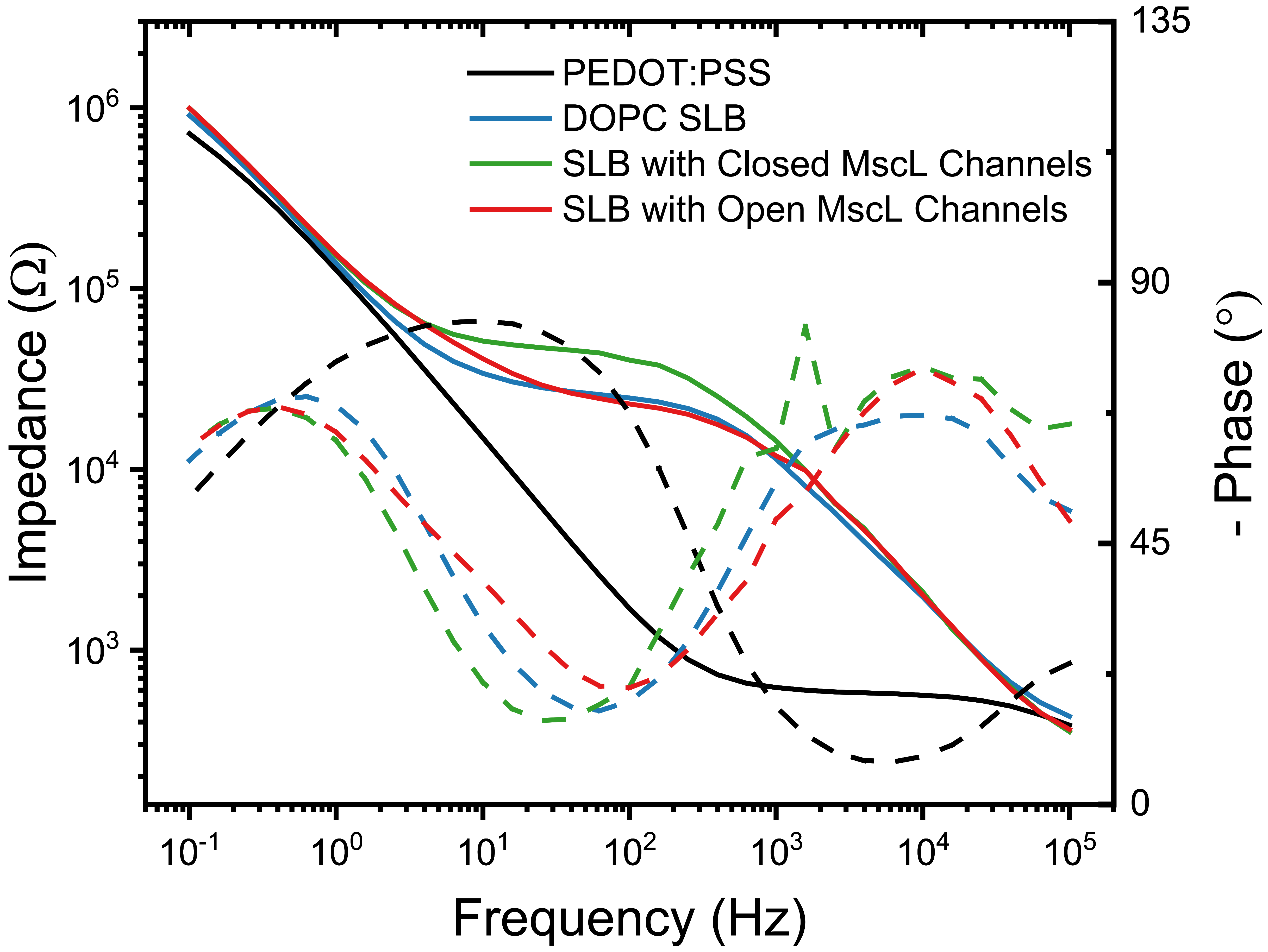
Schafer, *et al., ACS Appl Mat & Inter, 15, 20,* **2023**

Impedimetric Detection of Membrane Protein Activity

Cell-free expression







Manzer, *et al., ACS Appl Bio Mat, 4, 4,* **2021**

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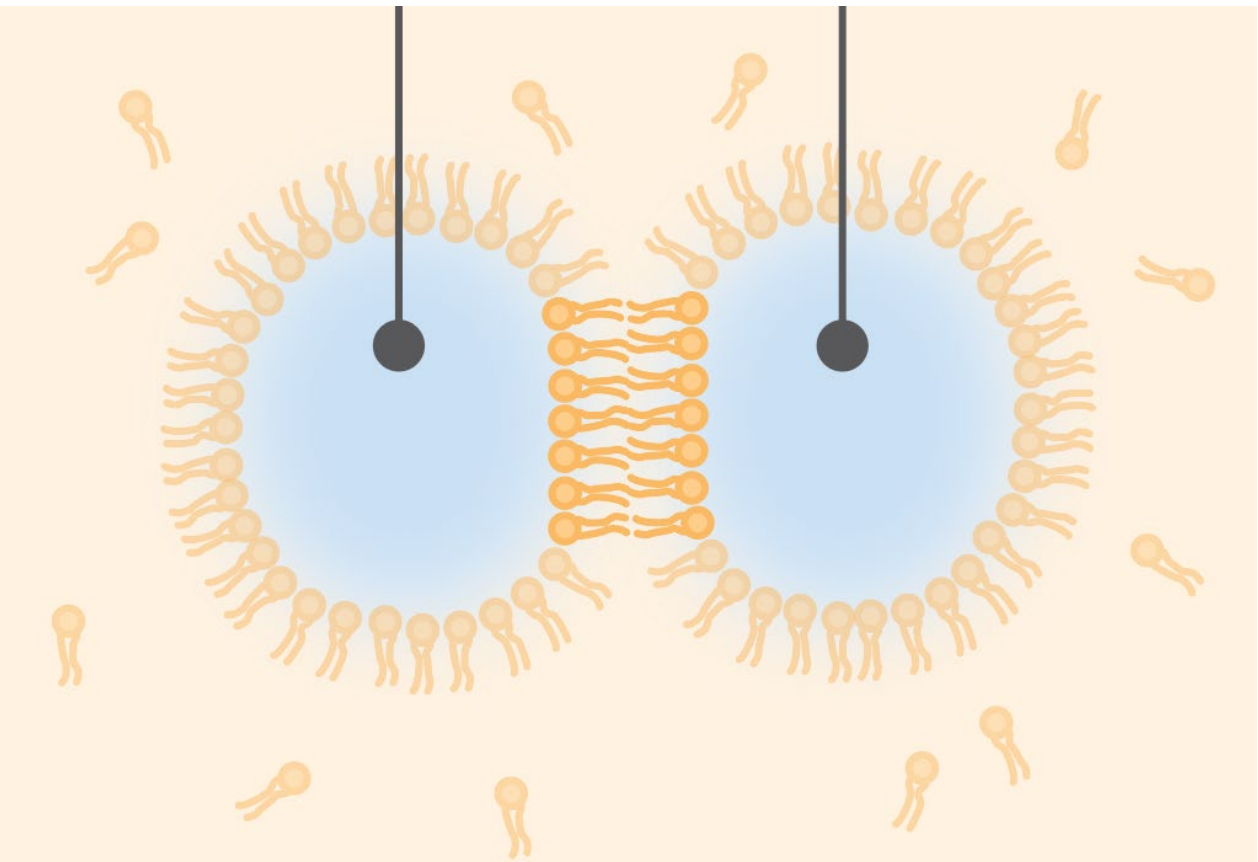
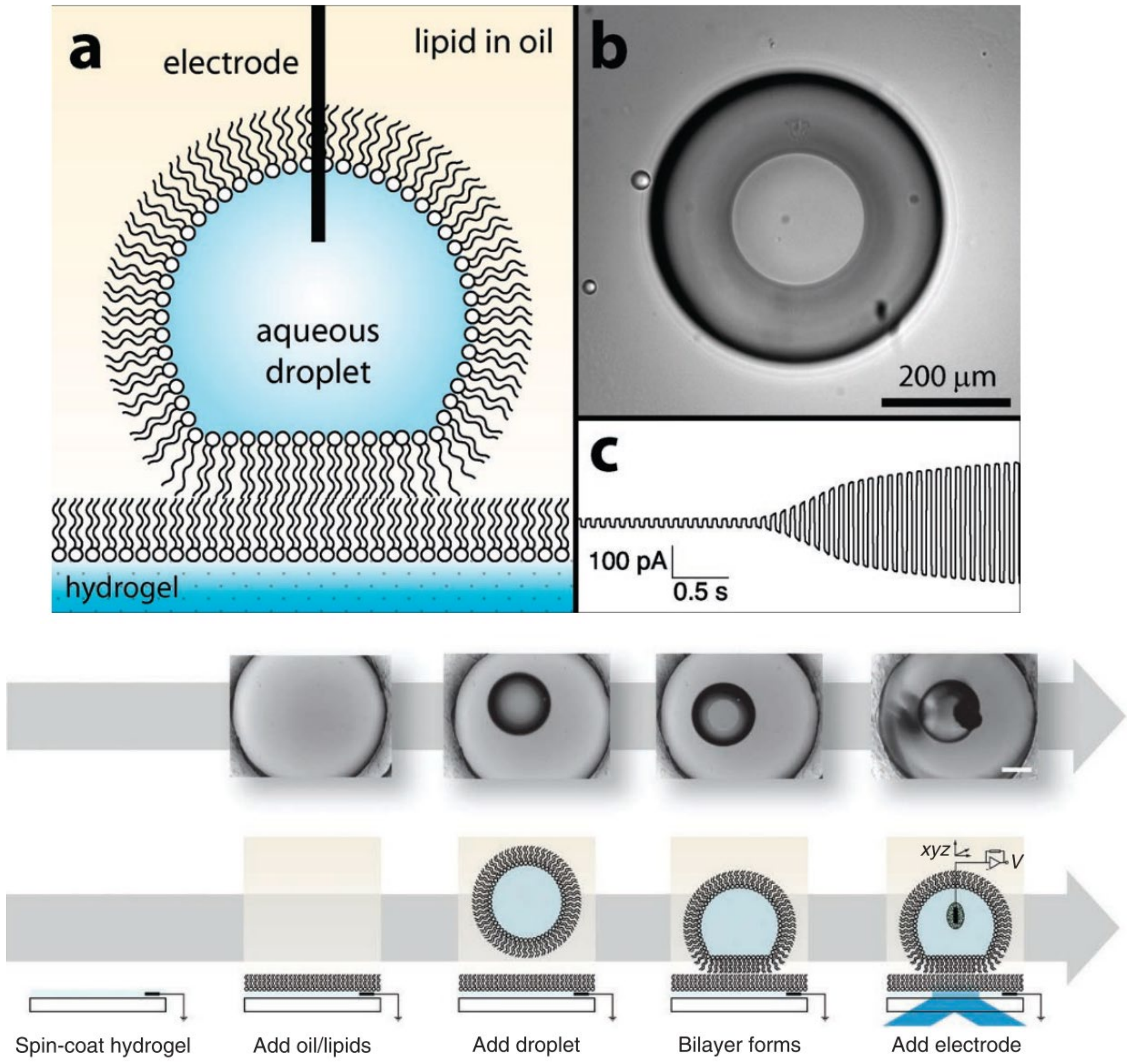
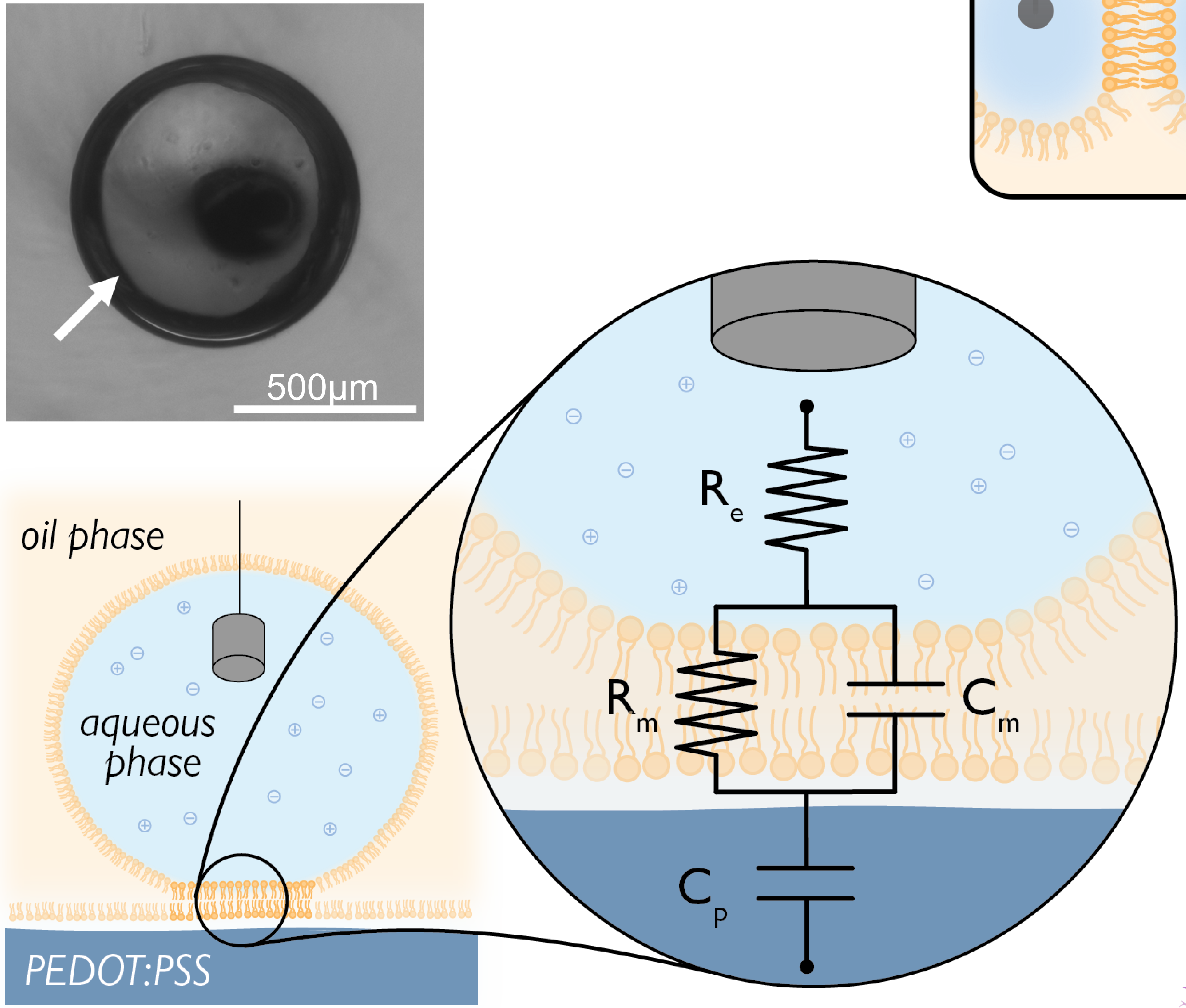
Decoupling Membrane Properties from the Interface

Droplet interface bilayers



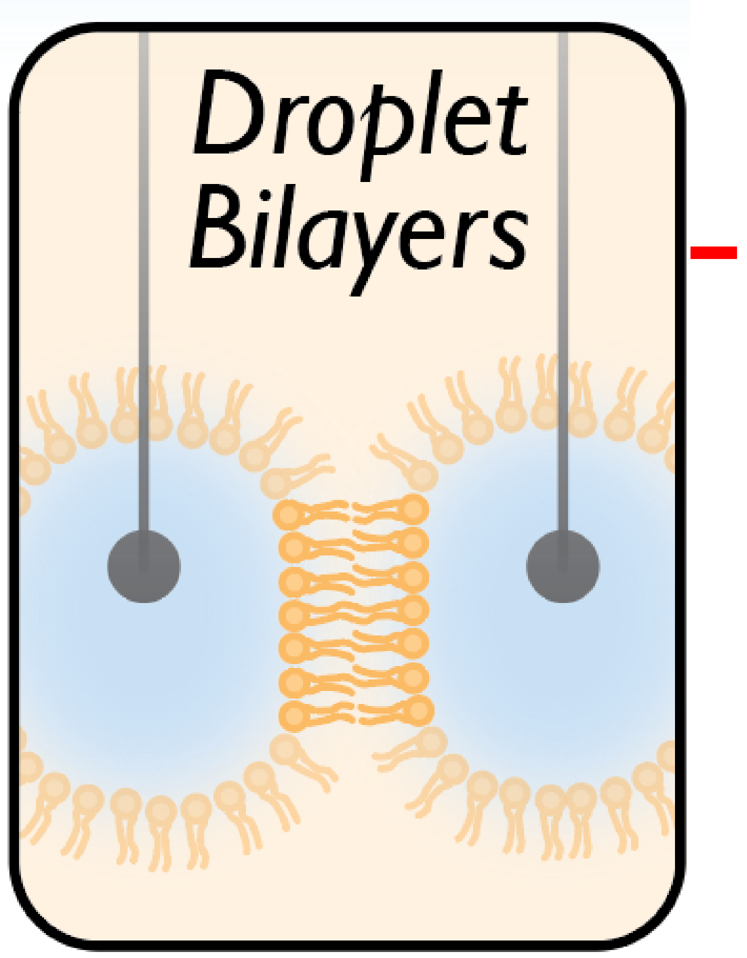
Droplet hydrogel bilayers

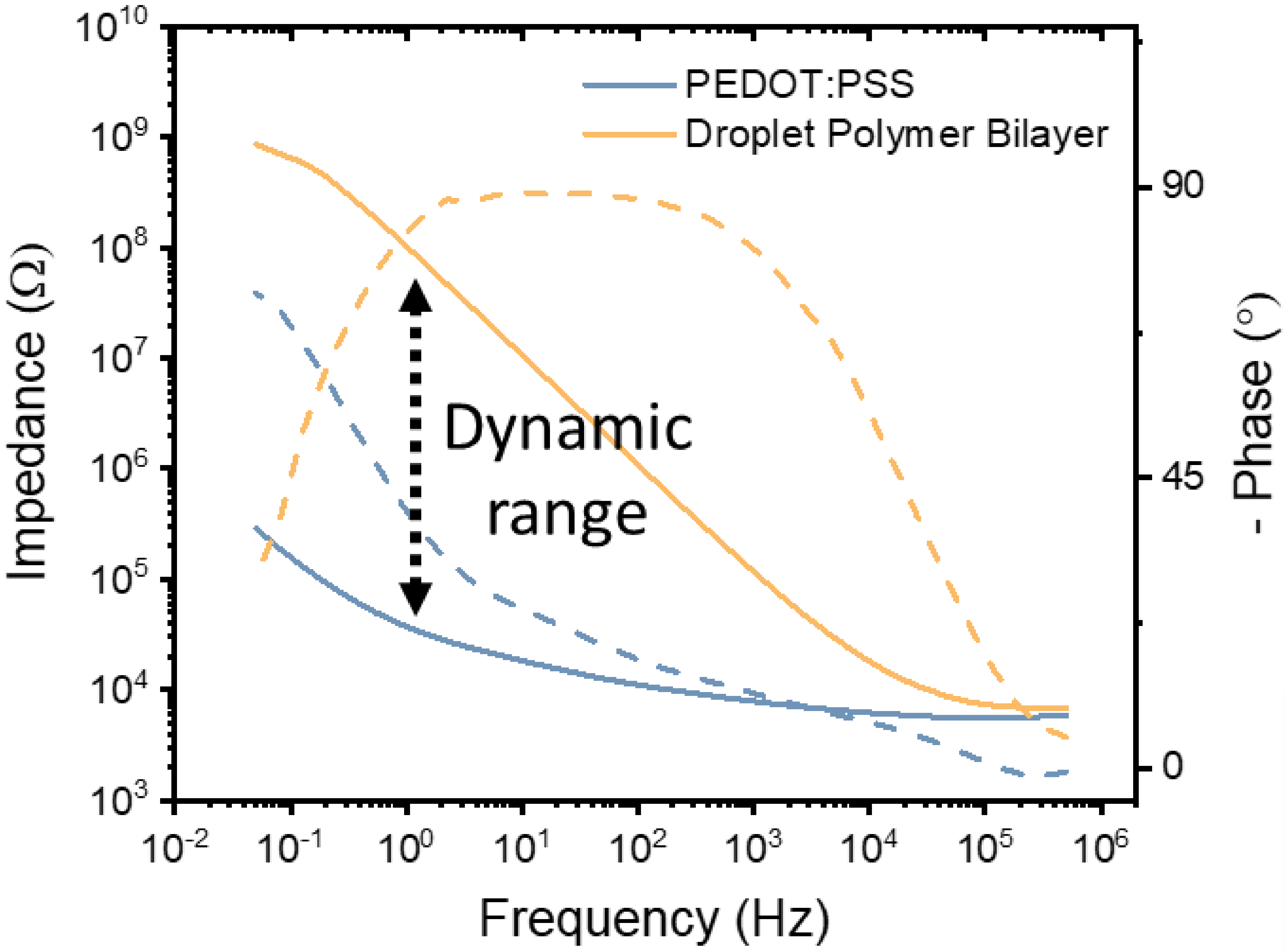


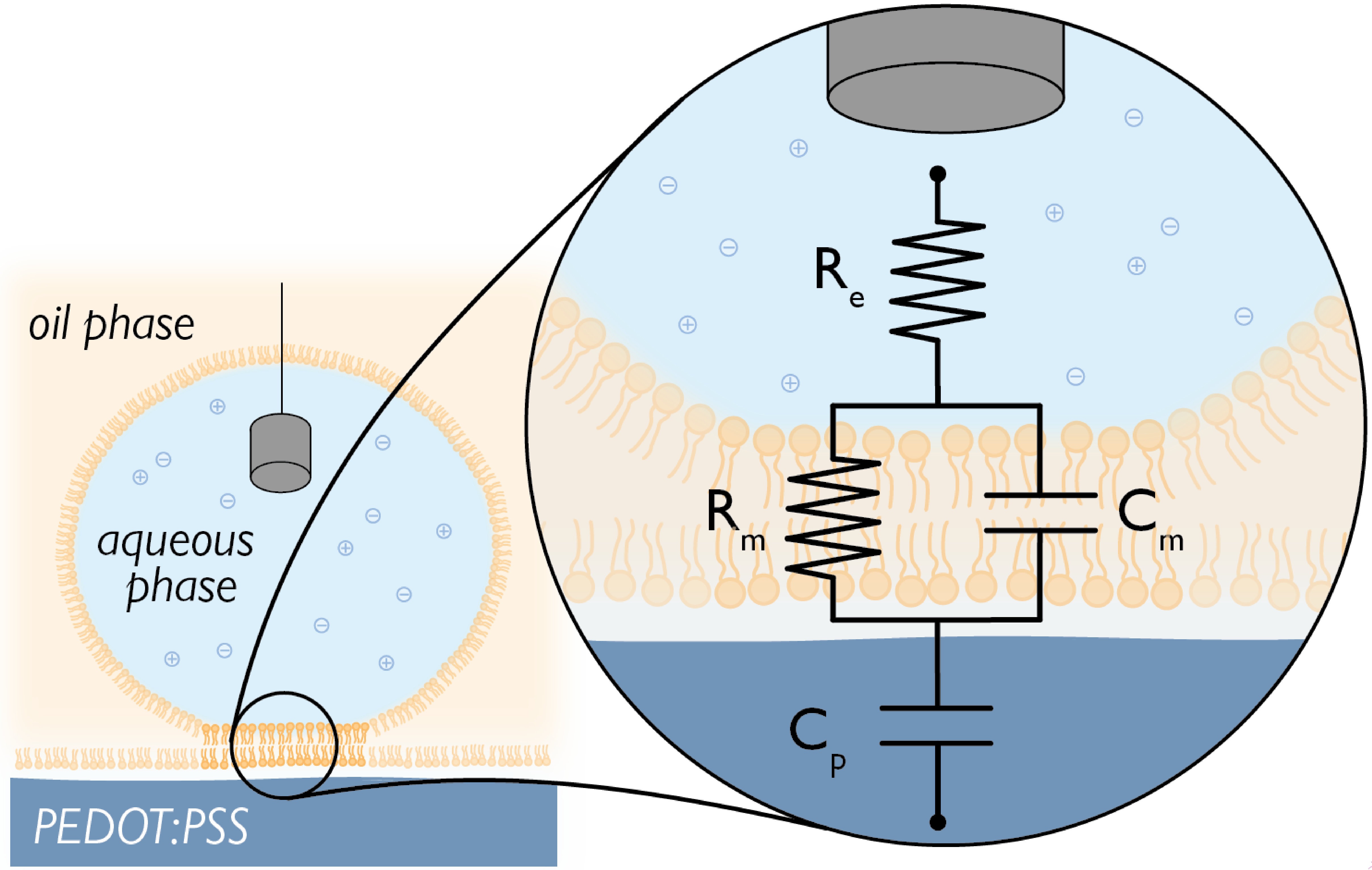


Schafer, *et al., JACS, 146, 21,* **2024**

Decoupling Membrane Properties from the Interface



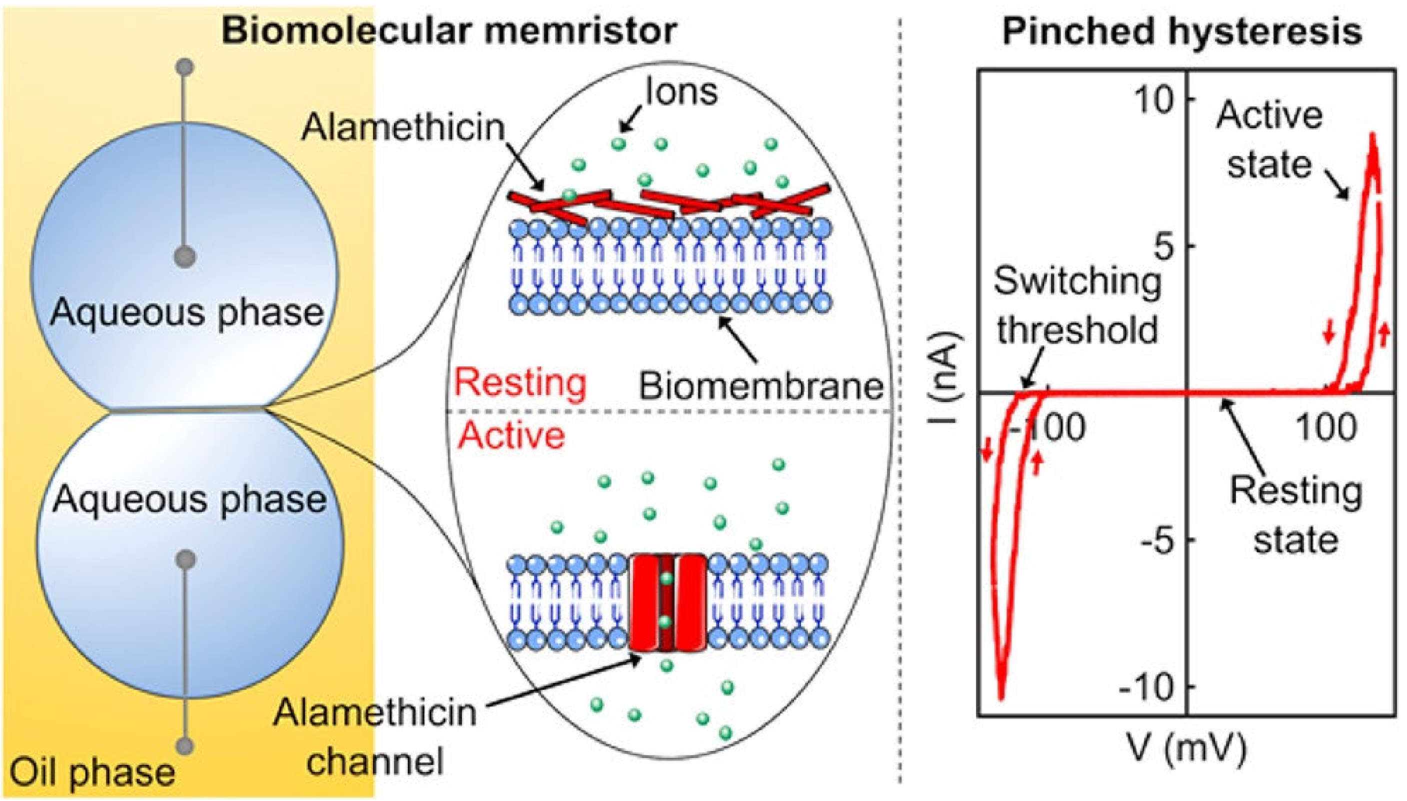


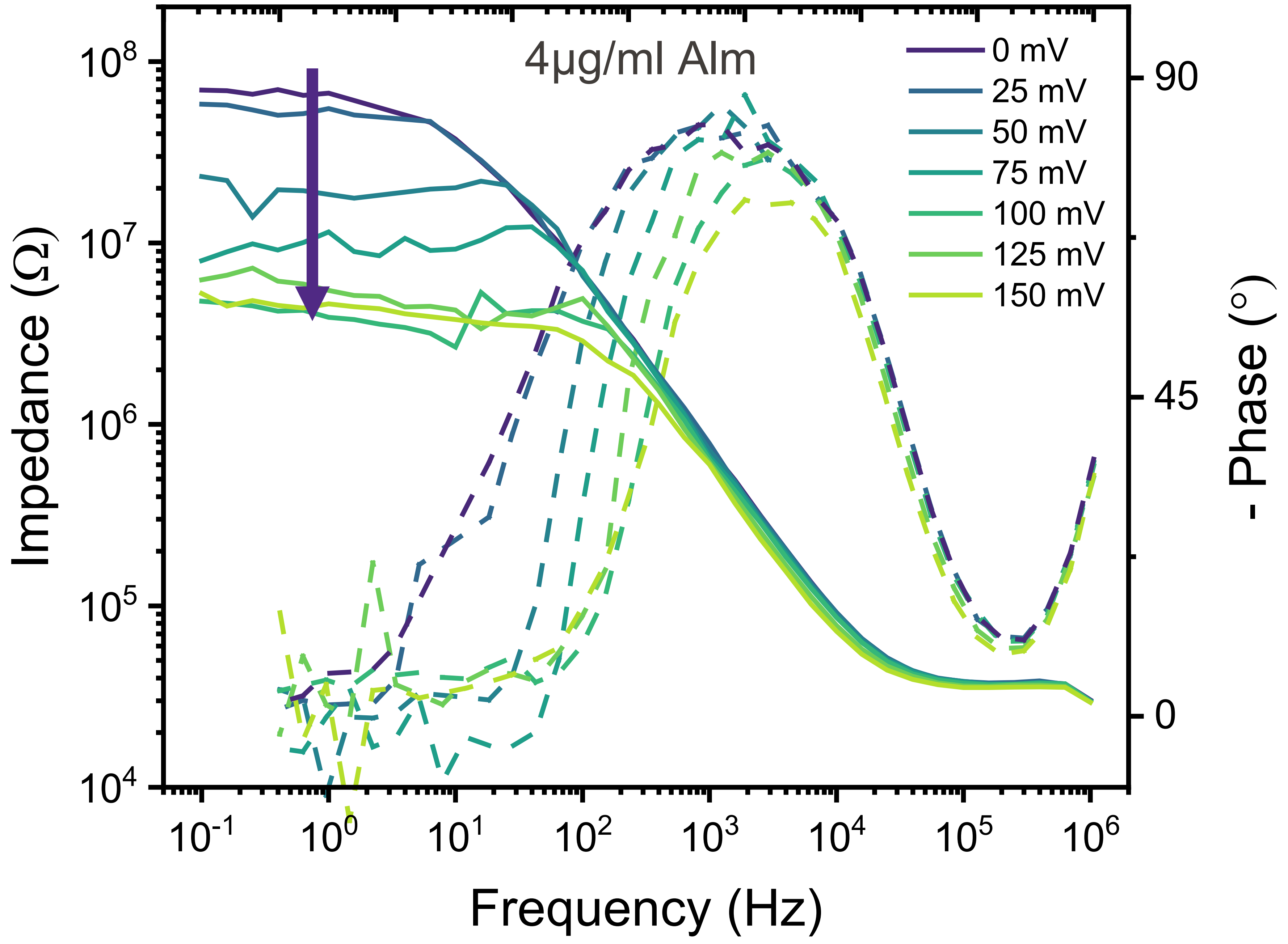


Schafer, *et al.*, *JACS*, *146*, *21*, **2024**

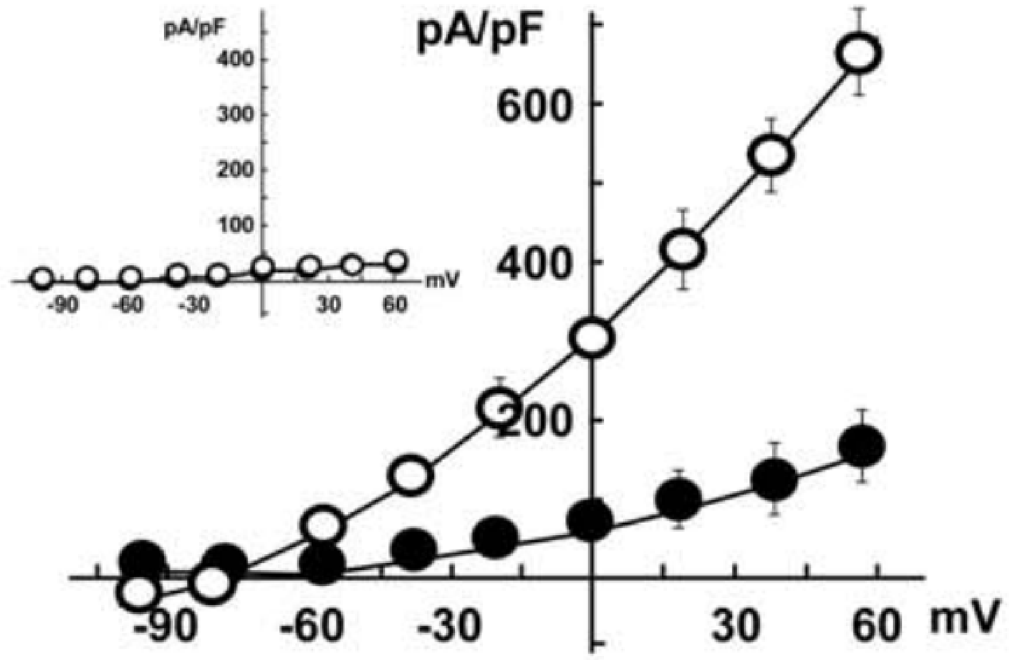
Voltage-Dependent Membrane Protein Activity

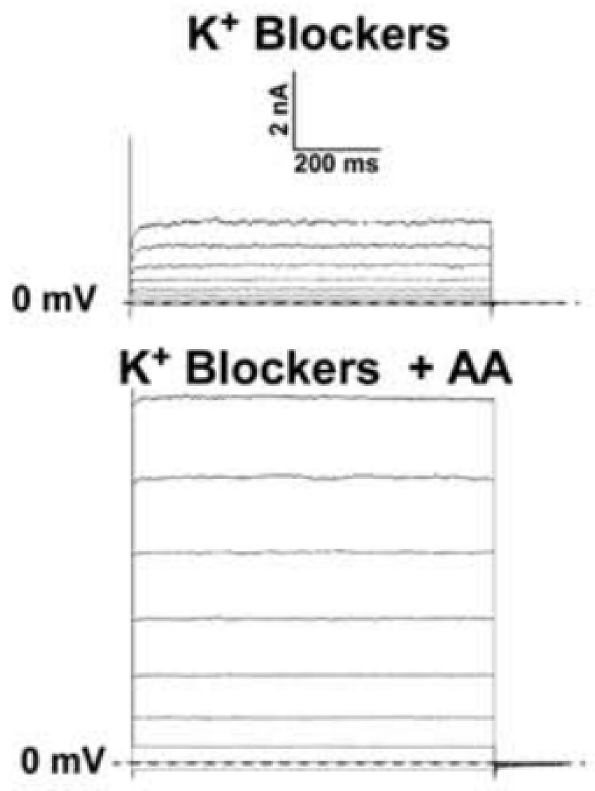
Alamethicin: voltage-gated, antimicrobial peptide

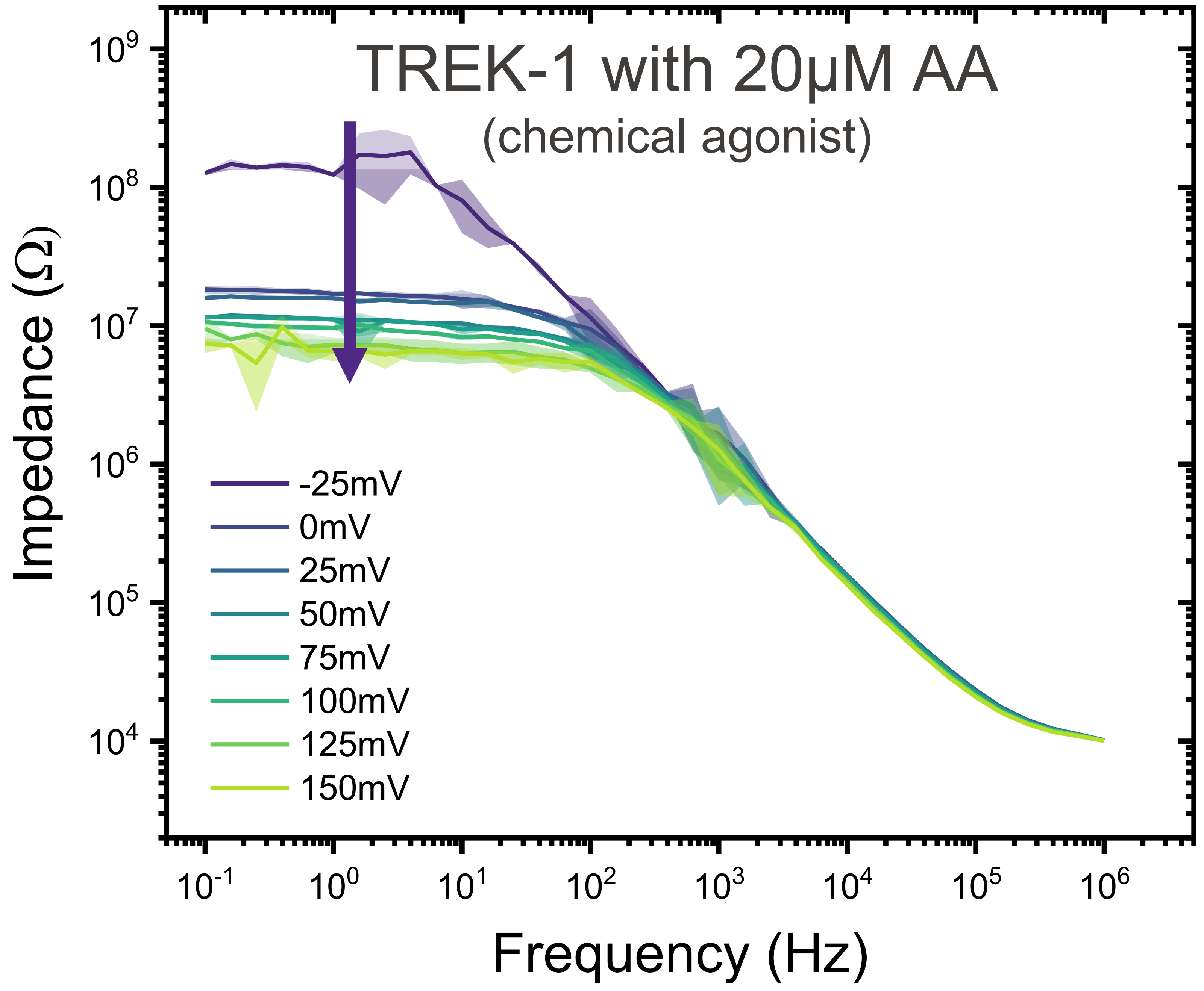




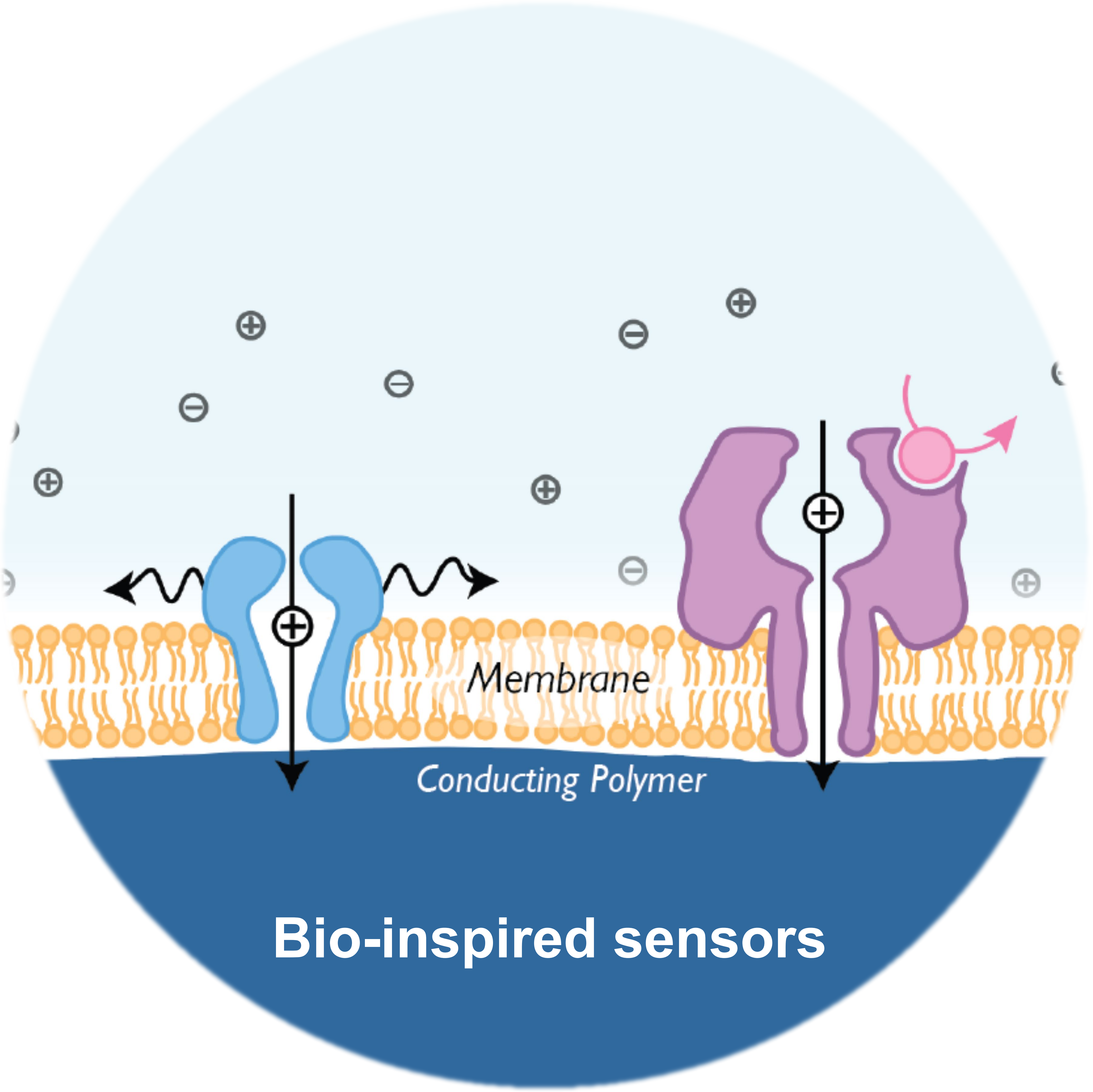
TREK-1: voltage-gated potassium ion channel



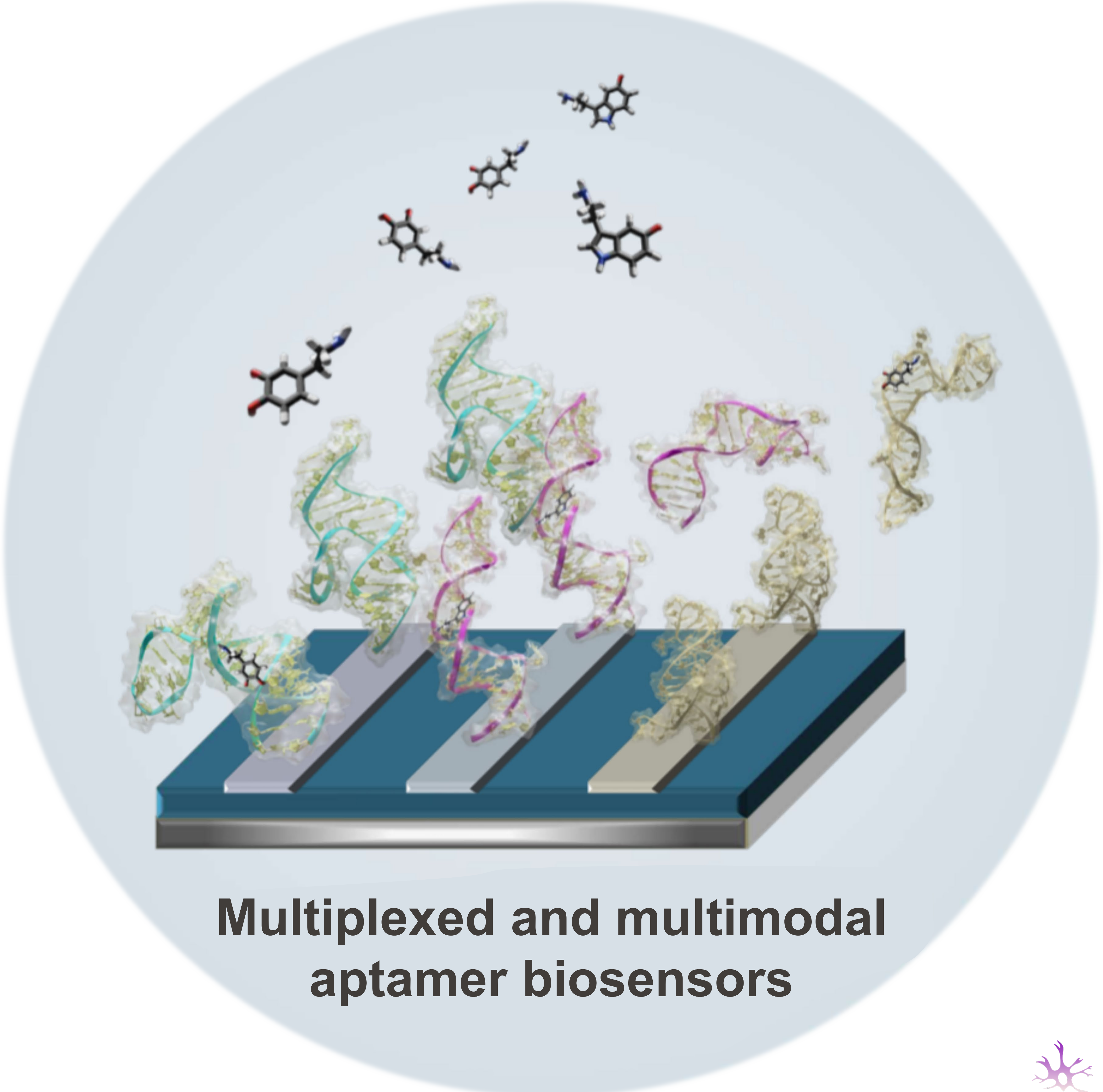




Organic Conducting Polymers in Biosensing

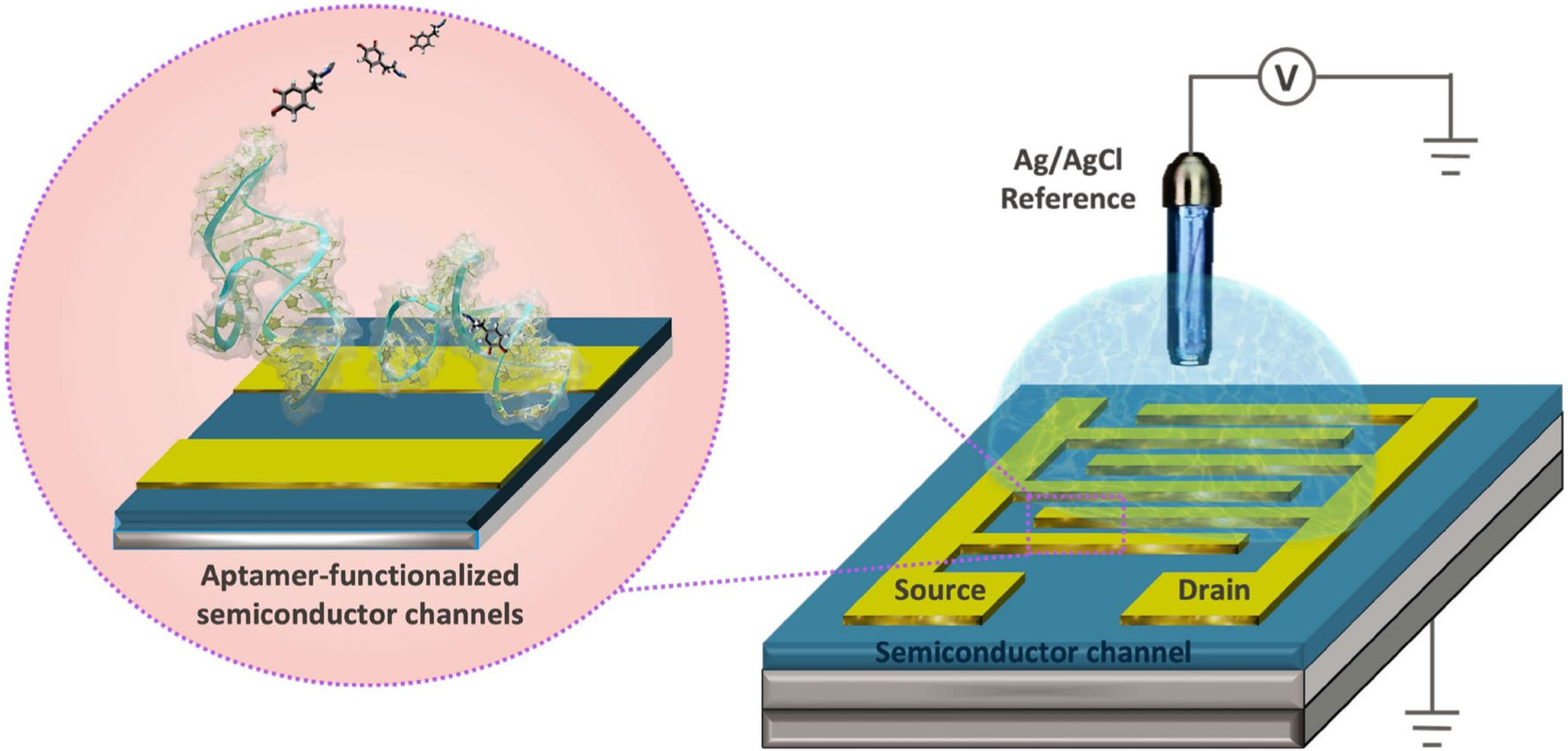


Bio-inspired sensors



Multiplexed and multimodal aptamer biosensors

Aptamers for Neurochemical Sensing



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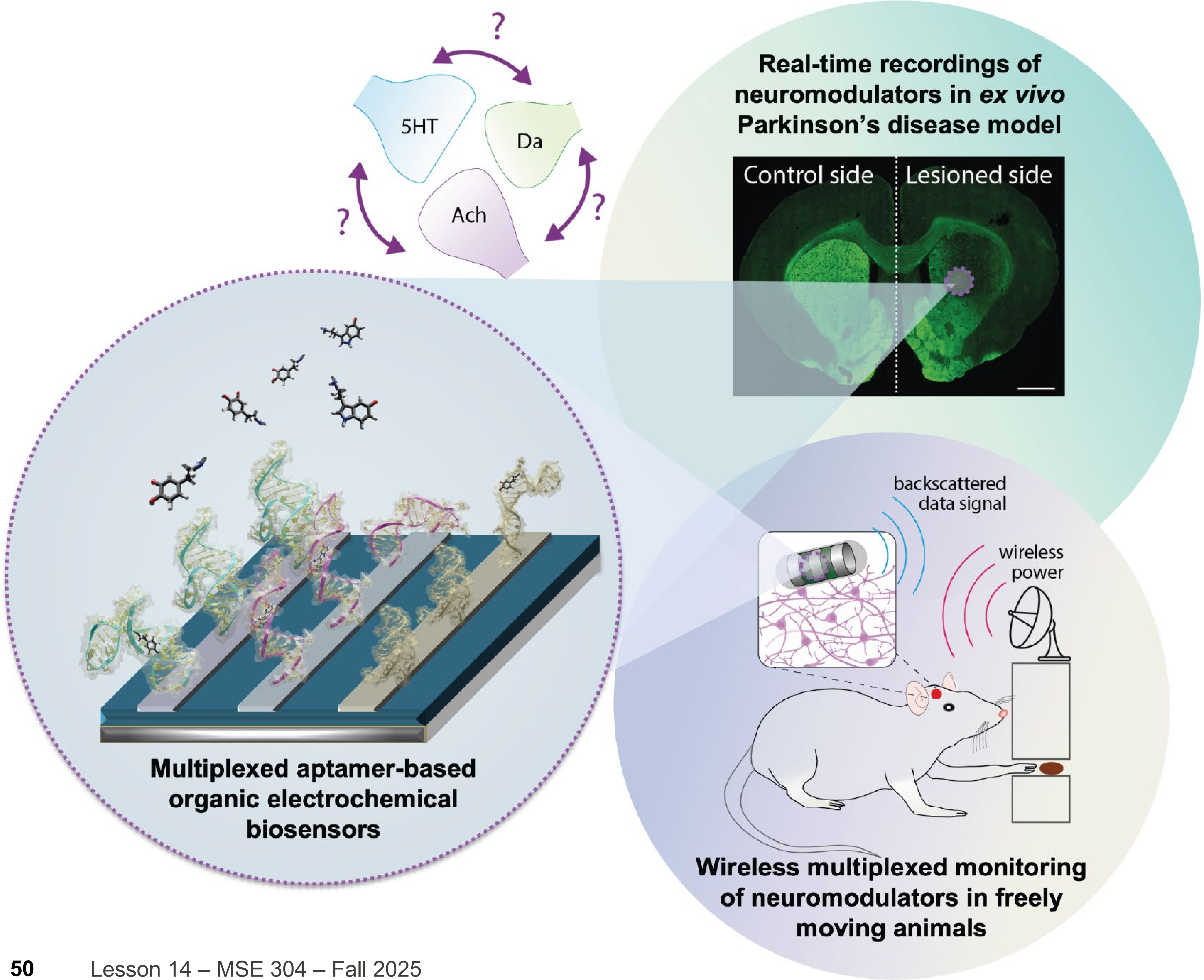
Aptamers for Neurochemical Sensing – with OECTs!

OECTs offer improved biocompatibility and amplification power that can benefit aptamer sensors for …

… multiplexed sensing

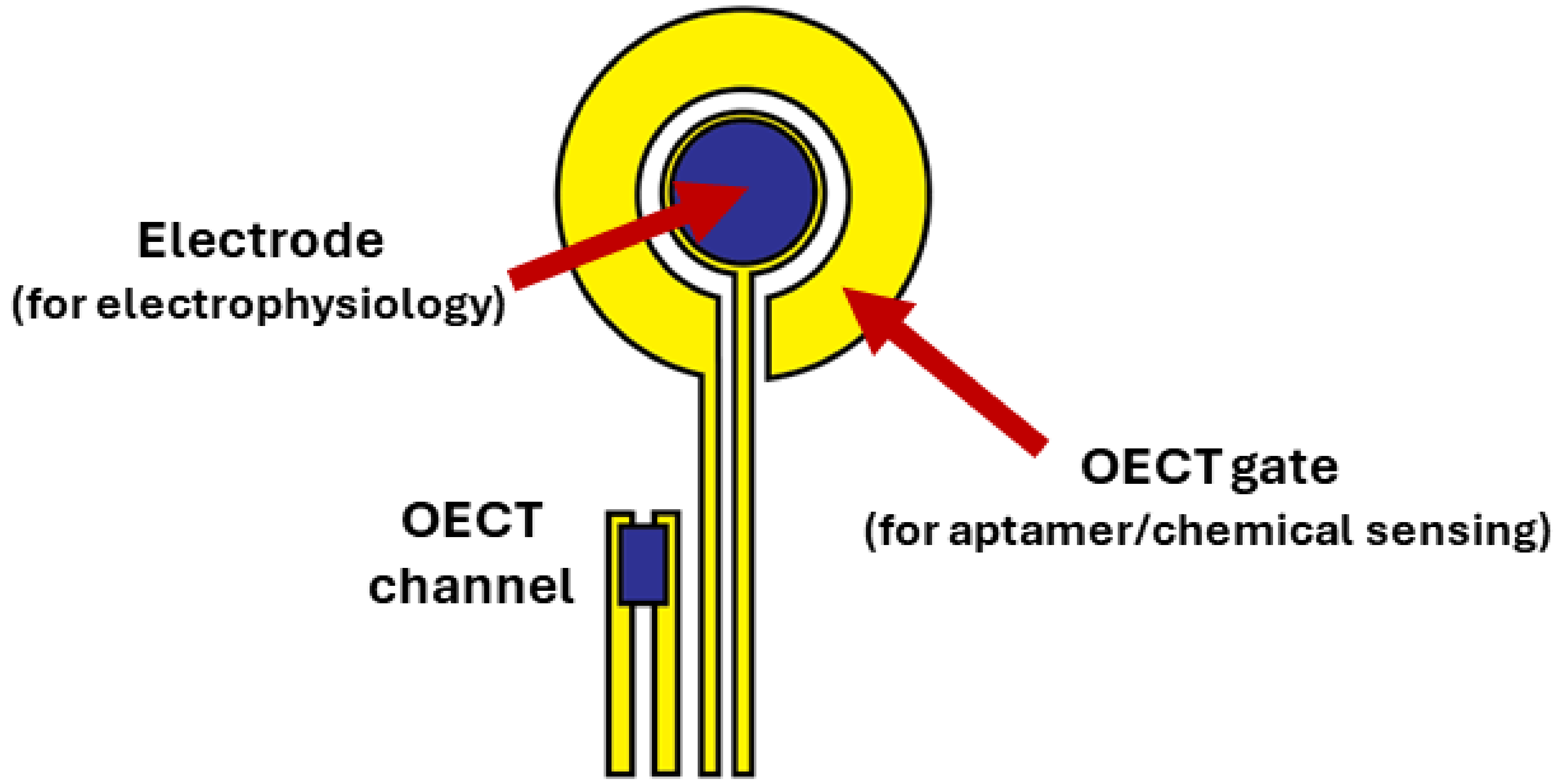


Real-time recordings of neuromodulators in *ex vivo* Parkinson's disease model

Multiplexed aptamer-based organic electrochemical biosensors

Wireless multiplexed monitoring of neuromodulators in freely moving animals

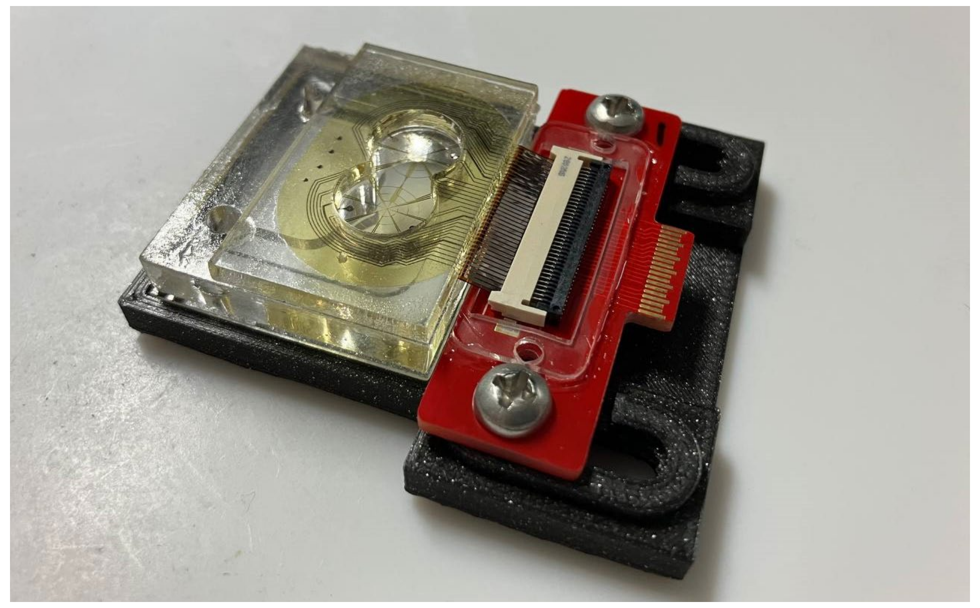
… multimodal sensing

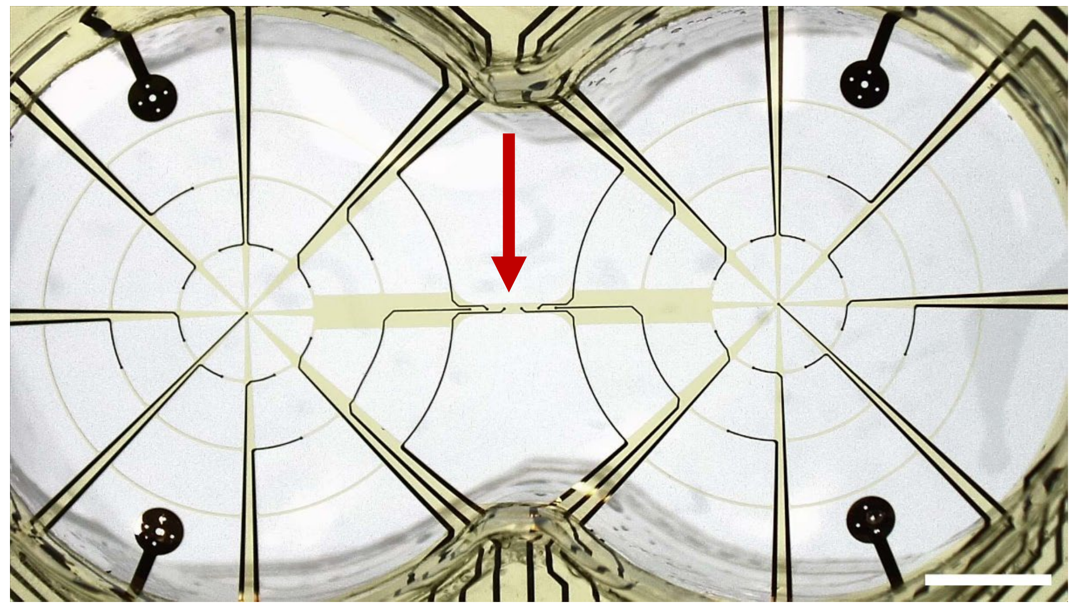


Electrode
(for electrophysiology)

OECT channel

OECT gate
(for aptamer/chemical sensing)



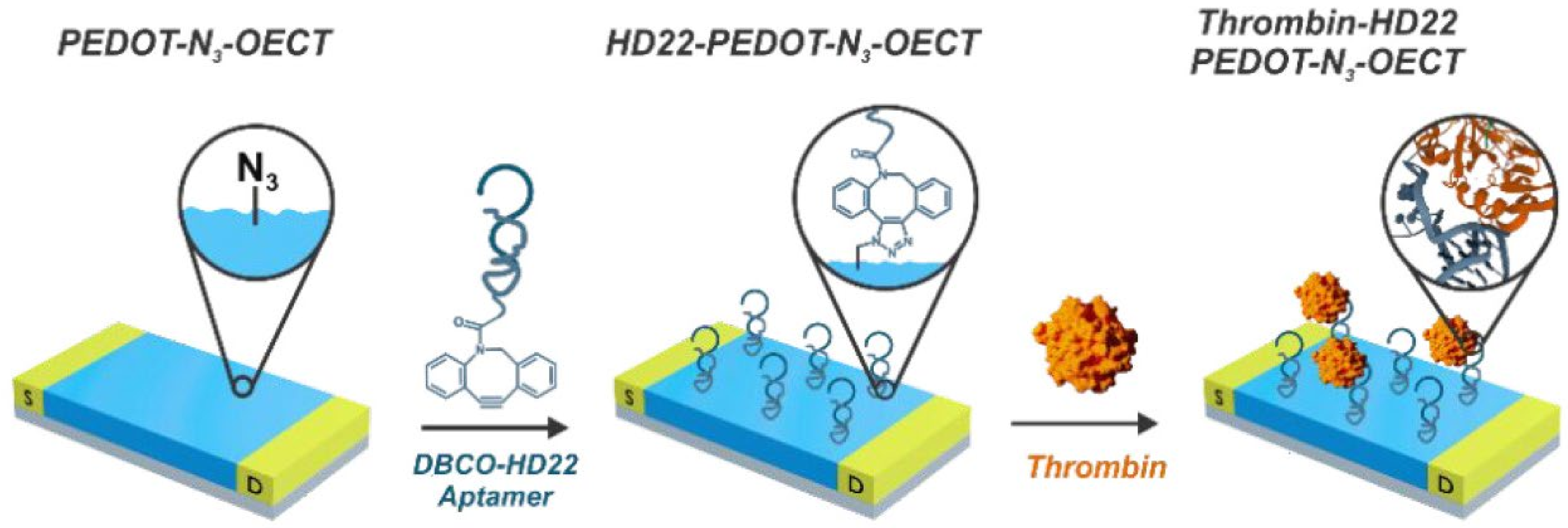


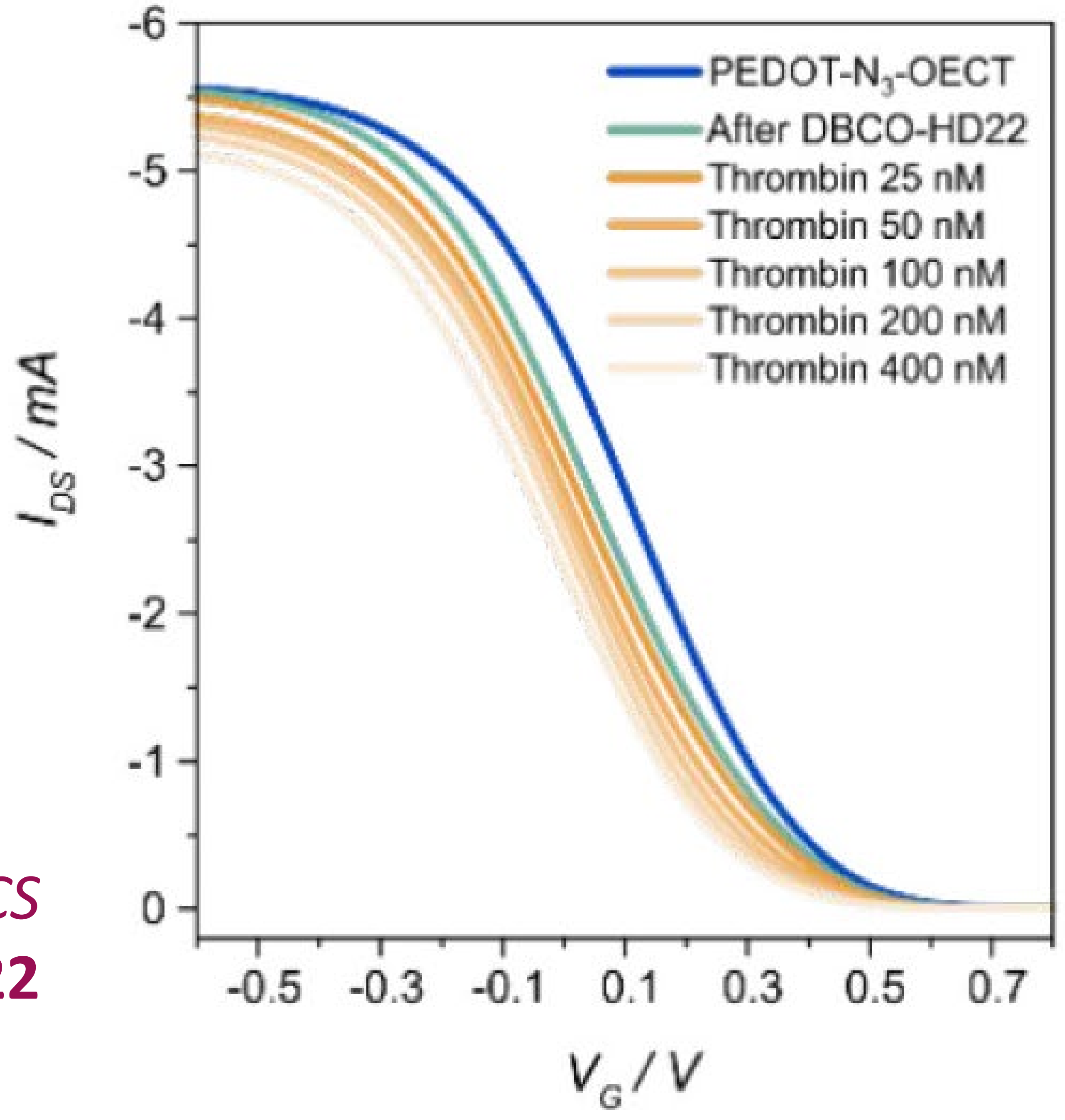
Different Strategies for Interface Design

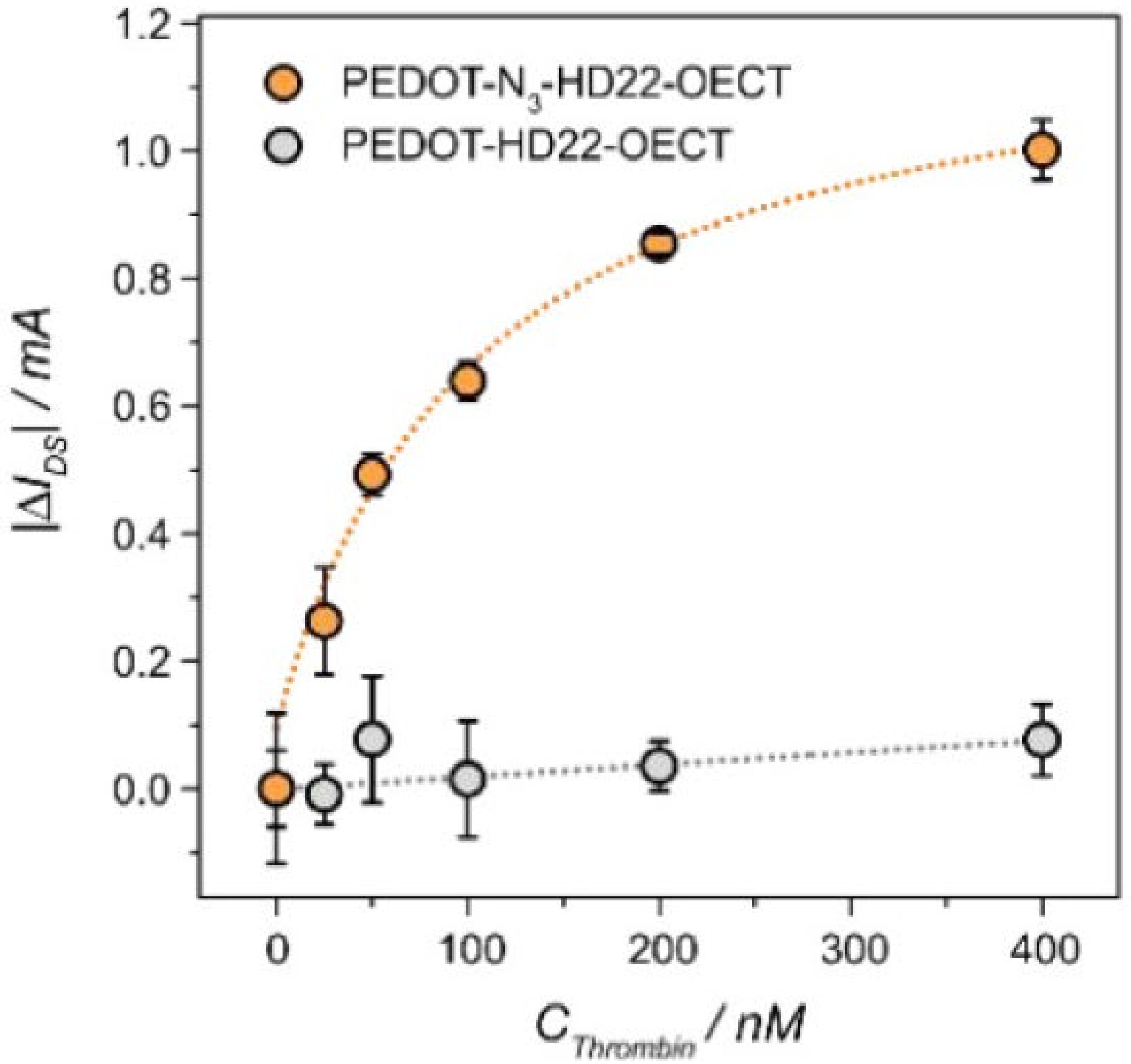
More straightforward surface chemistries
Larger device footprint

Challenging and complex surface chemistries
High density recordings

OECT Channel Functionalization for Aptamer Biosensors







Fenoy, *et al.*, *JACS Au, 2, 12,* ***2022***

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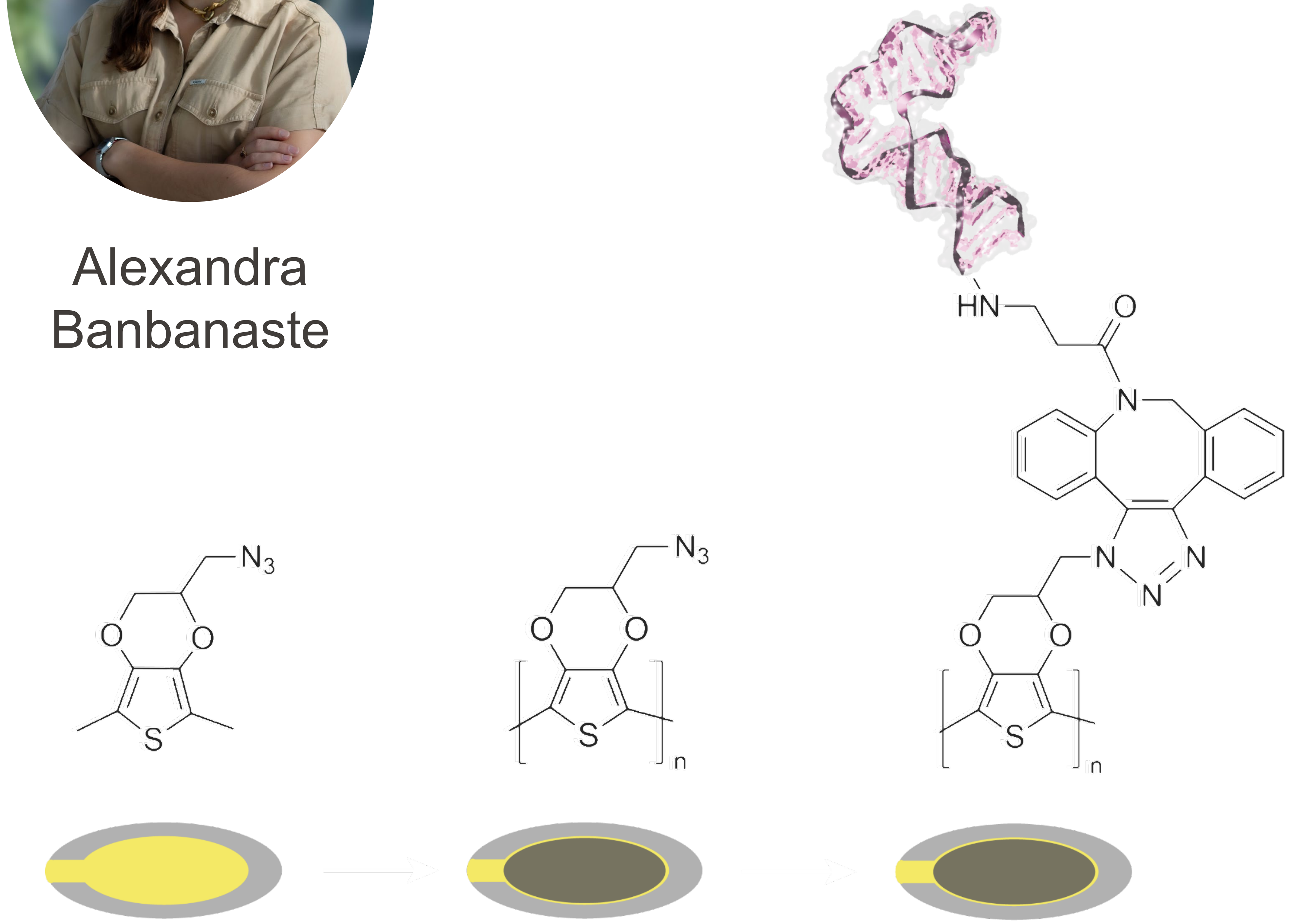
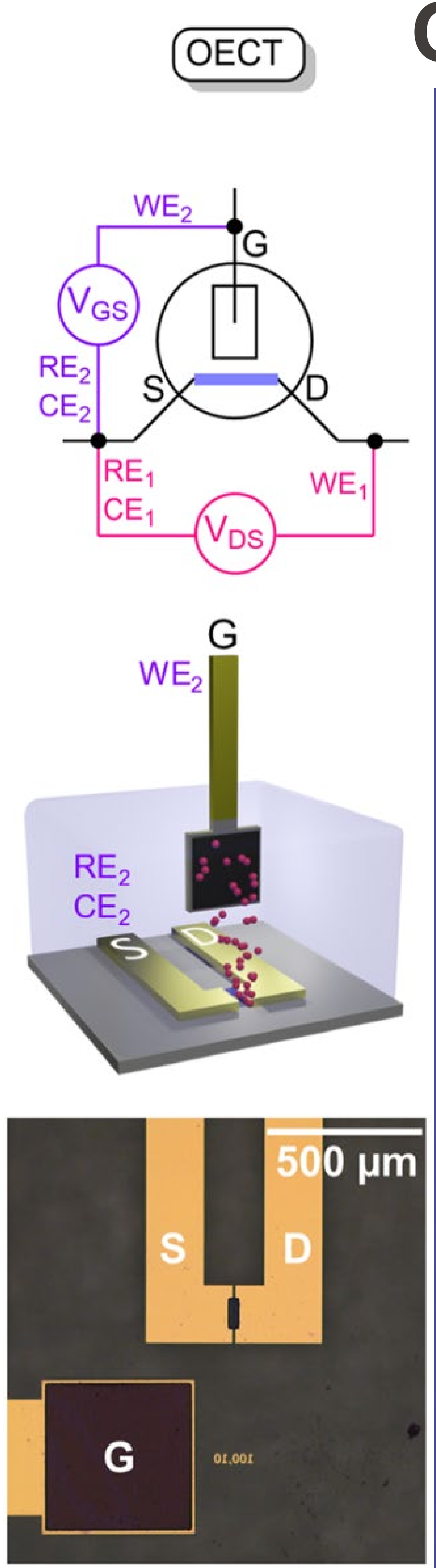
OECT Channel Functionalization for Aptamer Biosensors

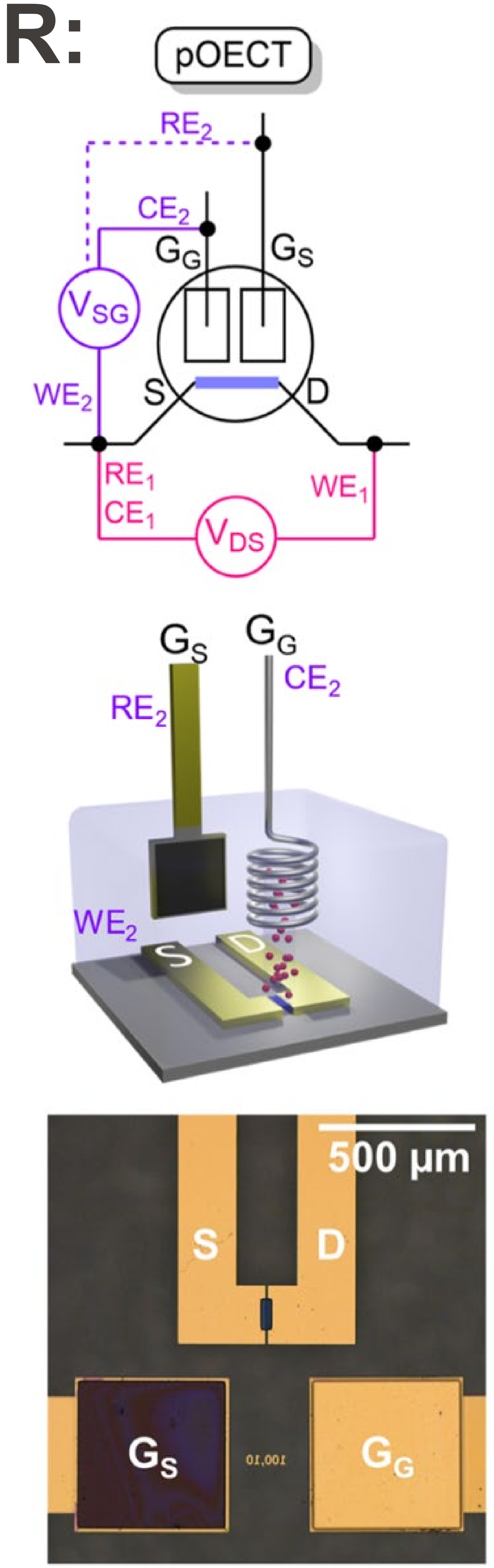
Alexandra
Banbanaste



OECT Gate Functionalization for Aptamer Biosensors

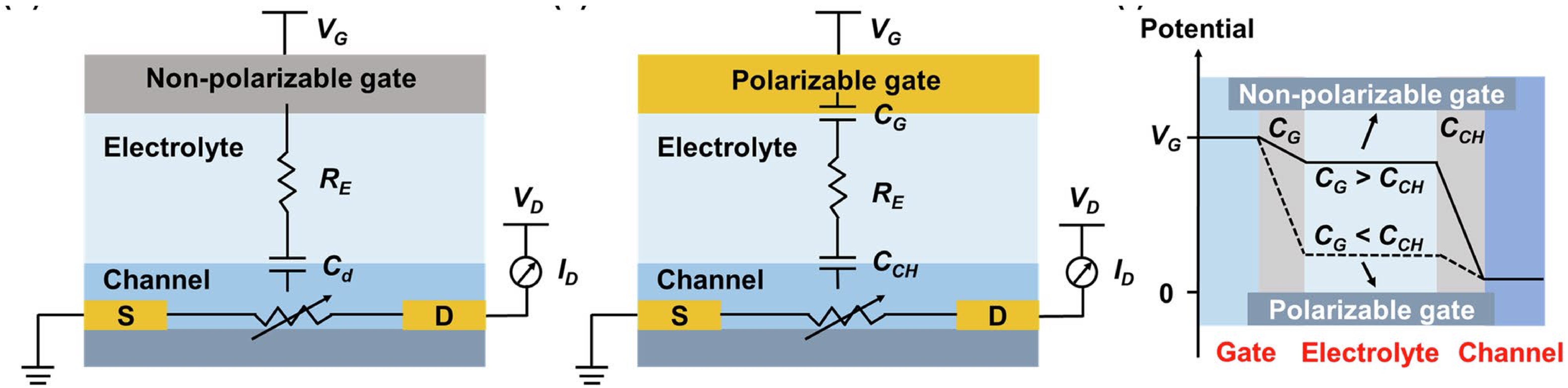


OR:

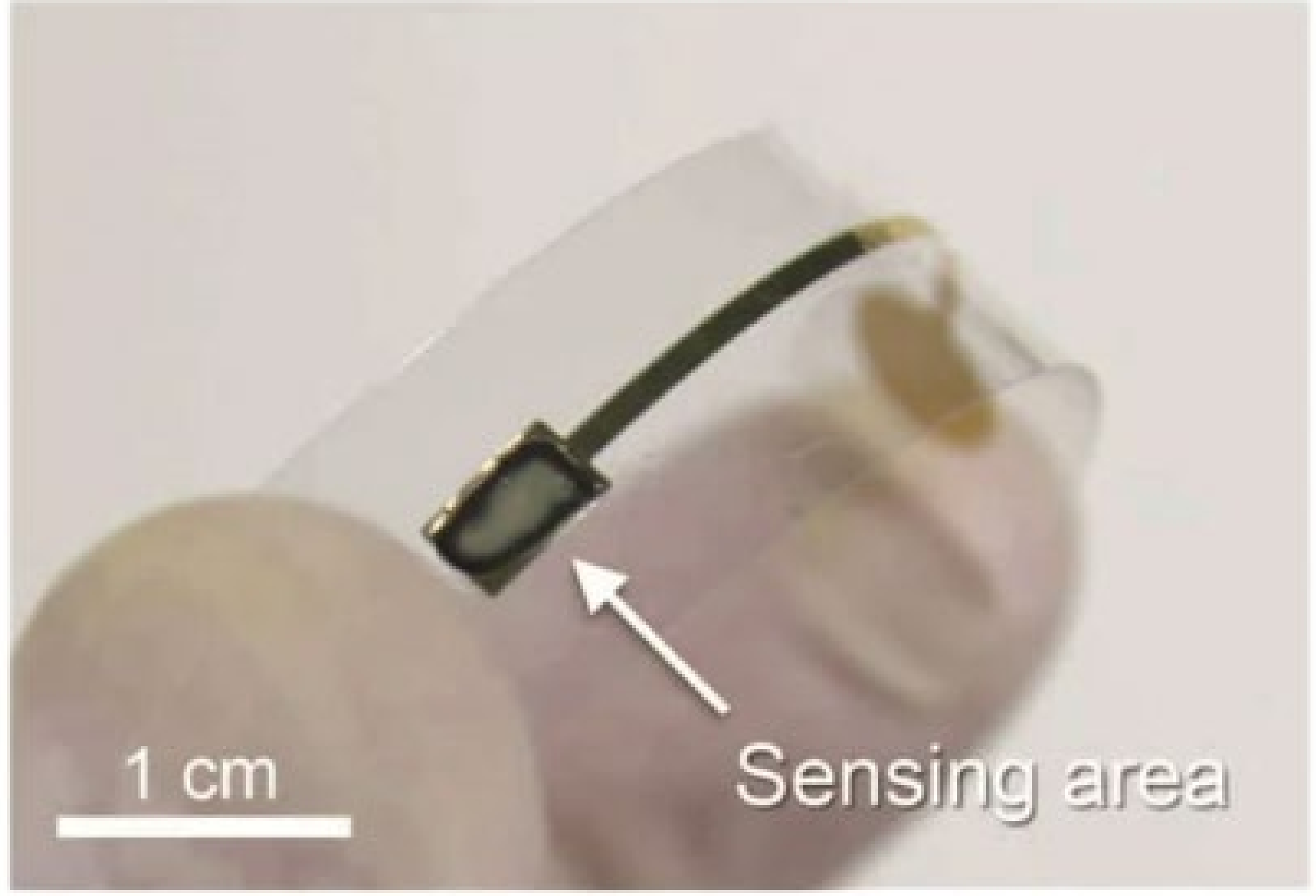


Ideal for a potentiometric sensor:

In real-life:



Potentiometric sensors can behave more "ideally" with a large gate area, but this sacrifices spatial resolution:



Salvigni, *et al.*, *Nat Comm*, *15*, **2024**
Lu, *et al.*, *npj flexible electronics*, *9*, **2025**
Shiwaku, *et al.*, *Sci Rep*, *8*, **2018**

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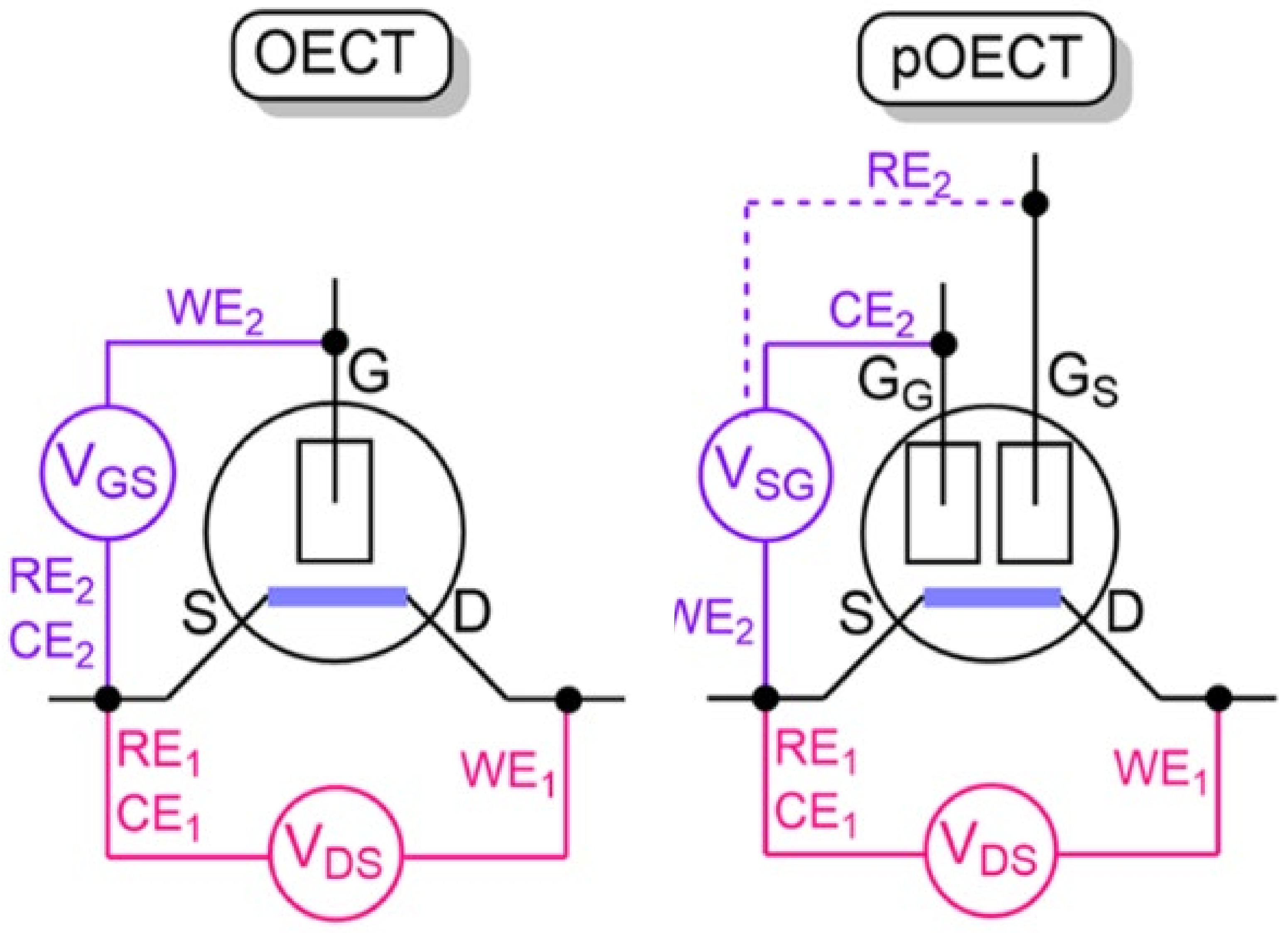
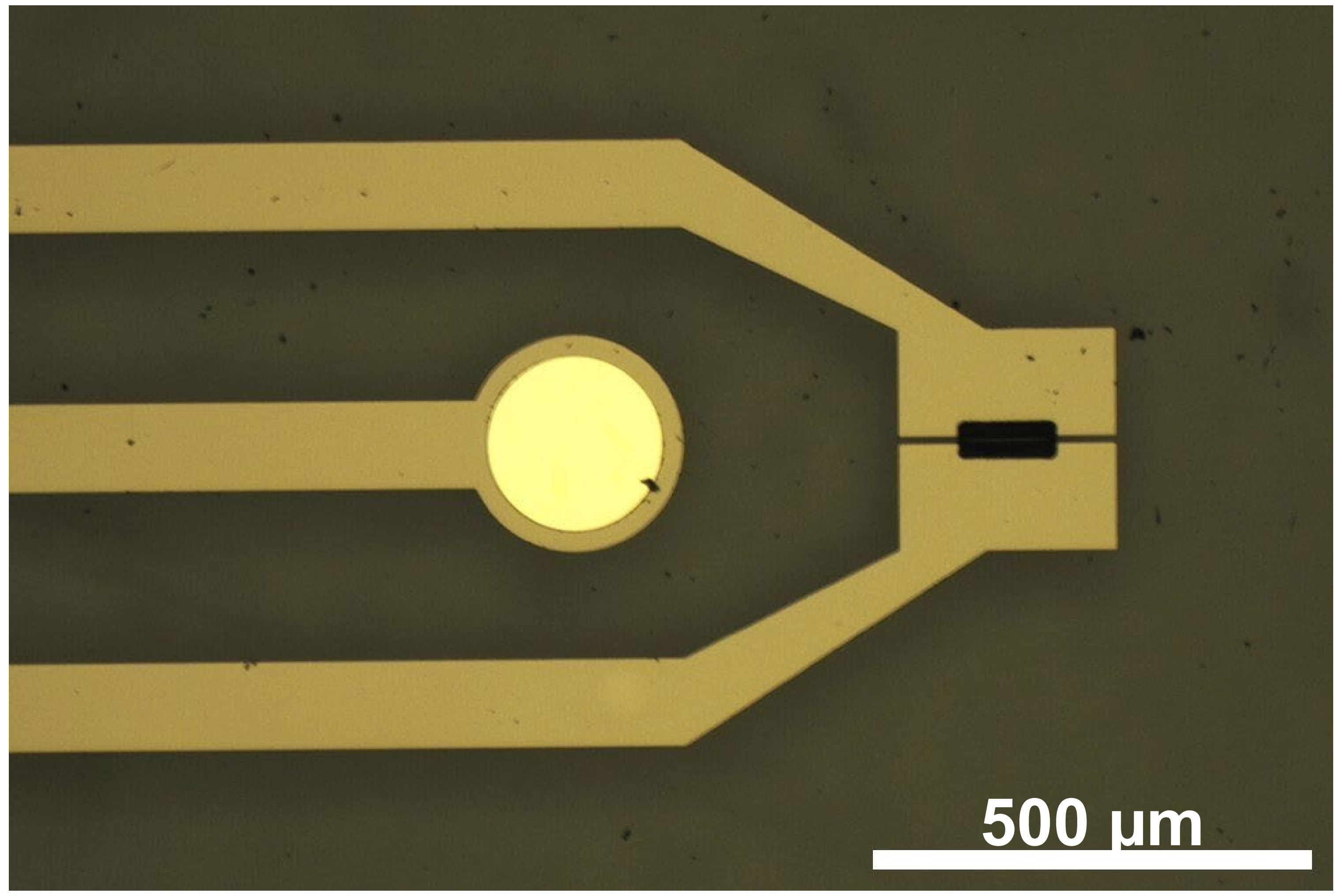
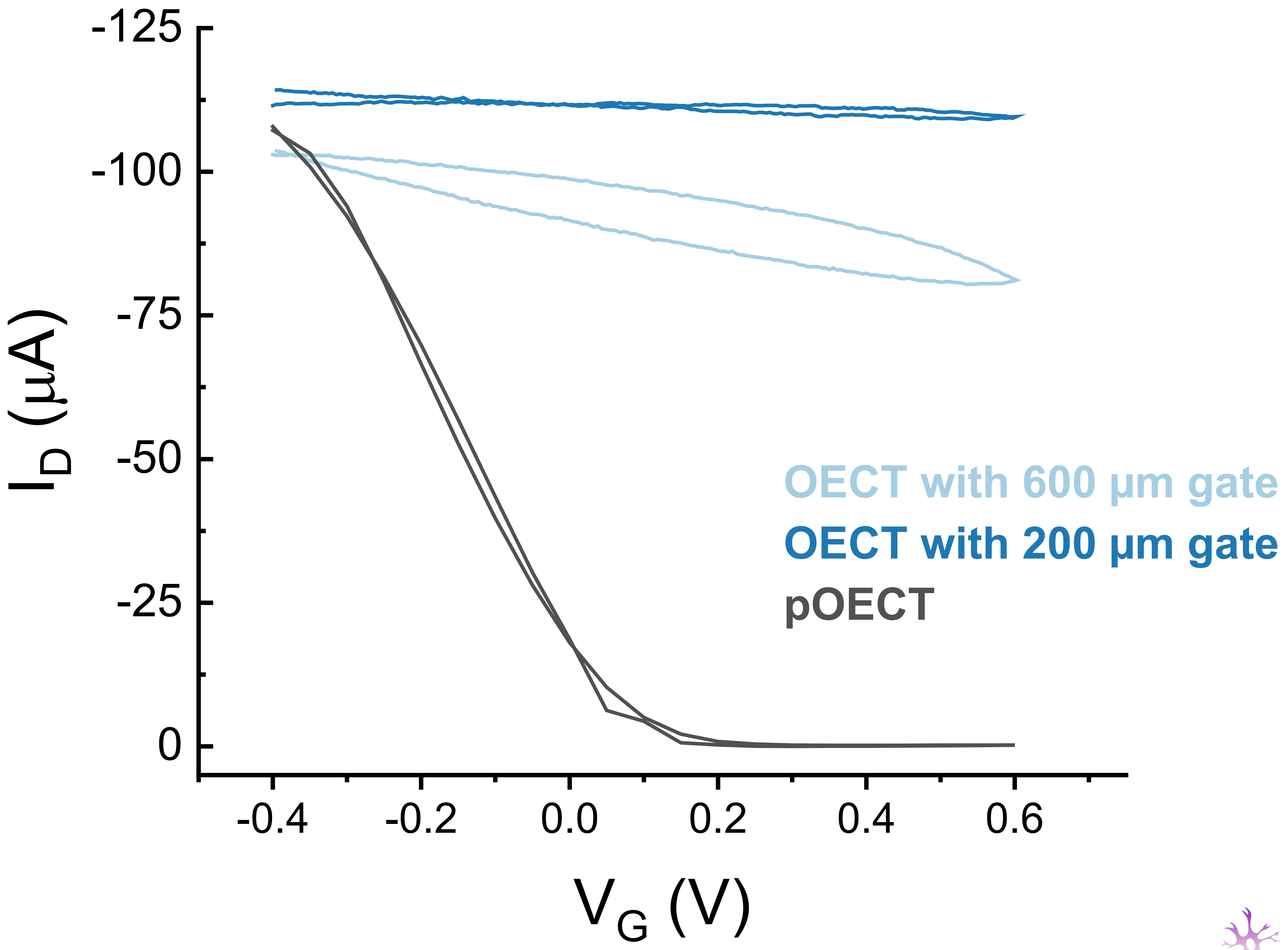
OECT Gate Functionalization for Aptamer Biosensors

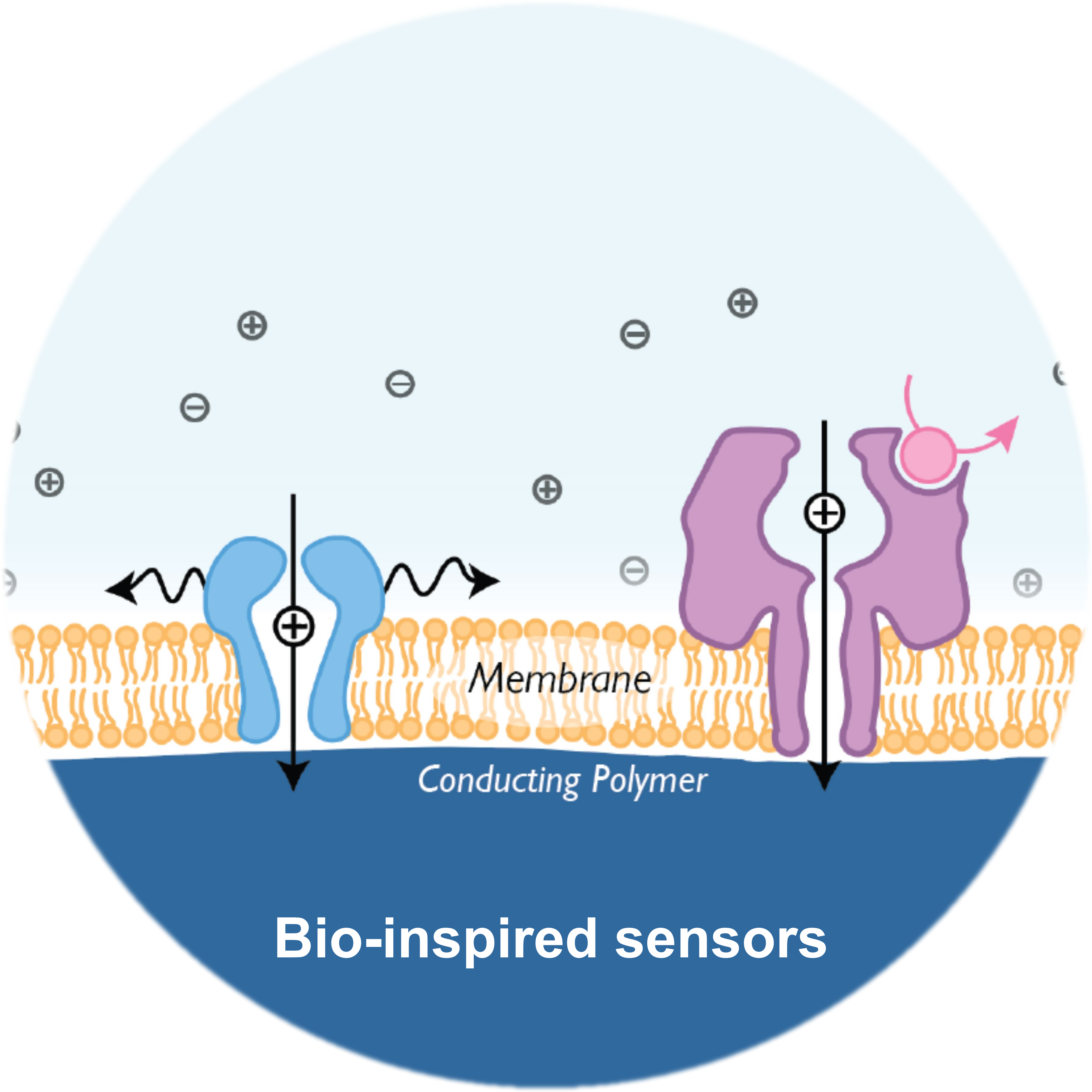




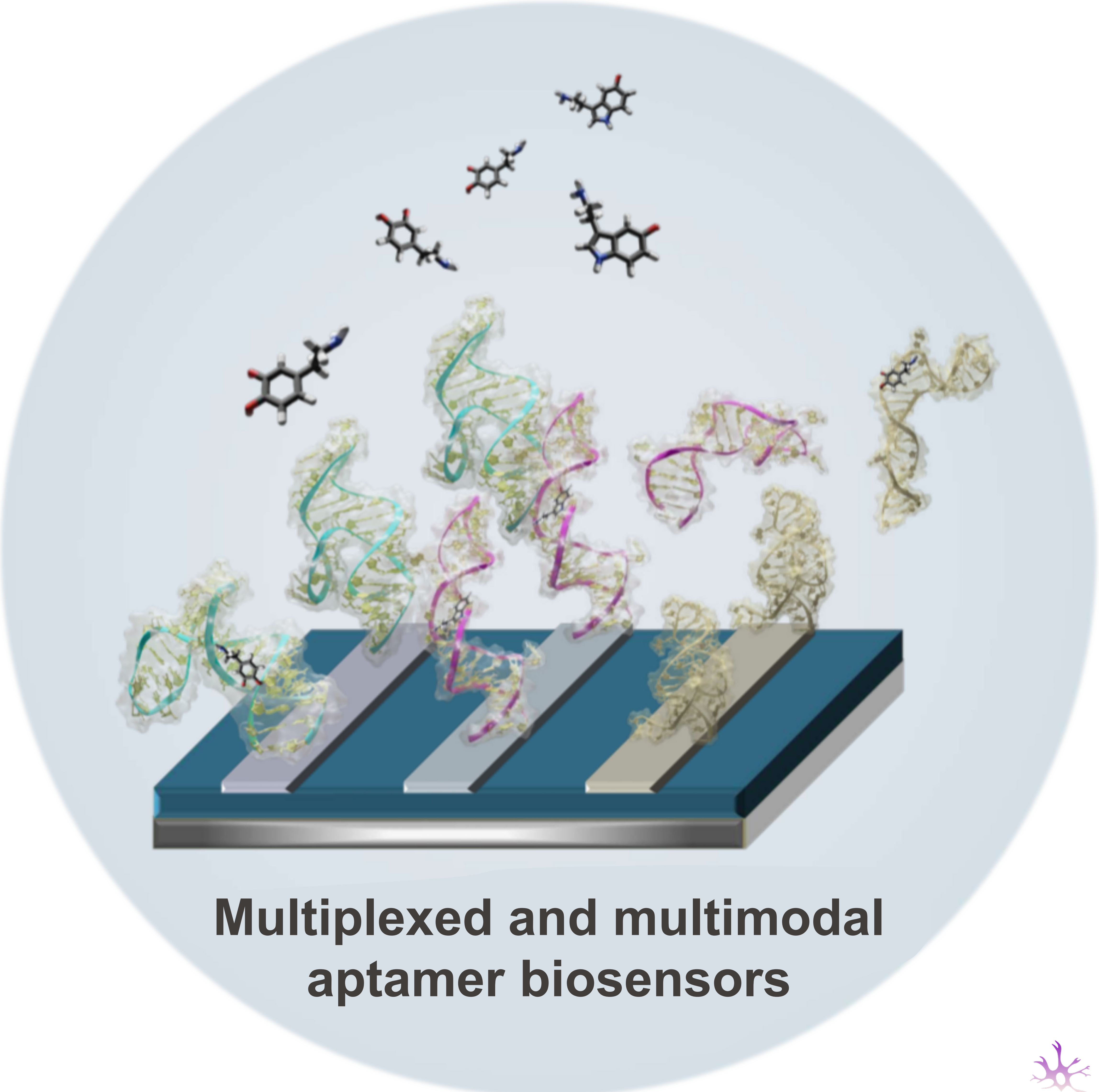


Salvigni, *et al.*, *Nat Comm*, *15*, **2024**

Organic Conducting Polymers in Biosensing



Bio-inspired sensors



Multiplexed and multimodal aptamer biosensors

Summary of Today's Class

- Bioelectronic devices must be carefully designed to match the time scale, length scale, and requirements of the intended application
- Semiconductors can be designed to "blur" the lines between bulk and interfacial properties
- Organic conducting polymers are a promising new class of materials for improving bioelectronic devices
- Successful bioelectronics using these conducting polymers necessitate informed design of the interface between semiconductors and biology

Acknowledgements

EPFL

Northwestern University

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