Ultra-low noise organic based devices to record bioelectrical signals in non-excitable cell populations: Applications in anticancer drug screening platforms

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Outline

- Novel electrophysiological sensing platform.
  (Ink-jet printed PEDOT:PSS electrodes and bacterial cellulose substrates)

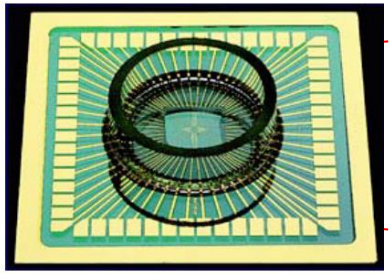
- Device physics, design rules and detection limits.

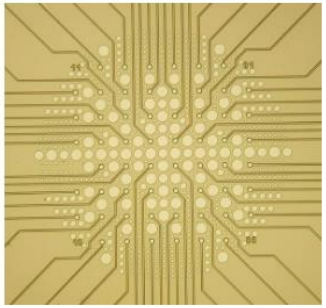
- The bioelectricity of ensembles of non-excitable cells.

- Applications in fundamental biological studies and in medicine:
  - Cancer research and treatment.
  - Cell migration.
  - Wound healing and tissue regeneration.
  - Biological rhythms and biological clocks.

- Summary (future therapeutic devices).

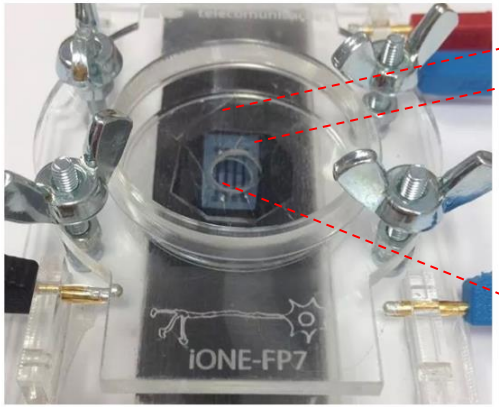
Electrodes for electrophysiological sensing

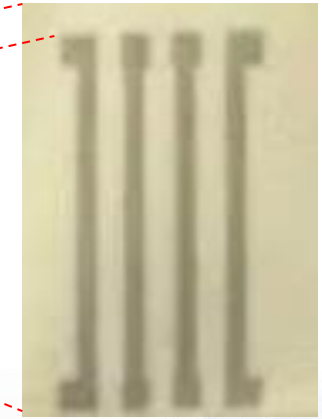




MEAs with 60 electrodes

multichannel systems
a division of Harvard Bioscience, Inc.



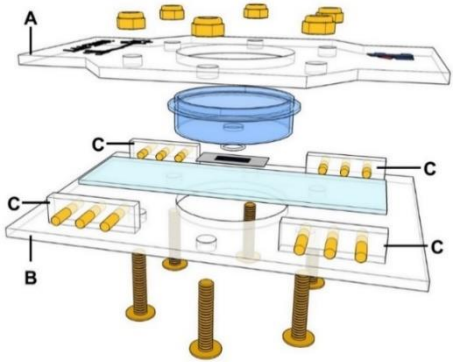


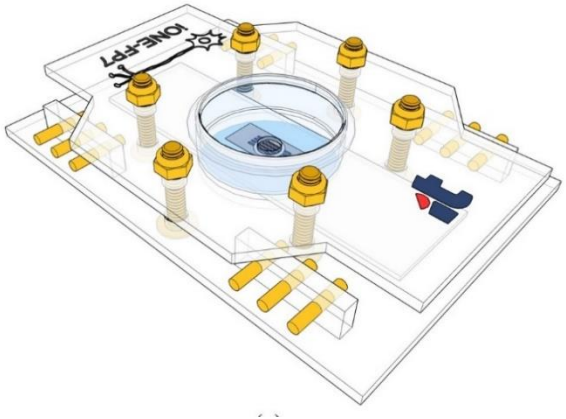
1 cm

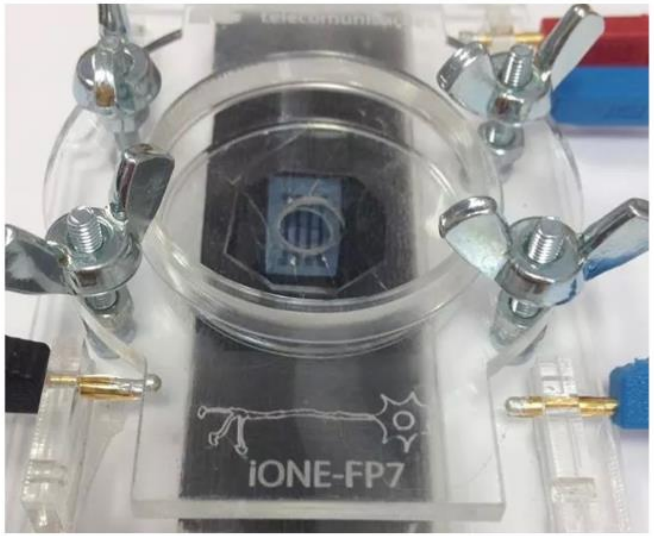
Our system

Ink-jet printed PEDOT:PSS in bacterial celulose substrates

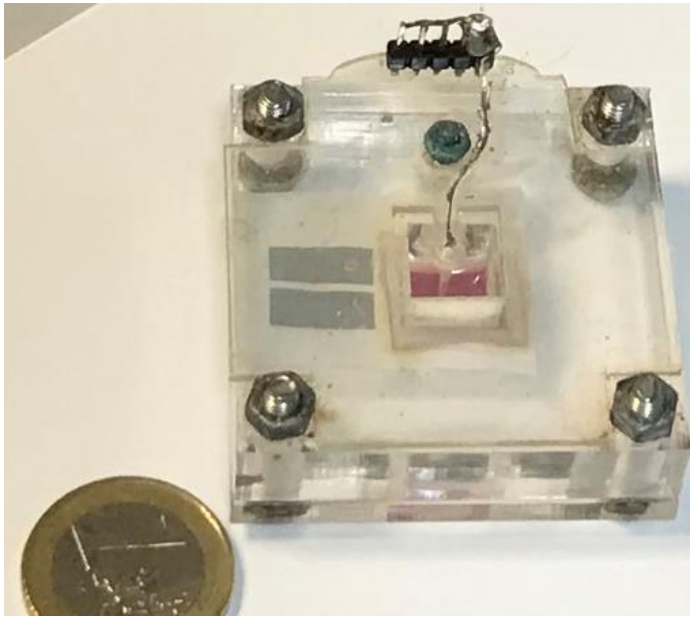
Ink-jet printed electrodes for electrophysiological sensing

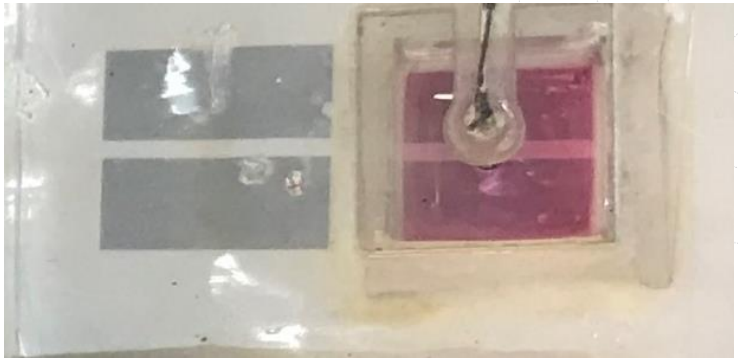




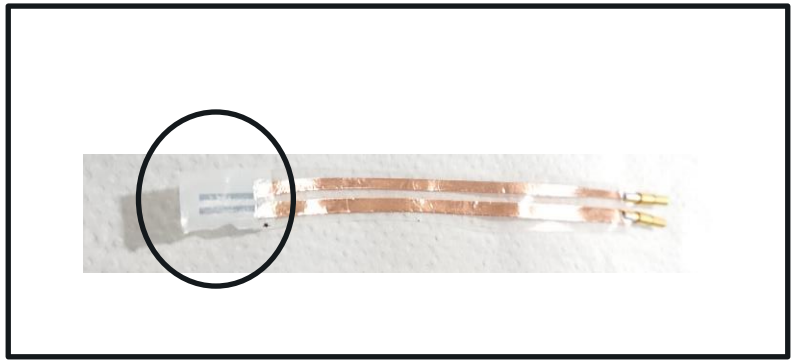


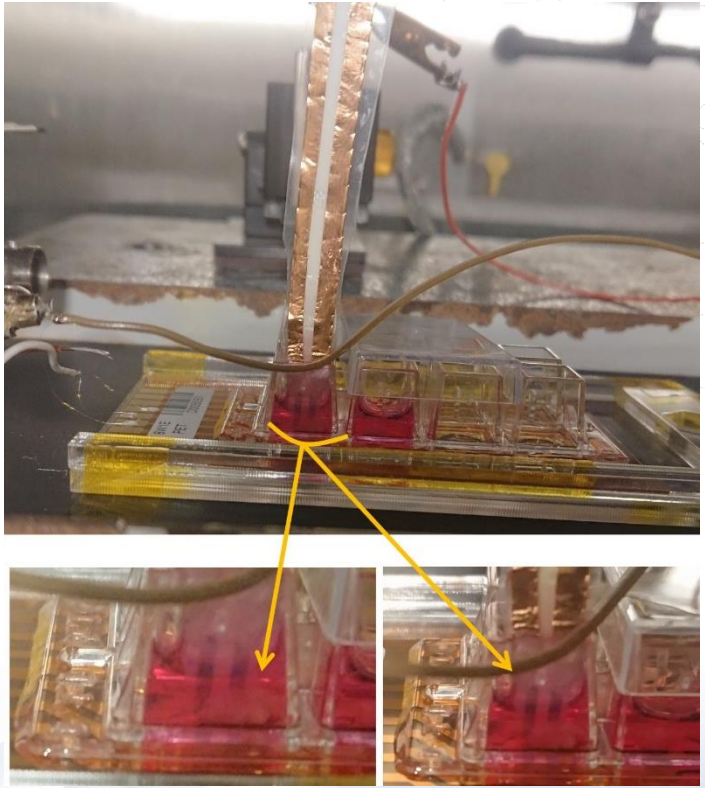
Ink-jet printed electrodes for electrophysiological sensing



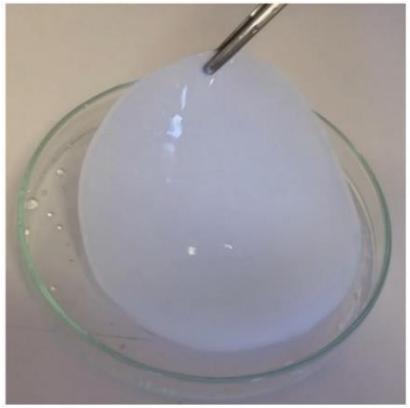


Ink-jet printed electrodes for electrophysiological sensing

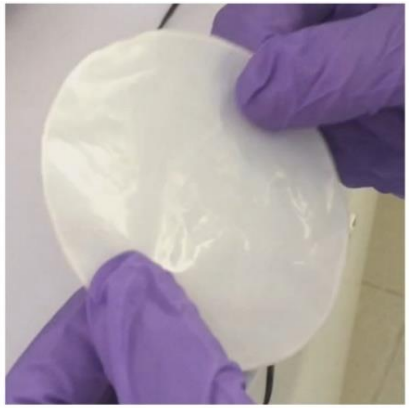




Bacterial cellulose substrates



(a)



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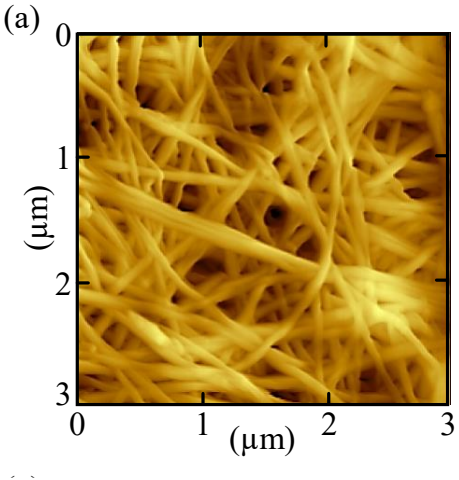
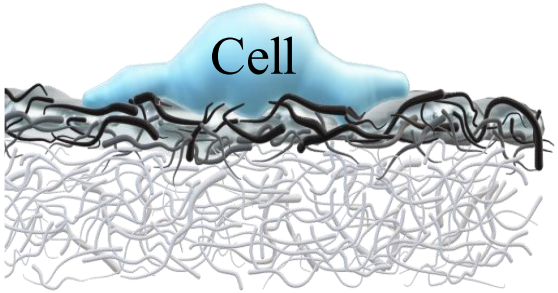
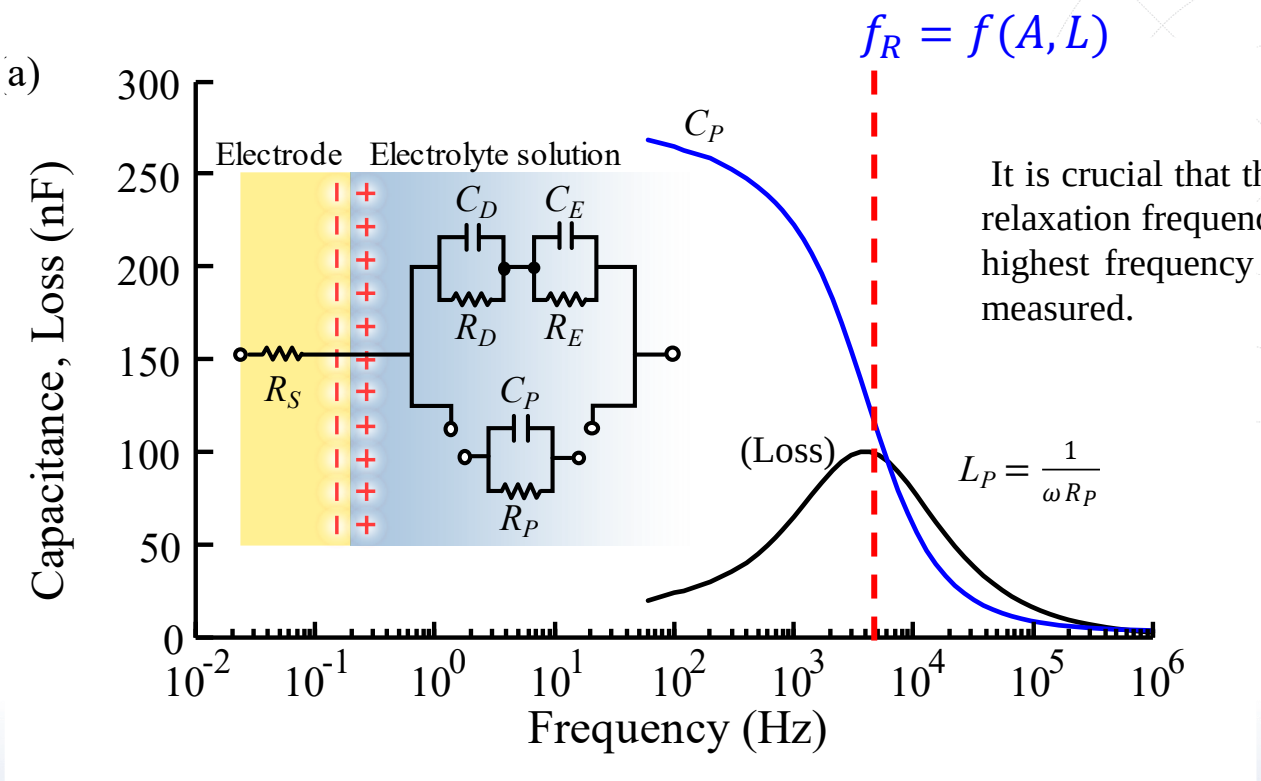




The impedance of the electrical double-layer



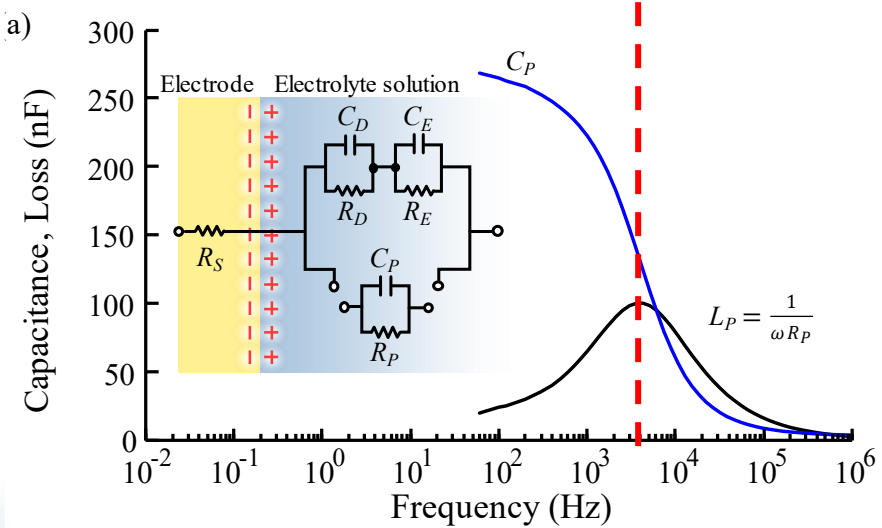
It is crucial that the Maxwell-Wagner relaxation frequency is higher than the highest frequency of the signal being measured.

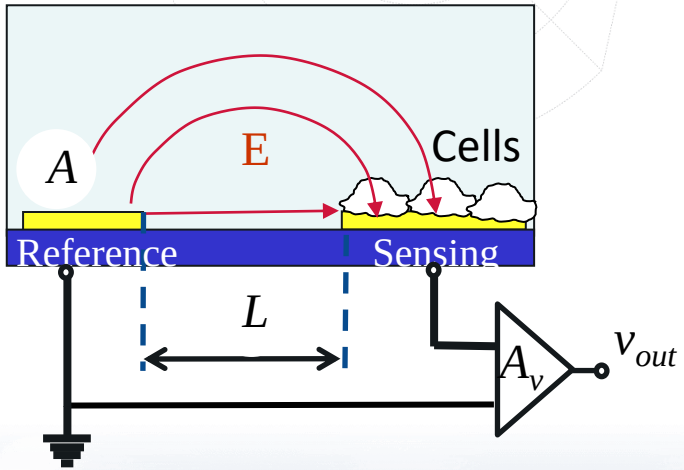
Design rules to optimize the sensor impedance

$$f_R = f(A, L)$$

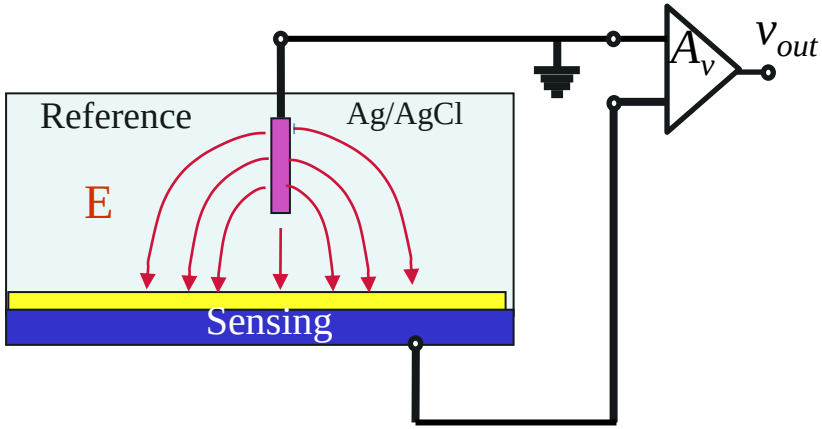
$$f_R = \frac{1}{2\pi R_E (C_D + C_B)}$$

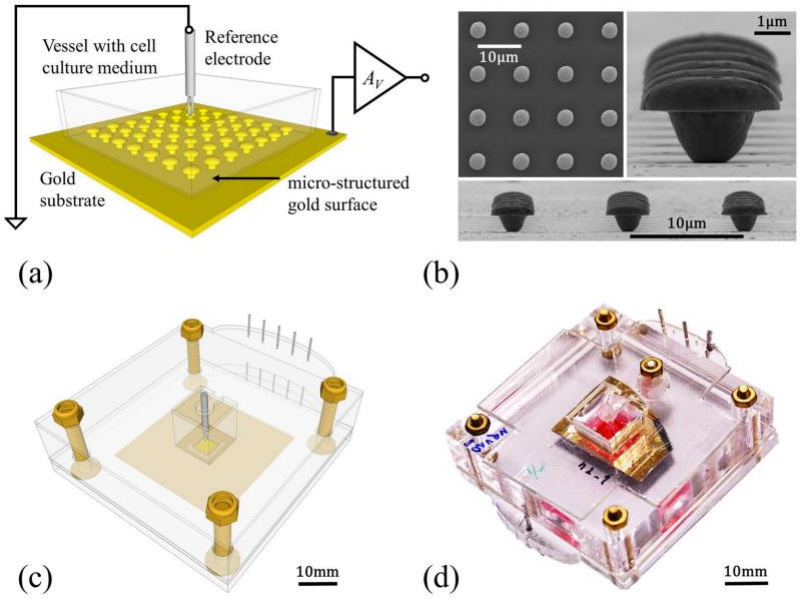
$$R_E = \rho \frac{L}{A}$$





Vertical configuration





SCIENTIFIC REPORTS

OPEN

Ultrasensitive gold micro-structured electrodes enabling the detection of extra-cellular long-lasting potentials in astrocytes populations

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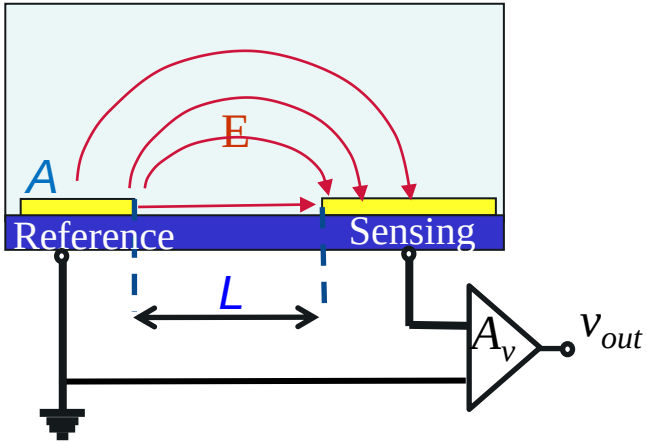
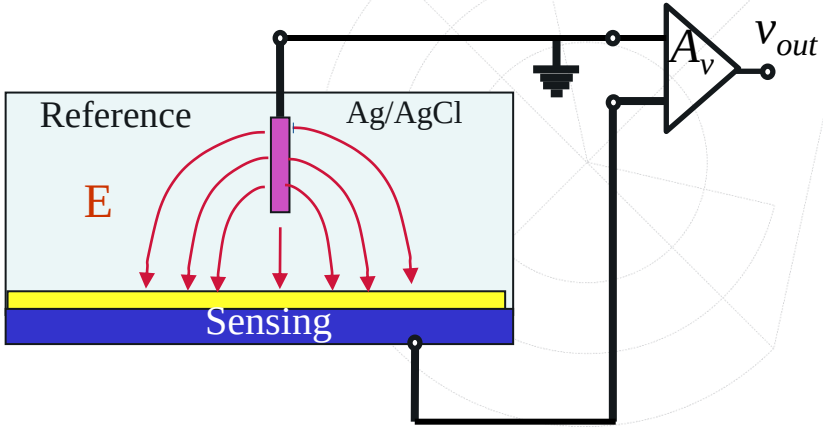
Ana L. G. Mestre[1,2], Mónica Cerquido[3], Pedro M. C. Inácio[1,2], Sanaz Asgarifar[1,2], Ana S. Lourenço[4,5], Maria L. S. Cristiano[1,6], Paulo Aguiar[7,8], Maria C. R. Medeiros[3], Inês M. Araújo[1,2], João Ventura[3] & Henrique L. Gomes[1,2]

Frontiers in Neural Circuits, Vol. 11 | Article 80

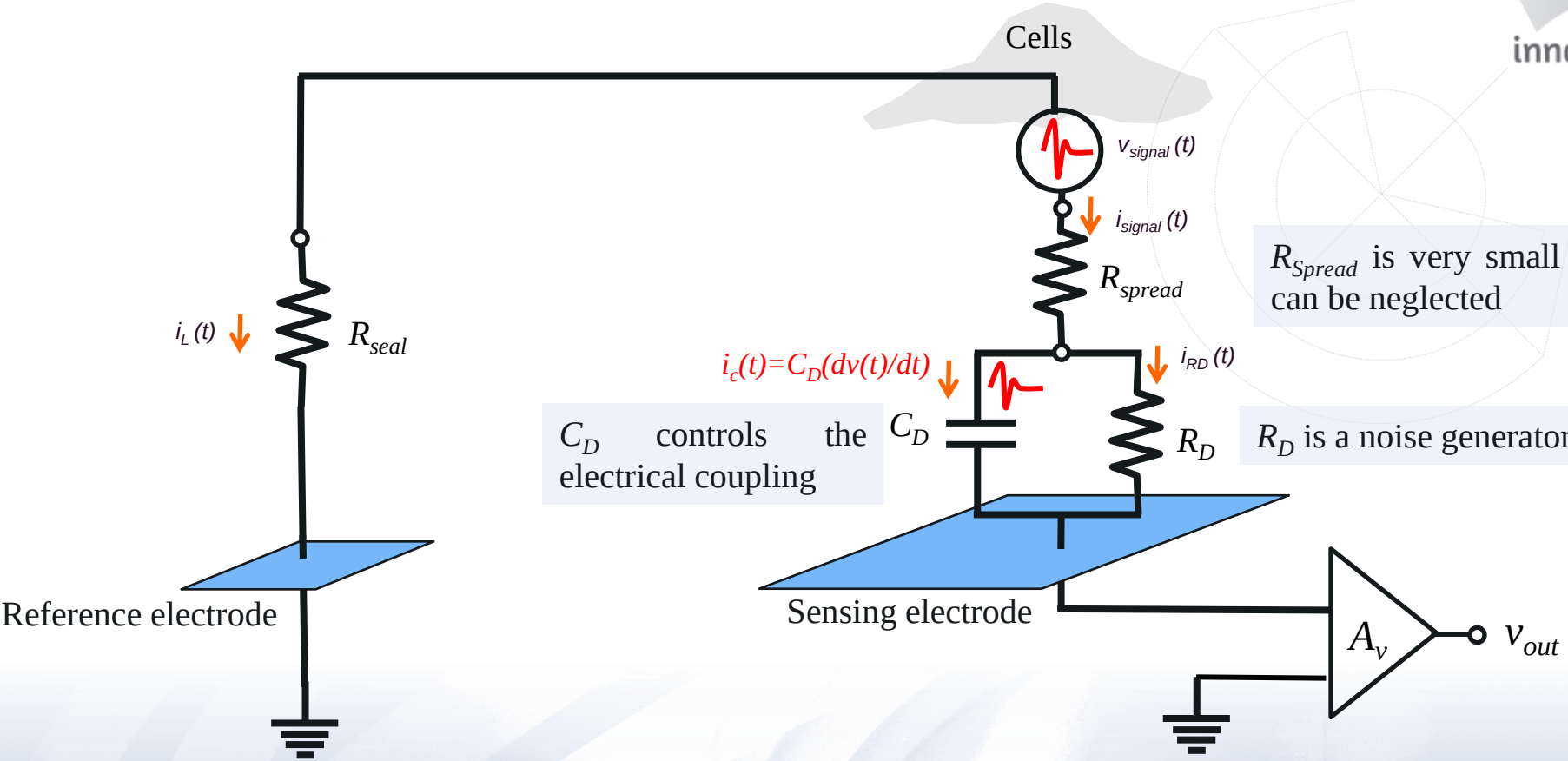
Planar and vertical electrode configurations





Co-planar systems perform better in terms of 1/*f* noise than vertical systems using Ag/AgCl.

The role of the impedance on the signal detection

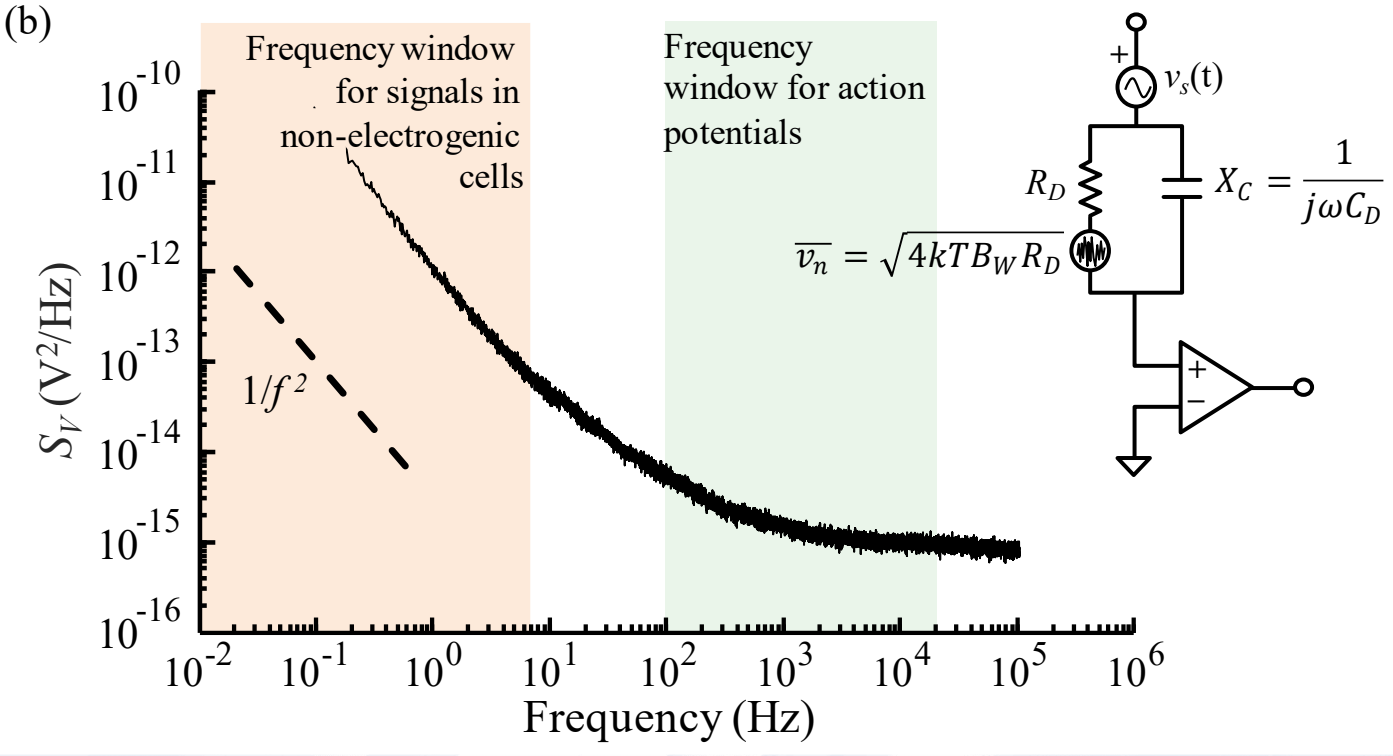


R_{Spread} is very small and can be neglected

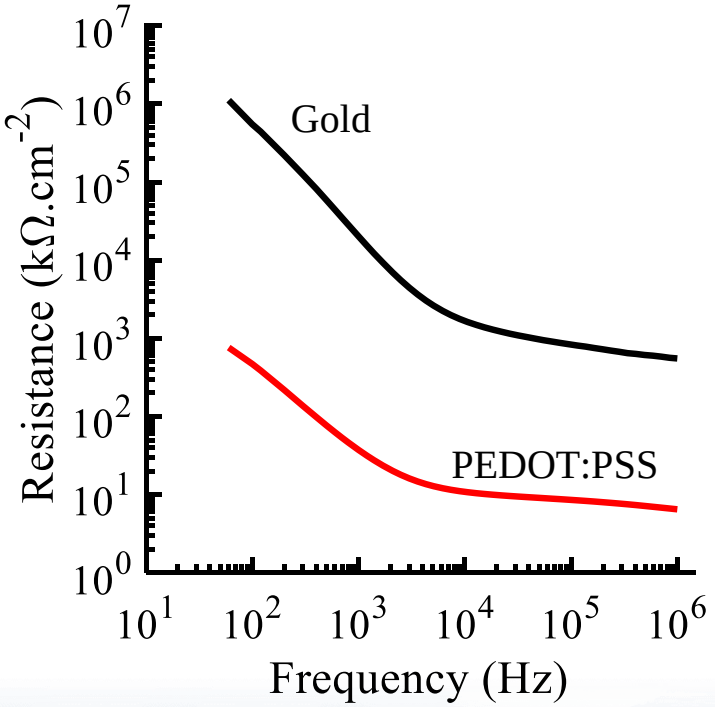
C_D controls the electrical coupling

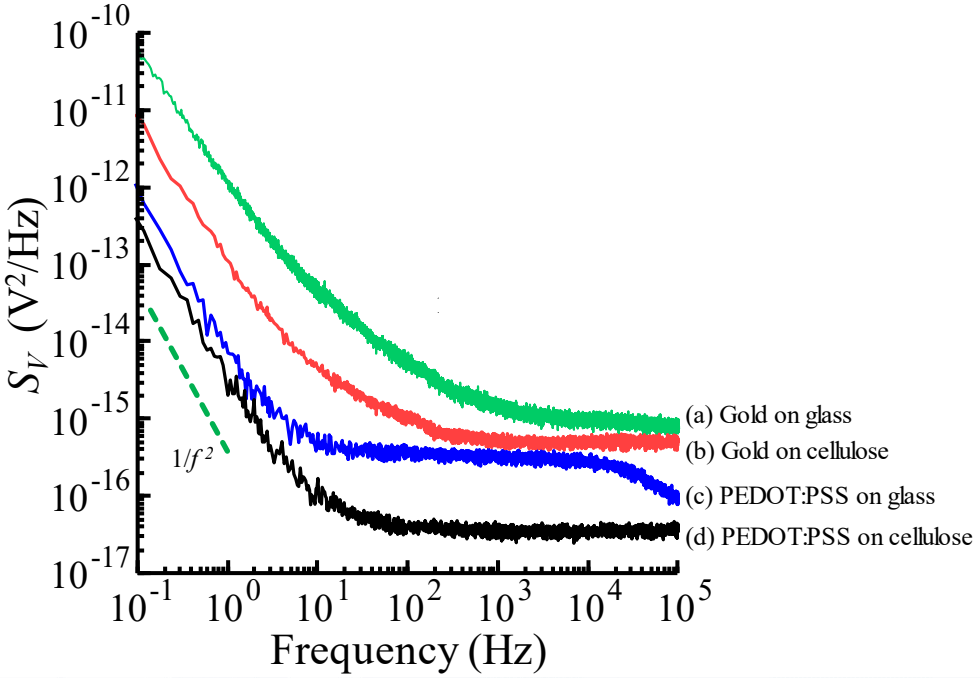
R_D is a noise generator

The importance of thermal and 1/*f* noise

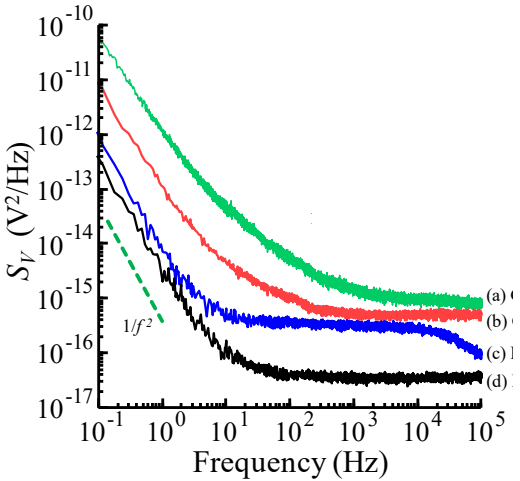


Interfacial resistance and intrinsic noise



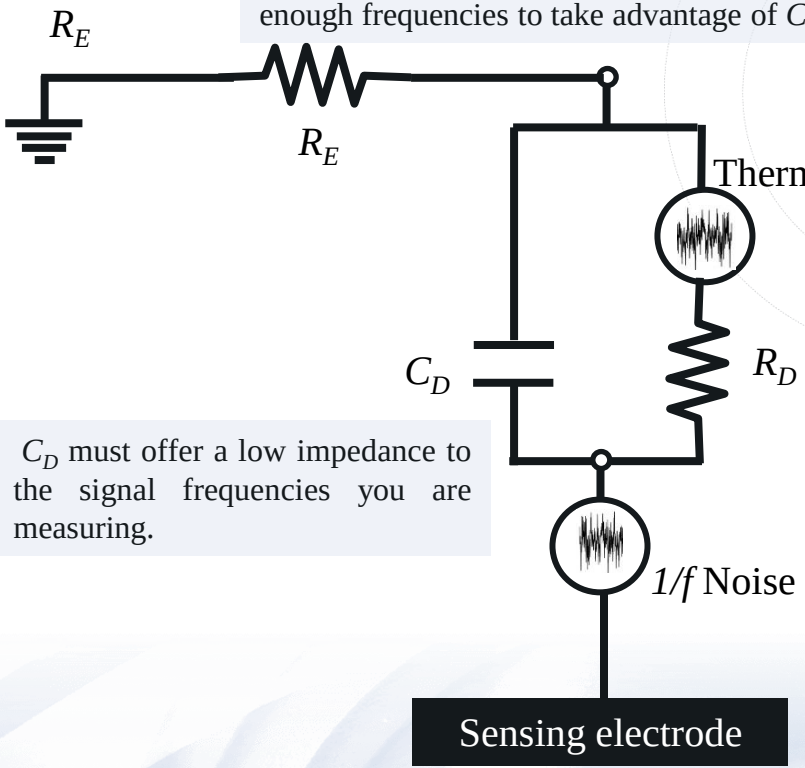


Design rules to maximize signal-to-noise ratio (SNR)



The noise curves shifts in a parallel fashion (lowering thermal noise also lowers 1/*f* noise).

R_E must guarantee a Maxwell-Wagner relaxation at high enough frequencies to take advantage of C_D.

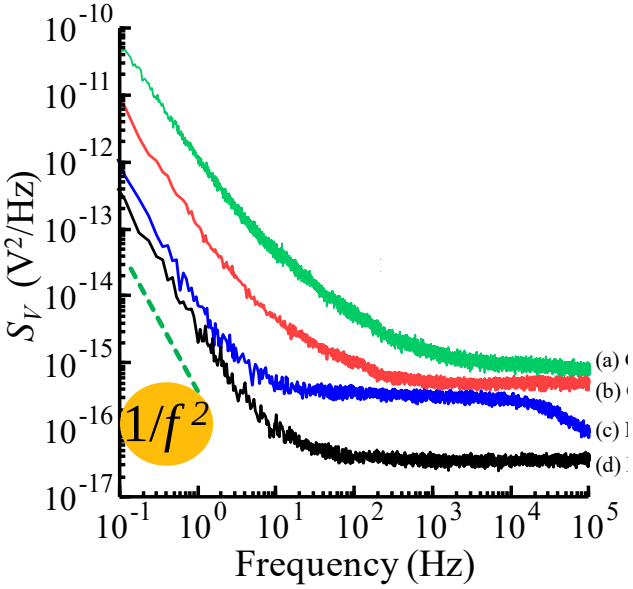


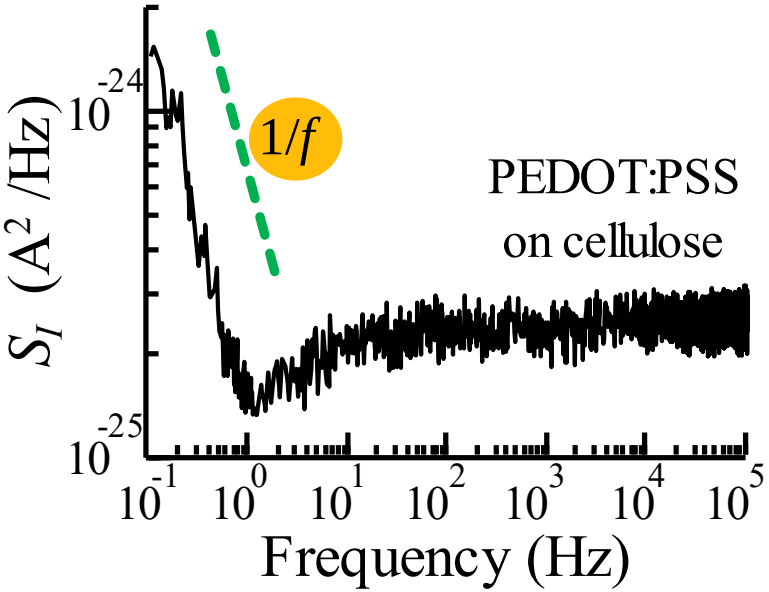
C_D must offer a low impedance to the signal frequencies you are measuring.

R_D must be small to minimize thermal noise.

(critical parameter in improving SNR).

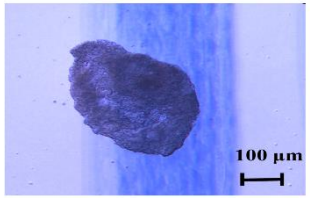
1/*f* noise in current and in voltage



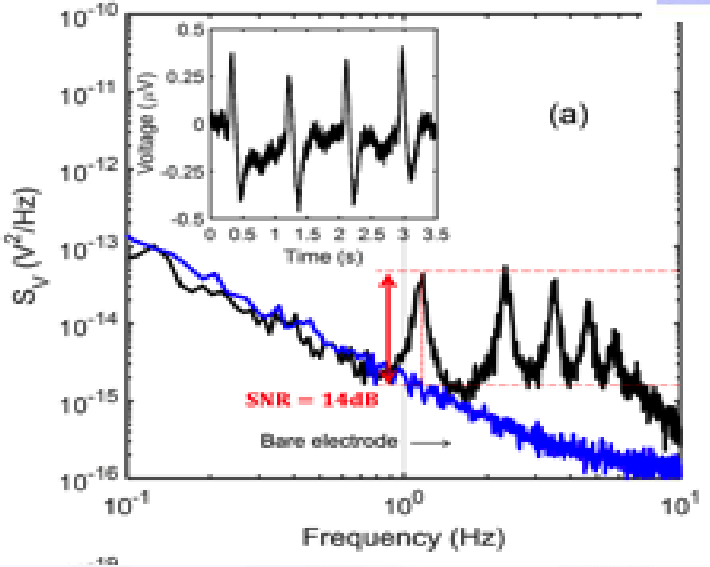


1/*f* noise in current and in voltage

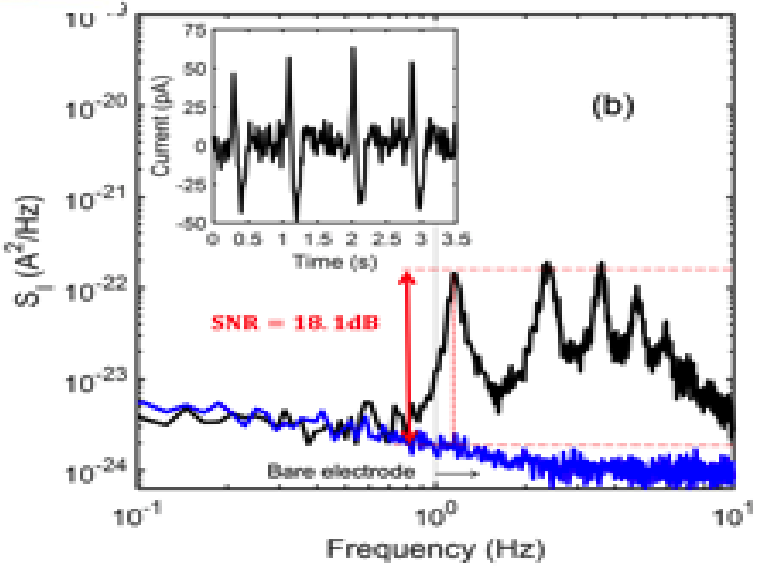
Embryoid body with autonomous cardiac contractile cells



IEEE SENSORS JOURNAL, VOL. 17, NO. 13, JULY 1, 2017

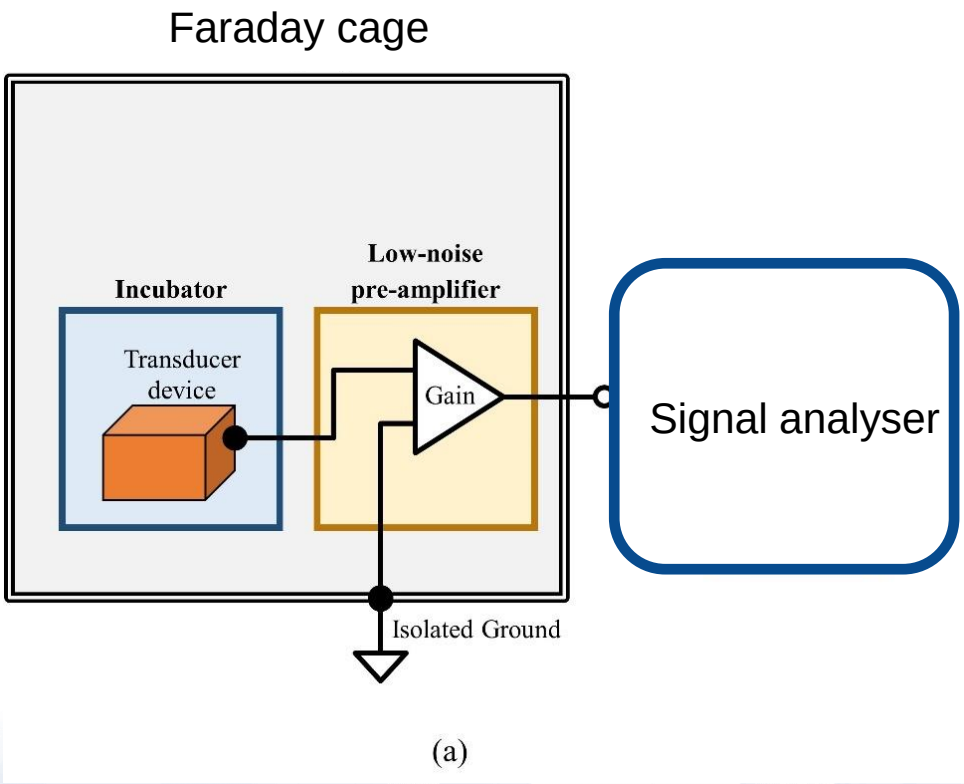


Signal detection in **voltage**

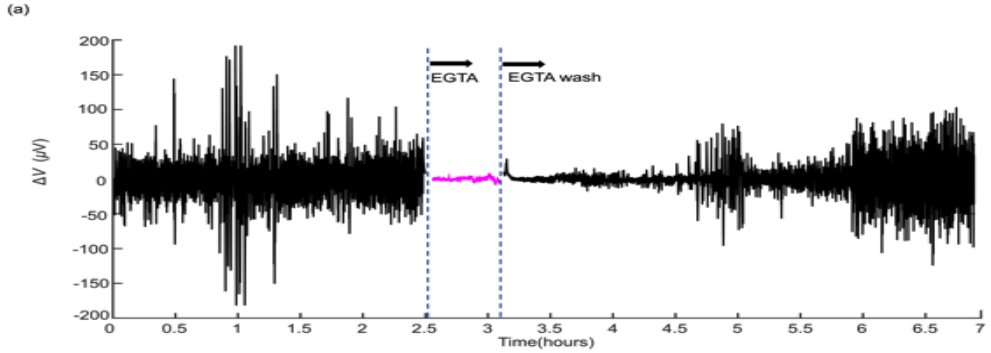


Signal detection in **current**

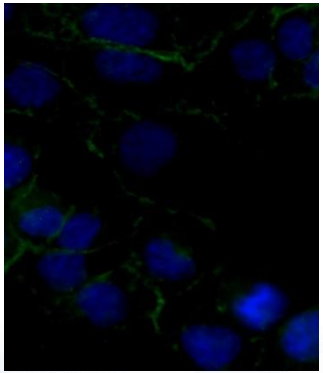
Experimental set-up

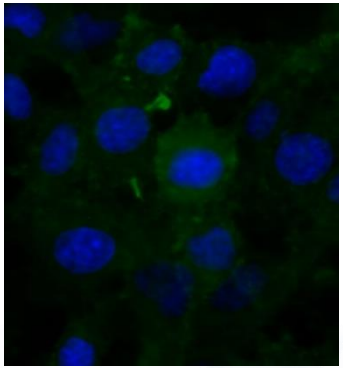


Non-excitable cells
Evidences for cooperative bioelectrical activity



Before adding EGTA

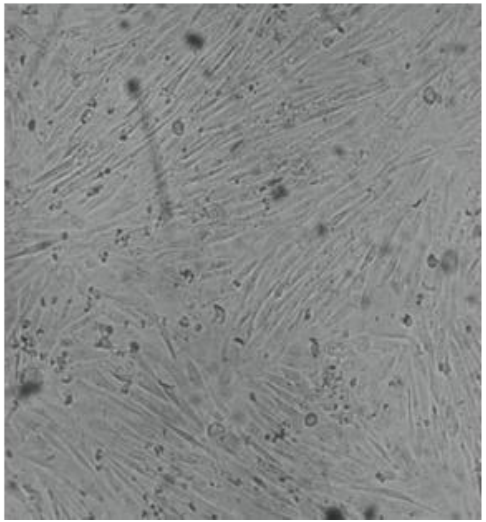


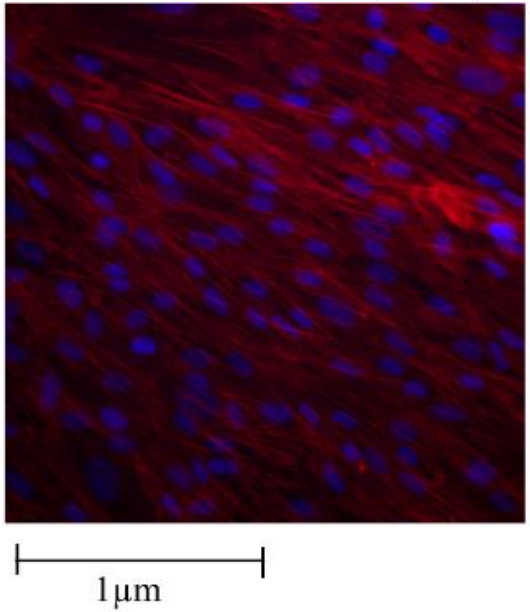


After EGTA exposure

Signals require the existence of cell-cell connections

Application:
Bioelectrical activity of dermal cells during wound healing

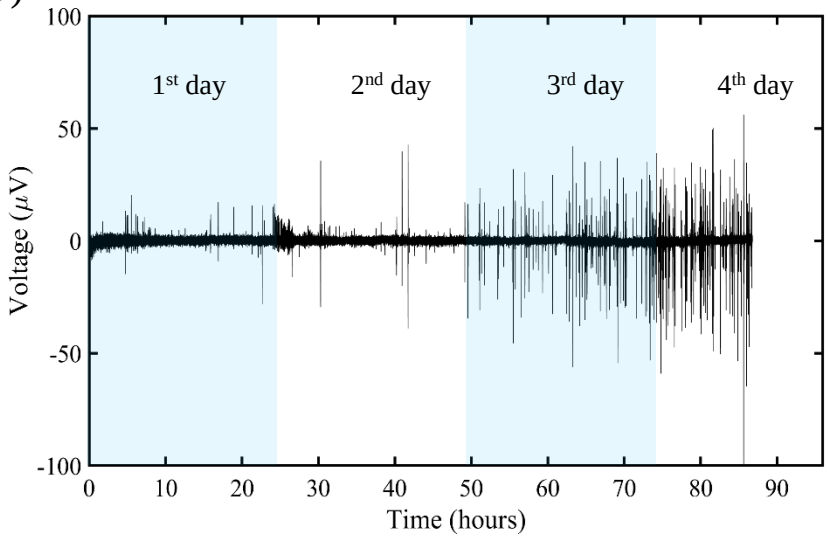




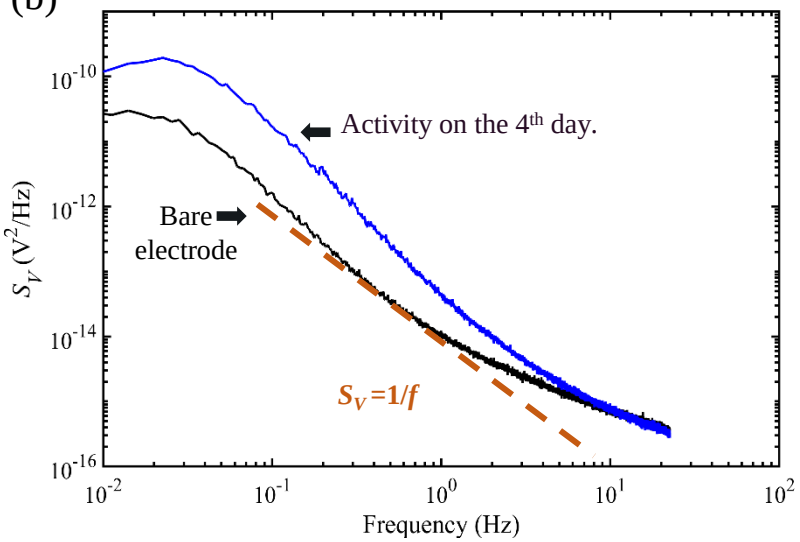
hTERT-immortalized fibroblast cell that was isolated from the foreskin of a male patient.

Spontaneous activity of dermal cells

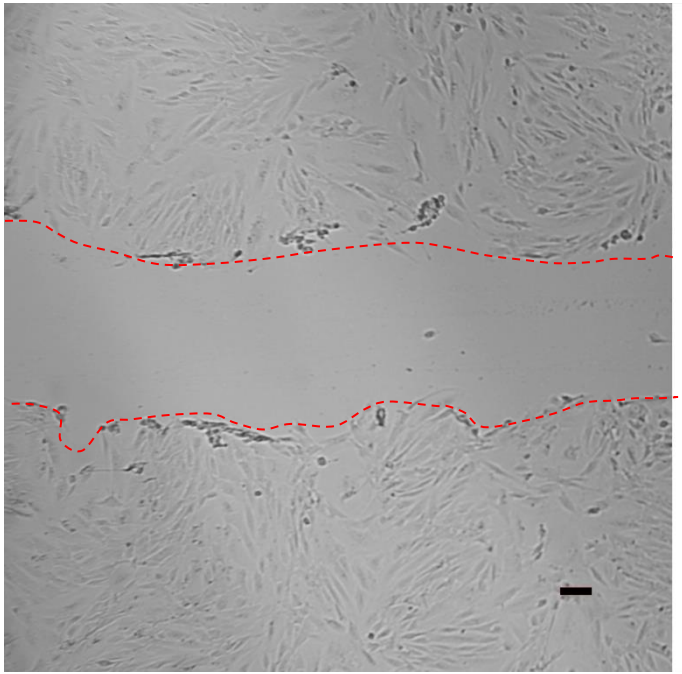
(a)

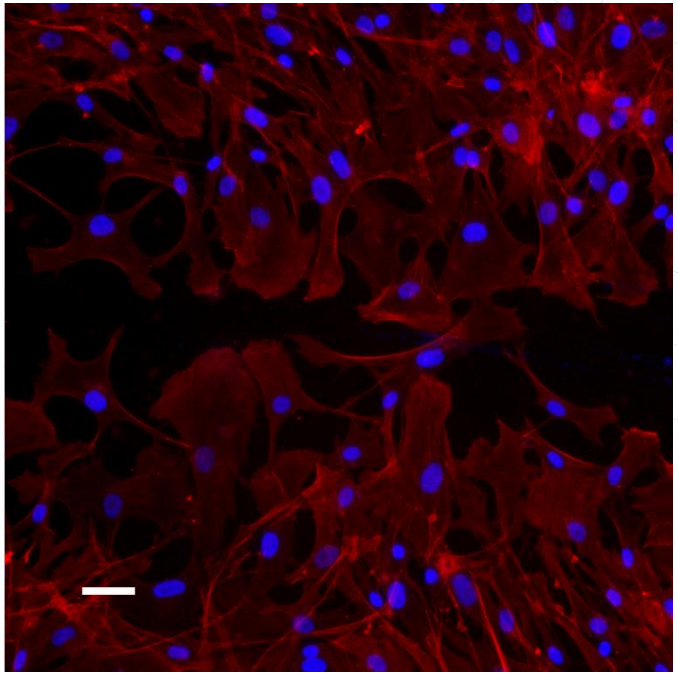


(b)

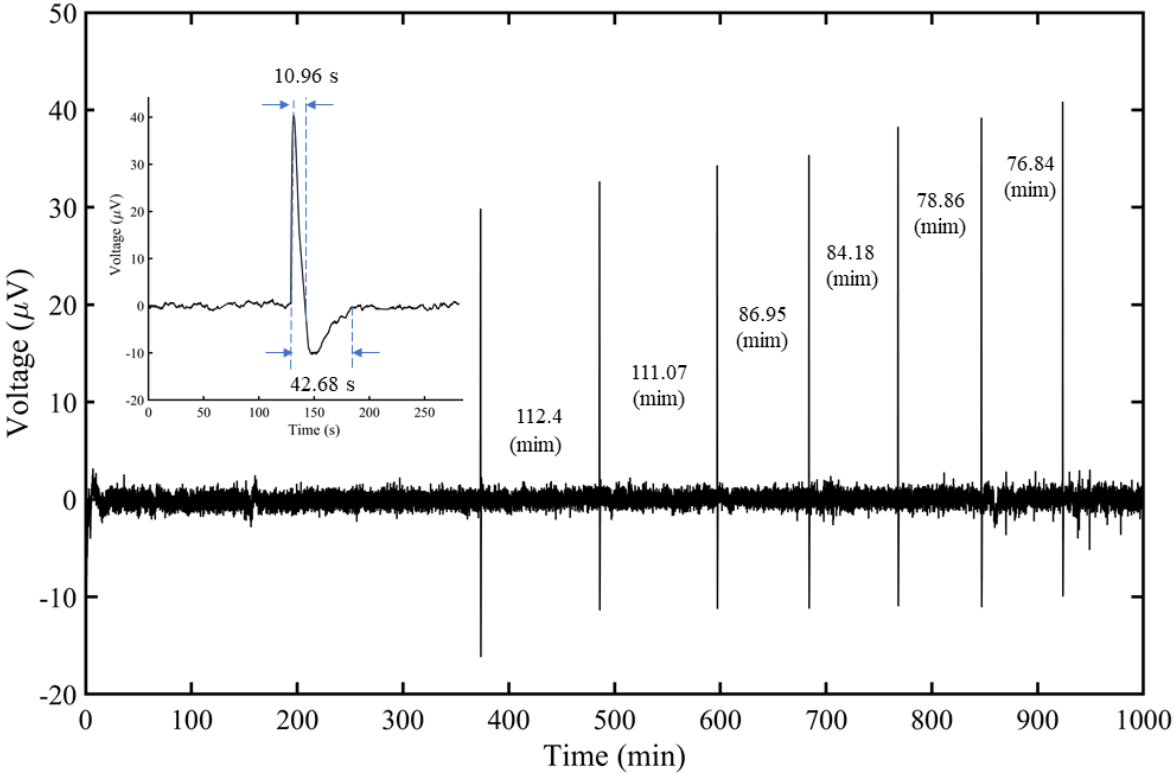


Wound in a confluent cell population

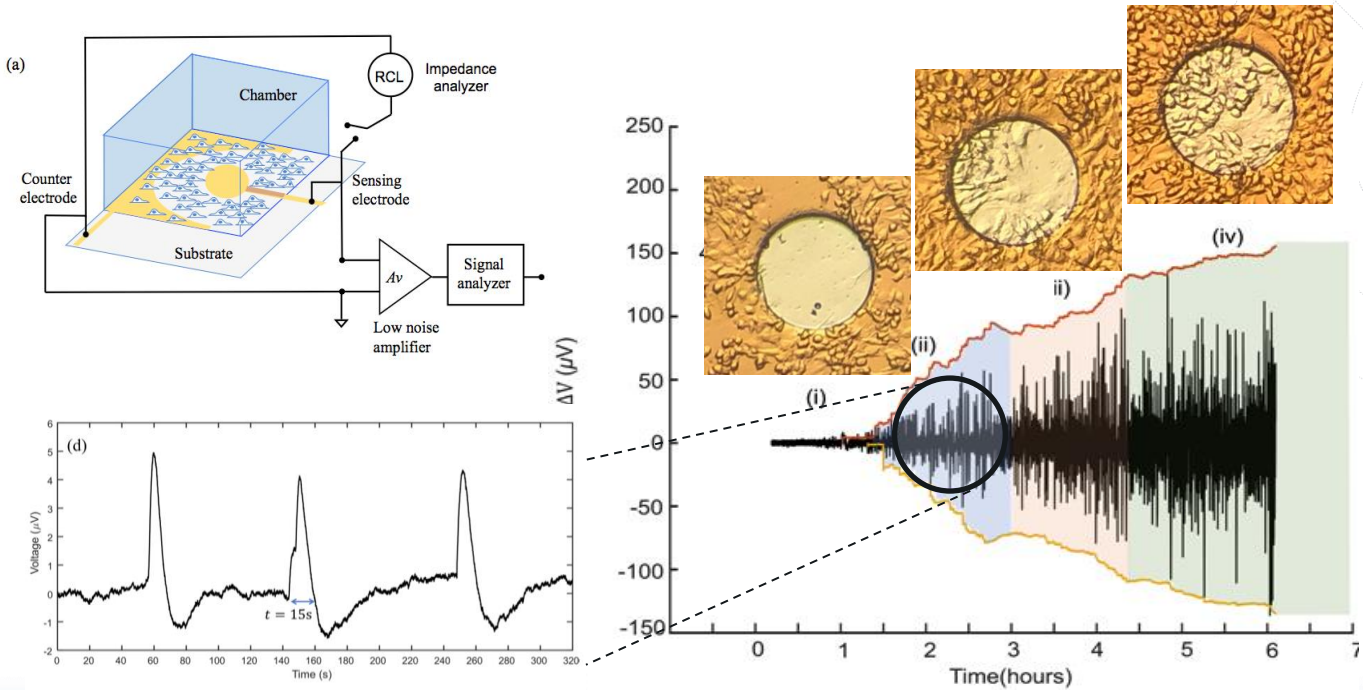




Biological clock activated by a wound ?



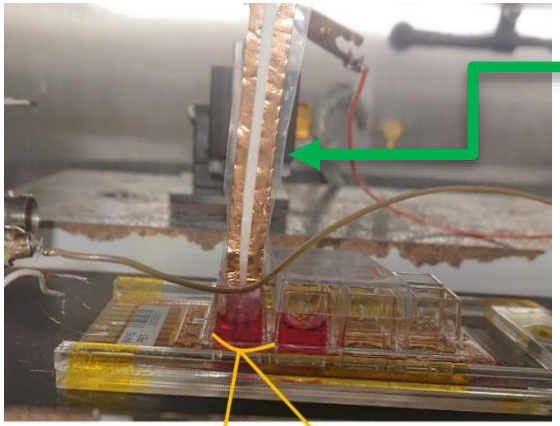
Application: Cancer cell migration

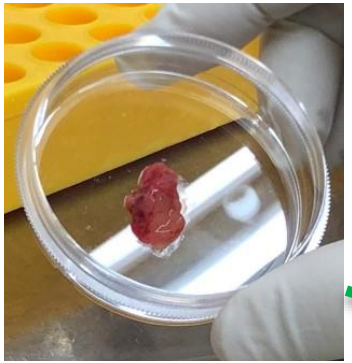


S. Asgarifar, et al. Biosensors and Bioelectronics 145 (2019) 1117082

Application:
bioelectrical activity of a glioblastoma (ex-vivo)

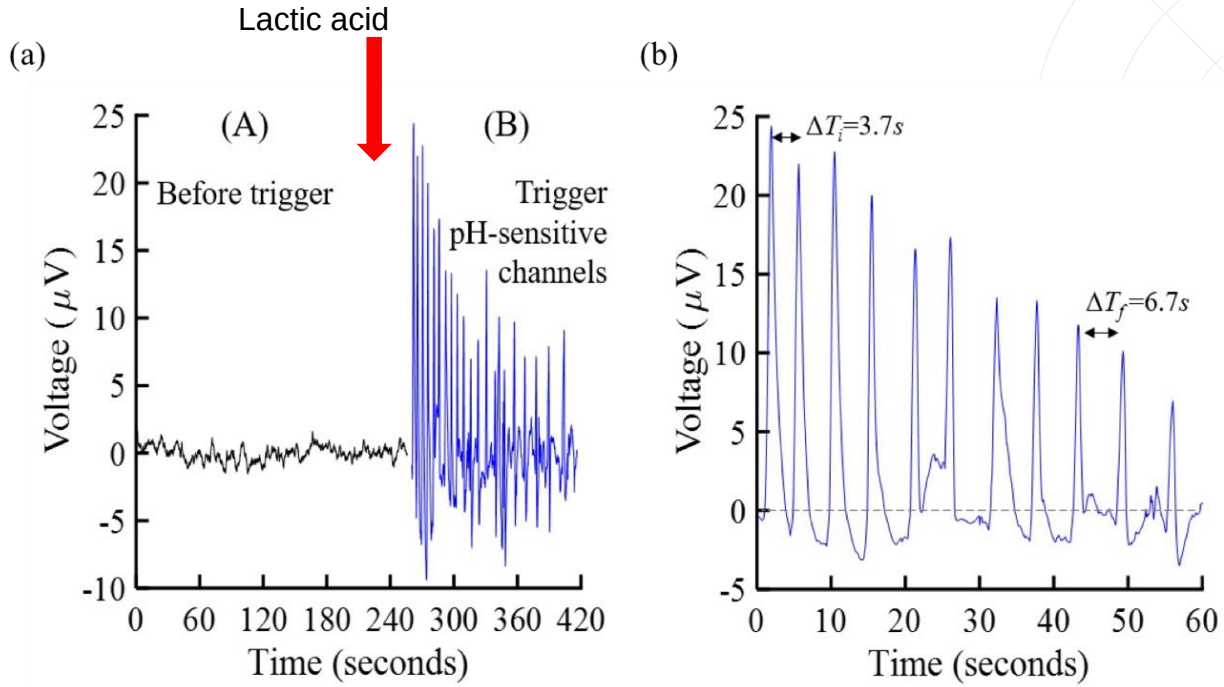
PEDOT:PSS on bacterial cellulose





Resected *ex-vivo* human glioblastoma tumour

Application:
Bioelectrical activityof a glioblastoma (ex-vivo)



Application;
bioelectrical activity of a glioblastoma (ex-vivo)

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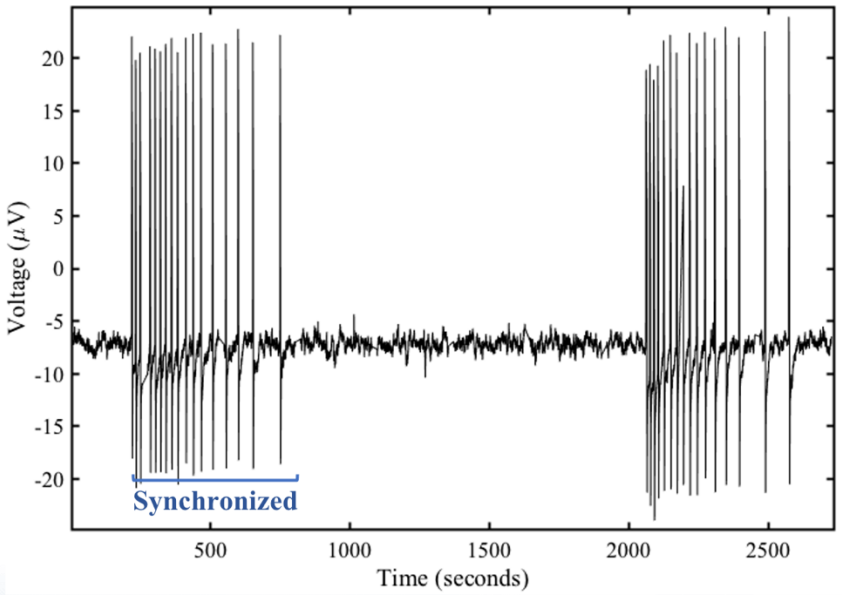
(a)



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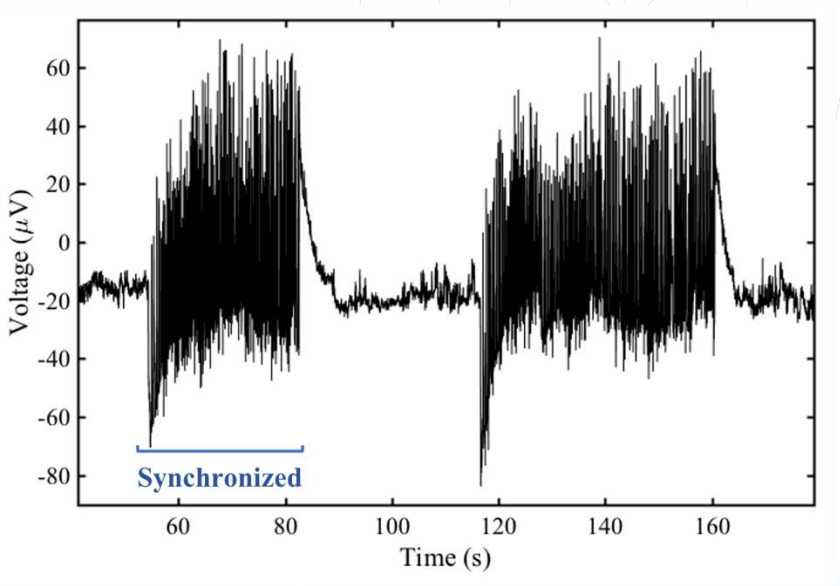
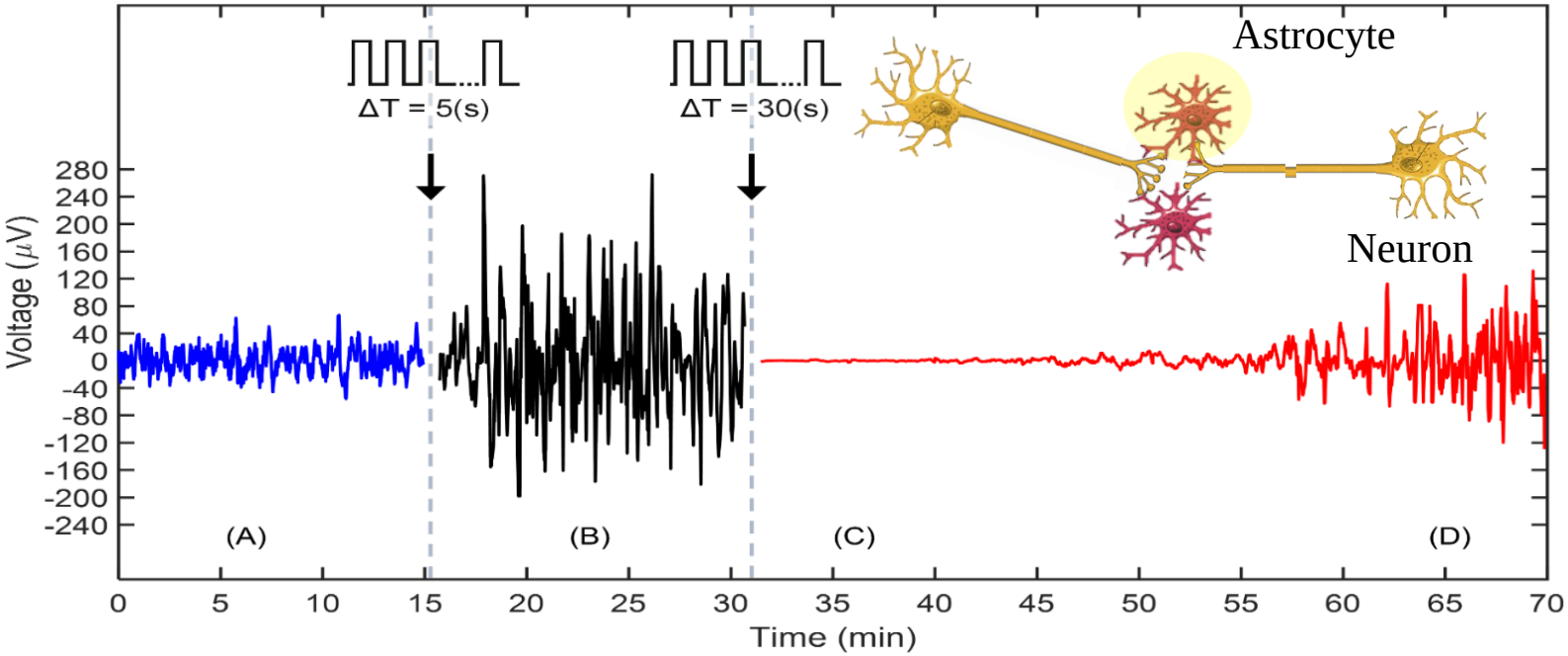


Electrical stimulation of astrocytes populations



Conclusions

- Conductive polymers form an electrical double layer that has a low interfacial resistance, resulting in minimal intrinsic thermal noise

- This low noise level in the electrode allows for the detection of ultra-weak bioelectrical signals that were previously unattainable.

Is it possible to decipher the language of the cells and establish a two-way communication with cells and tissues for therapeutic devices?

Acknowledgements


Maria Medeiros


Leonor Cancela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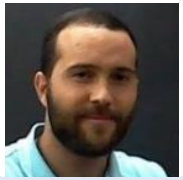
Inês Araújo

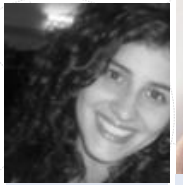

Deborah Power

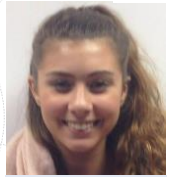

Ana Mestre


Pedro Inácio


Youssef Elamine


Sanaz Asgarifar


Rute Félix


Rita Monteiro

Thank for you attention

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