Electrical Cell Biology Workshop

Bio Electrical Engineering Innovation Hub at Warwick

UNIVERSITY OF BATH

Detecting minuscule electrical activity of cell populations

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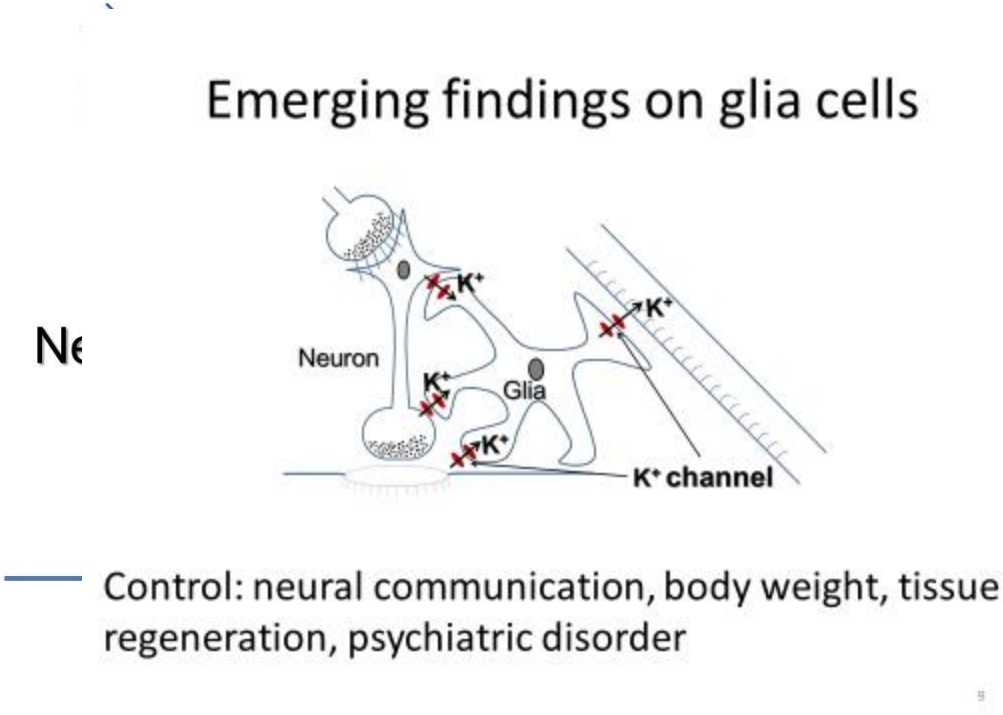
Session 4: Electro-biophysics and bioengineering

29th March, 2019

Motivation

- Brain tumours are the biggest cancer killer of children and adults under 40
- Over 5,000 people lose their lives to a brain tumour each year
- Brain tumours reduce life expectancy by on average 20 years – the highest of any cancer
- Glioma is the most aggressive form of brain cancer
    - **Epileptic seizures**

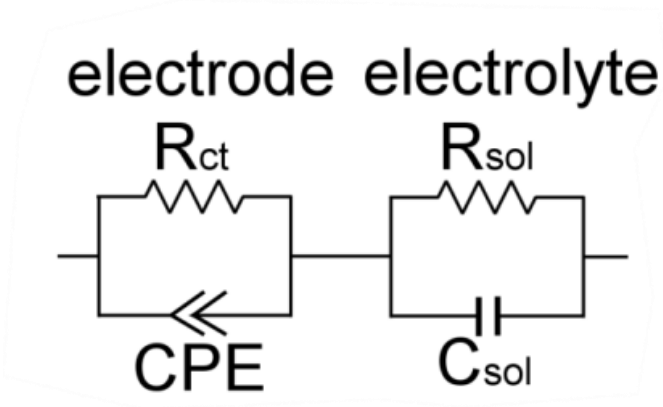
Emerging findings on glia cells



Control: neural communication, body weight, tissue regeneration, psychiatric disorder

Characterization of sensitive transducers

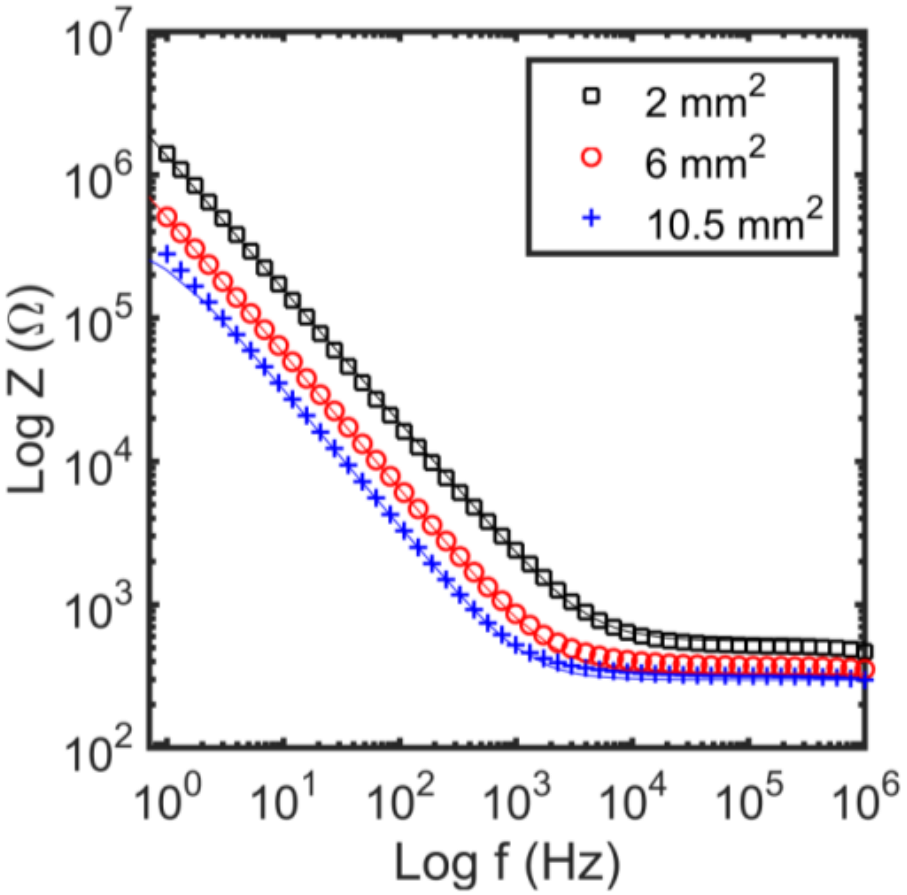
Noise and impedance analysis of Au/Electrolyte



$$Z' = R_{sol} + R_{ct}\left(\frac{1 + R_{ct}Q\omega^{n}\cos(n\pi/2)}{1 + \left(R_{ct}Q\omega^{n}\right)^{2} + 2R_{ct}Q\omega^{n}\cos(n\pi/2)}\right)$$

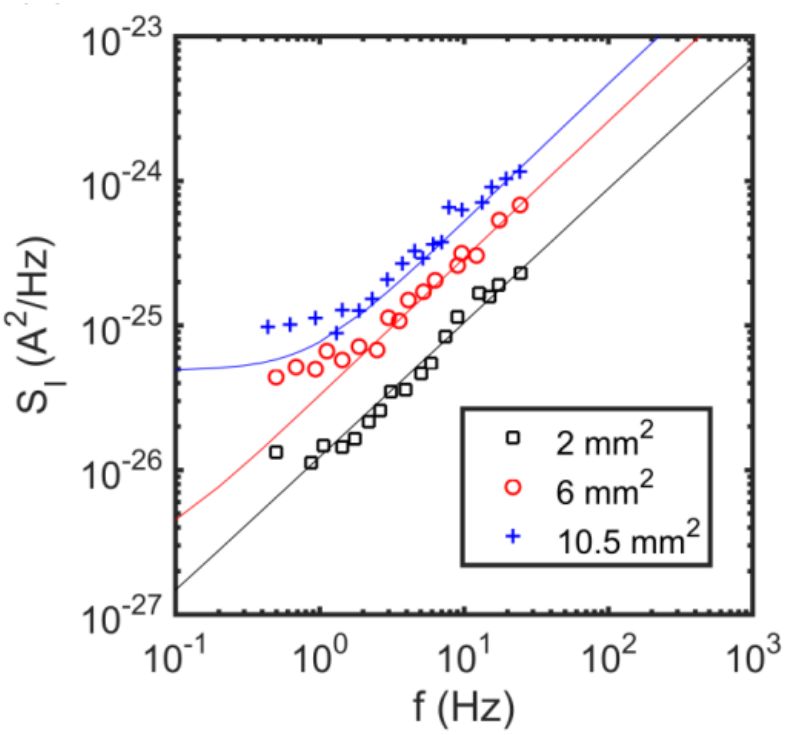
Characterization of sensitive transducers

- Noise and impedance analysis of Au/Electrolyte



Characterization of sensitive transducers

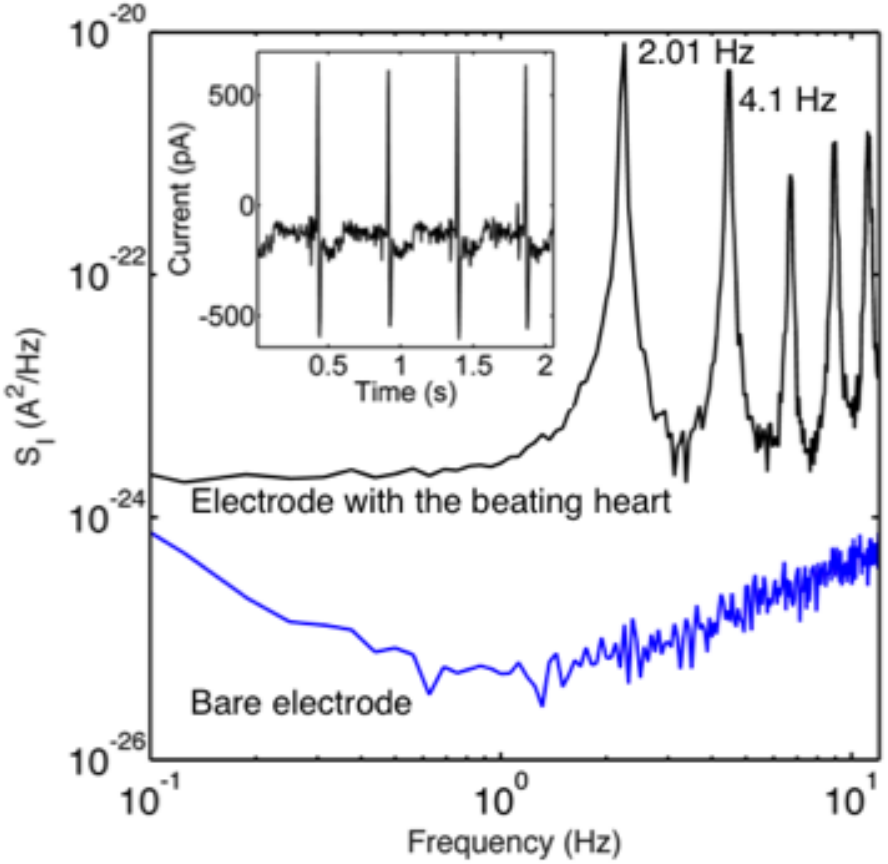
$$S_I(\omega) = 4kTY'(\omega)$$



Background noise is mainly due to the Re($Y_{electrode}$)

Rocha *et al*, *Scientific Reports , 2016, 6, 34843*

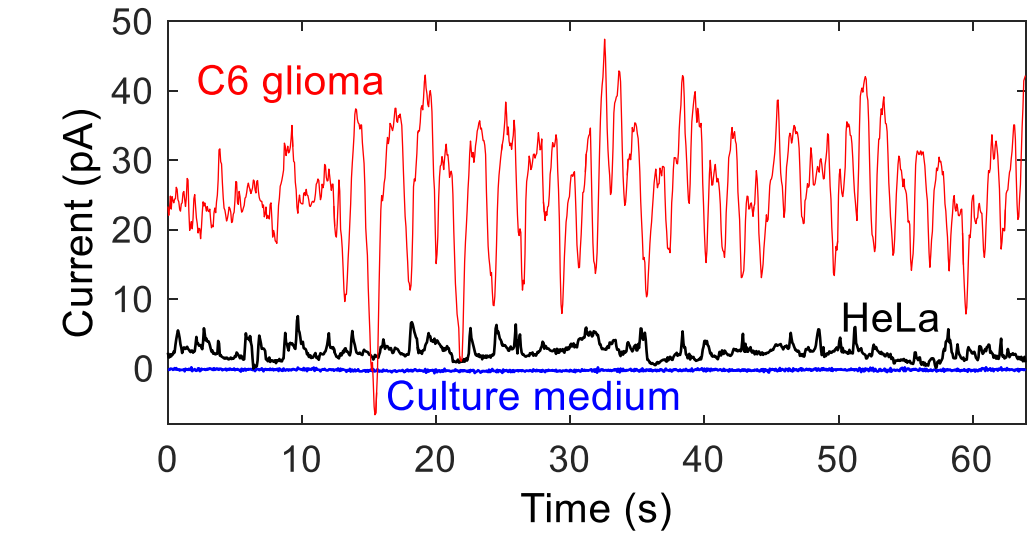
Benchmark - Zebra fish heart

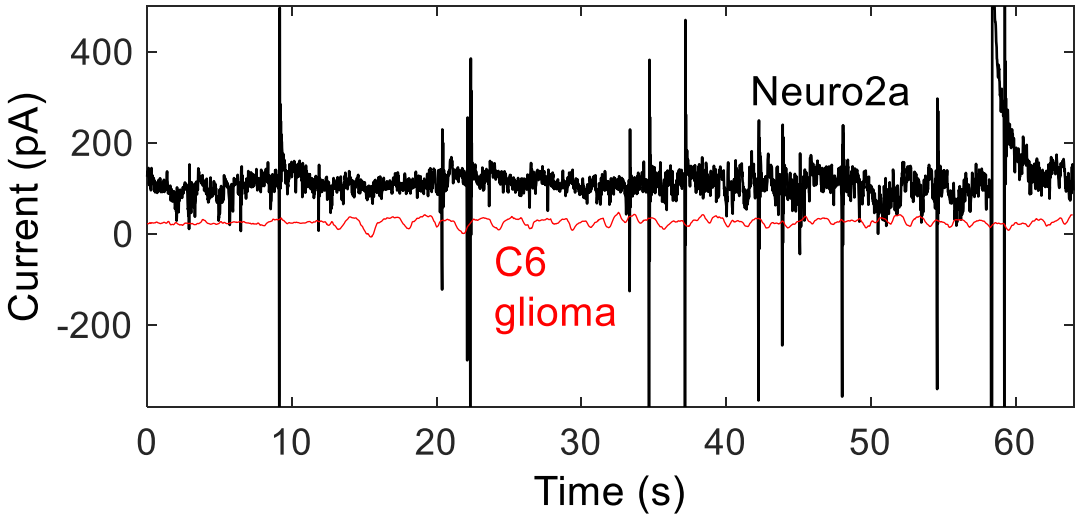


- Measure electrically quiescent cells
  - HeLa cells and Glioma cells

Medeiros et al, Sensing and Bio-Sensing Research, 2016,10, 1-8

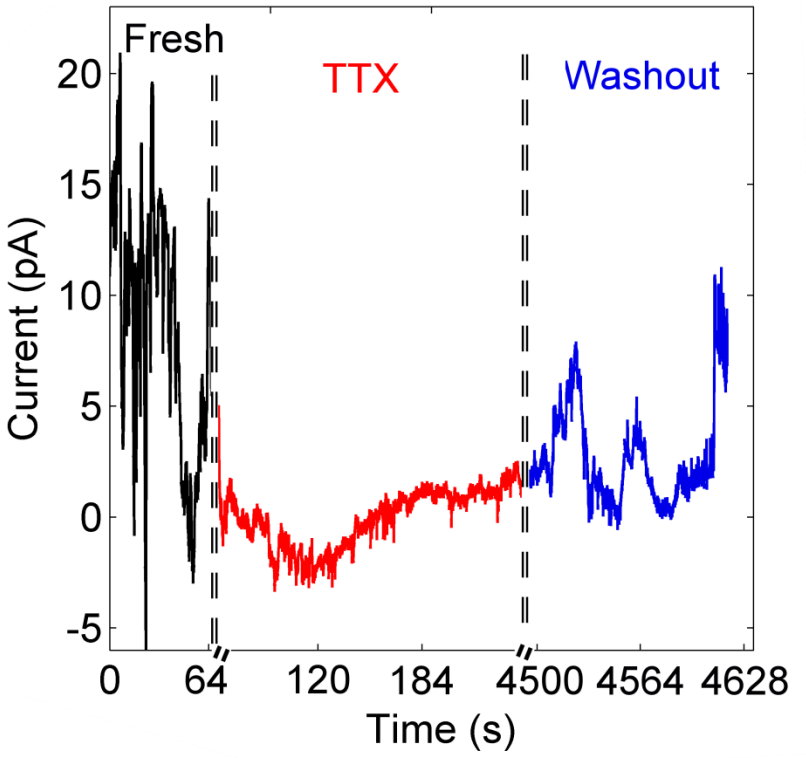
Setup validation

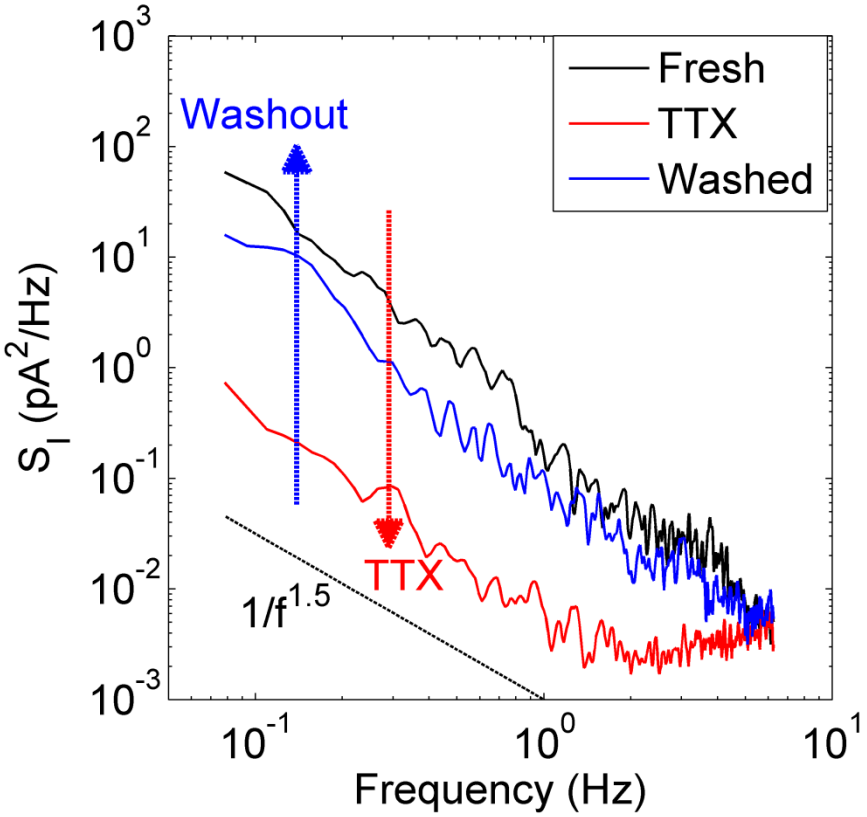




Rocha et al, J. Mater. Chem. B, 2015,3, 5035-5039

Inhibiting Na^+ channels using tetrodotoxin



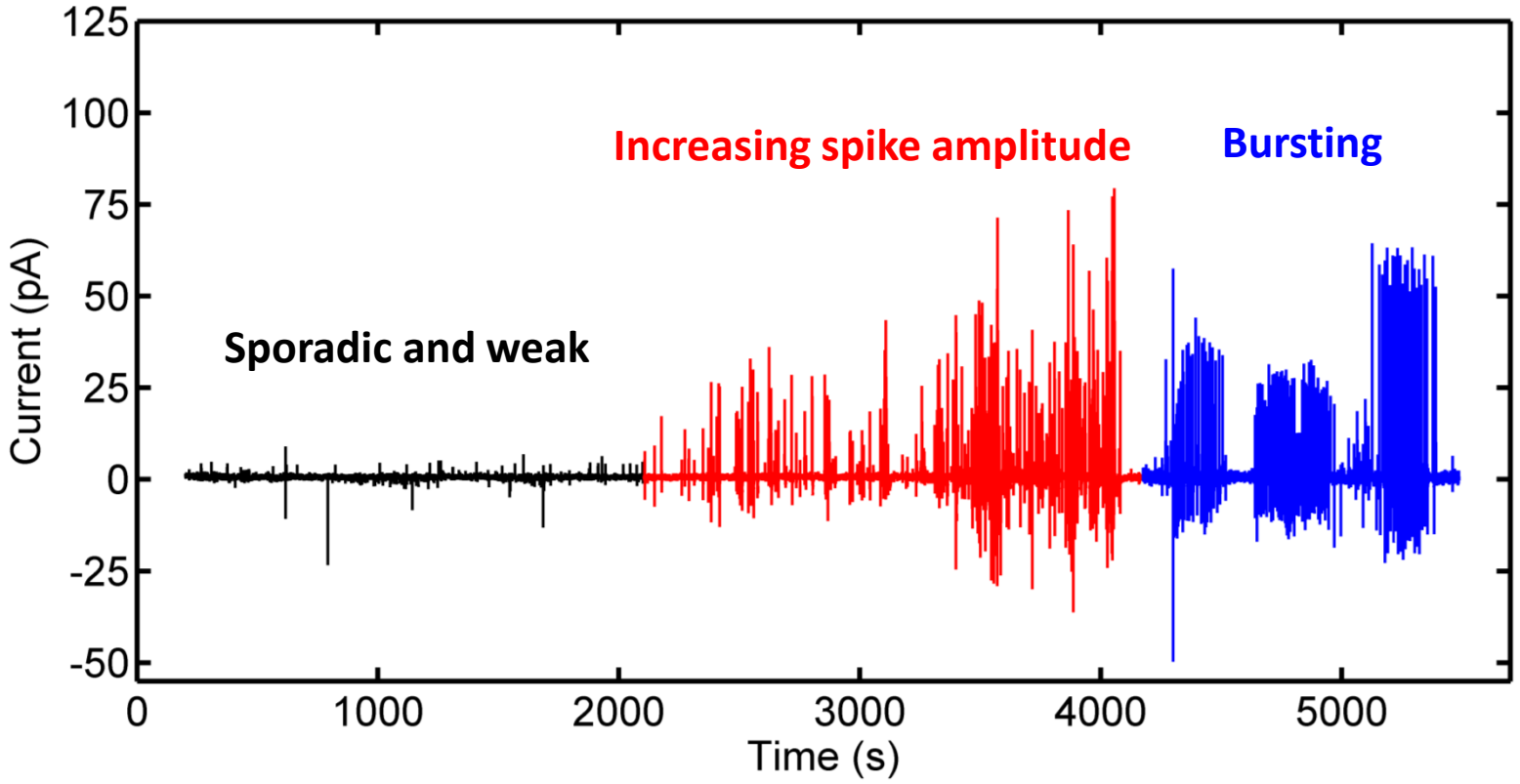


Glioma communication is primarily caused by the opening of voltage-gated Na^+ and K^+ ion channels

Efficiently abolished with specific pharmacological inhibitors.

Rocha et al, J. Mater. Chem. B, 2015,3, 5035-5039

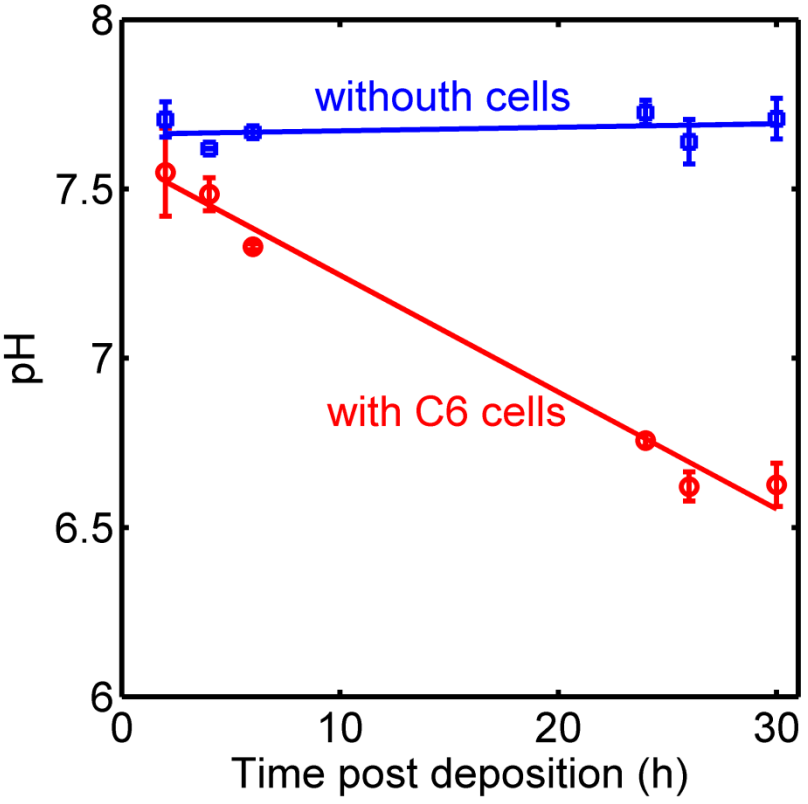
Evolution of current signal

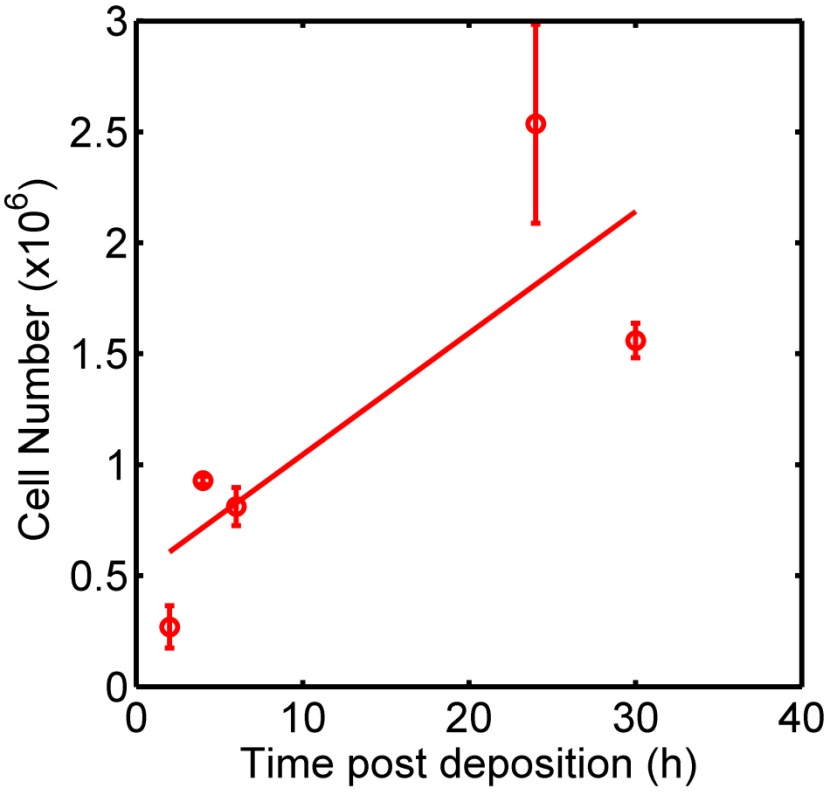


Electrical fluctuations of glioma cells unexpectedly evolve with time to an bursting activity

Rocha et al, Science Advances 2016, 2, 12, e1600516

pH inspection

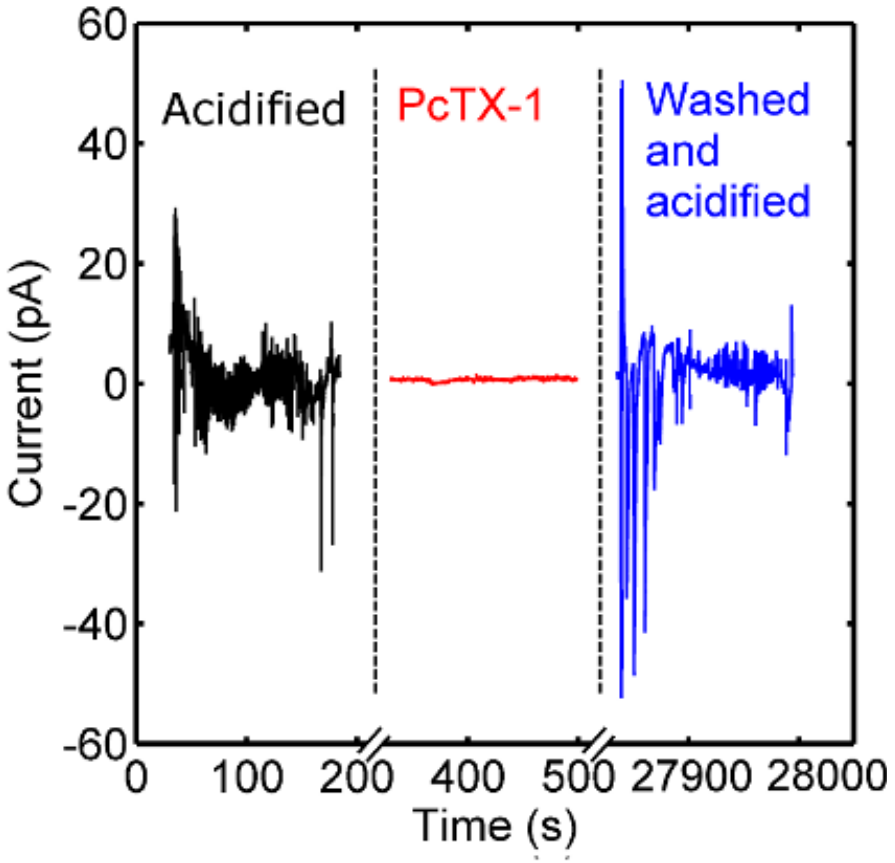


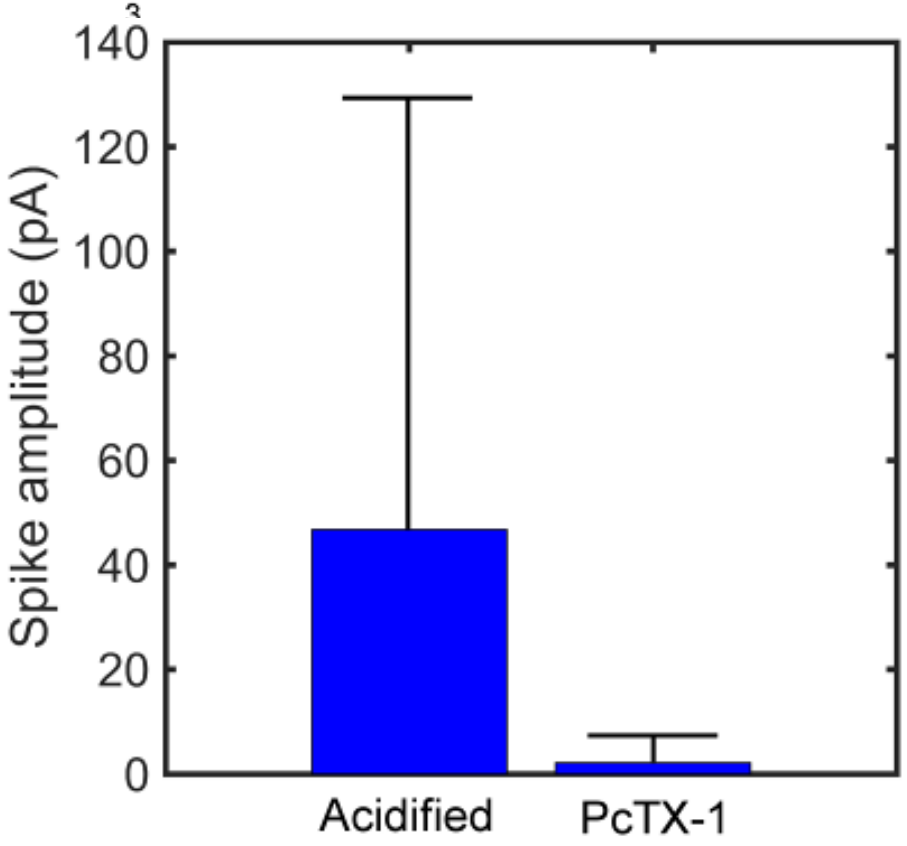


- Not apoptosis; Ph change

Rocha et al, Science Advances 2016, 2, 12, e1600516

Role of Acid Sensing Channels





Electric bursting is prompted by extracellular pH changes

Conclusions

- We have develop a highly sensitive system
- We can measure cancer cells communicating
  - Basal communication is primarily caused by the opening of voltage-gated Na^+ and K^+ channels in Glioma
  - Electrical detection reveals a cooperative bursting upon acidification
    - Link with pH triggered Ca^{2+} waves?
- A unique approach for studying electrophysiological properties of large cancer cell populations as an *in vitro* reference for tumour bulks *in vivo*

Acknowledgements

Bio Electrical Engineering Innovation Hub at Warwick

Imperial College London

Boehringer Ingelheim

PHILIPS

Holst Centre
Open Innovation by imec and TNO

DPI
DUTCH POLYMER INSTITUTE

Newbury Electronics

UNIMORE
UNIVERSITÀ DEGLI STUDI DI MODENA E REGGIO EMILIA

TU Delft

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UCL

Thank you for your attention