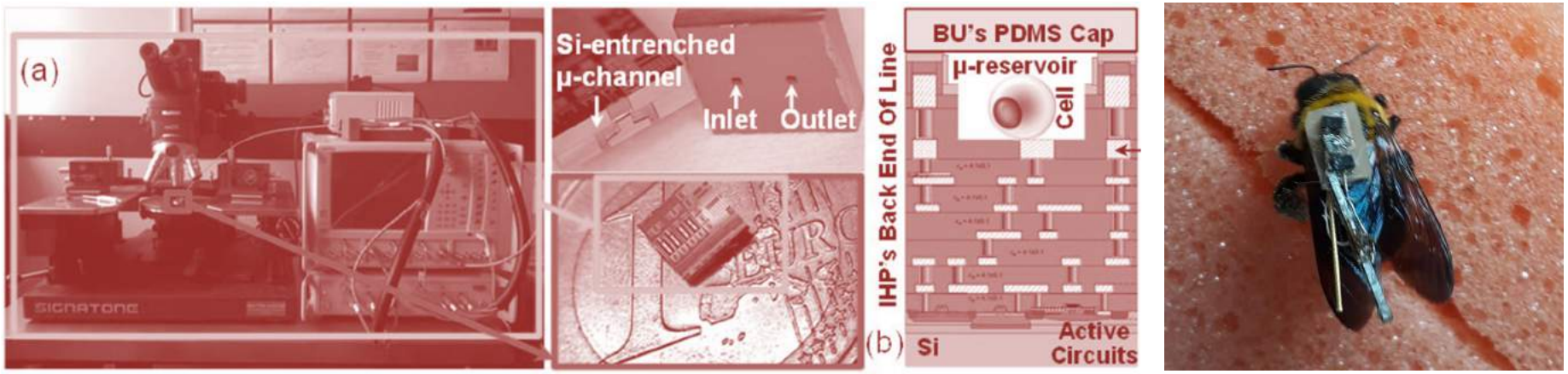
Cardiff, 22/10/2018



Tiny chips: from bee wearable electronics to cancer stem cells seek and destroy

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Outline

- Introduction: Multiphysics, multiscale problems
- Insect tracking
- Fluid characterization
- Cell tracking and stimulation

My research group

- Dr Nissar Karim: lab-on-chip module for cell stimulation
- Ilan Davies, PhD Candidate @ Creo: Hi-V ns pulse generator

- Jake Shearwood, PhD candidate: bee tracking /harvester
- Nawaf Alqathani, PhD Candidate : nanomaterials, Asian Hornet tracking

A word of winsdom

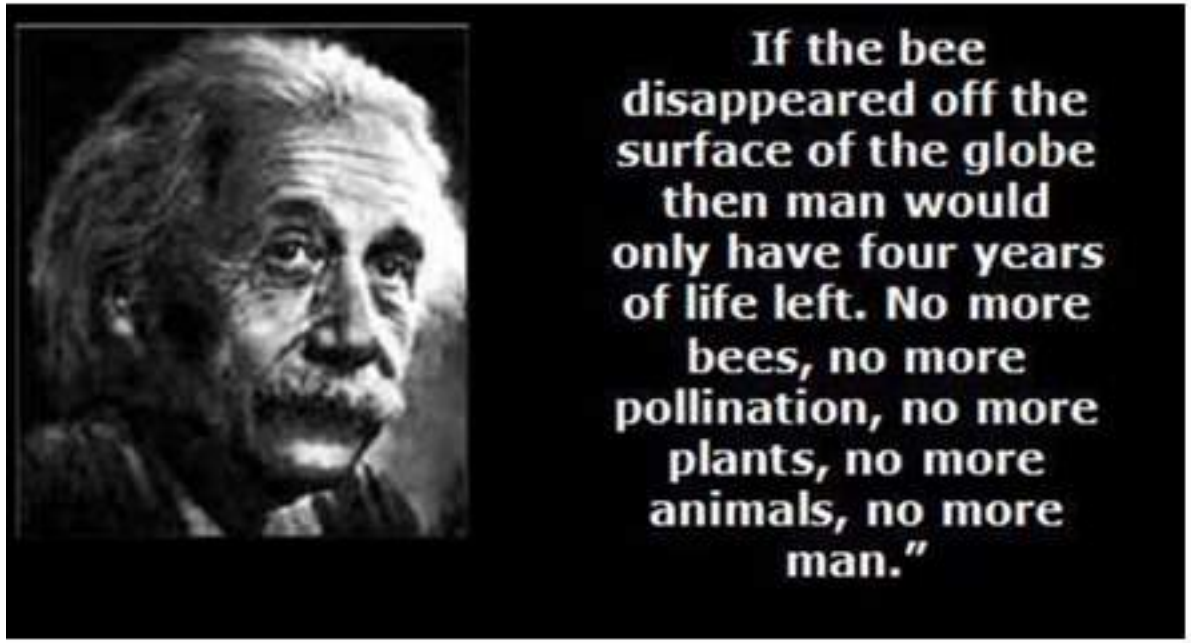
- *“According to recognized aero technical tests, the bumblebee cannot fly because of the shape and weight of his body in relation to the total wing area. The bumblebee doesn't know this, so he goes ahead and flies anyway. “*

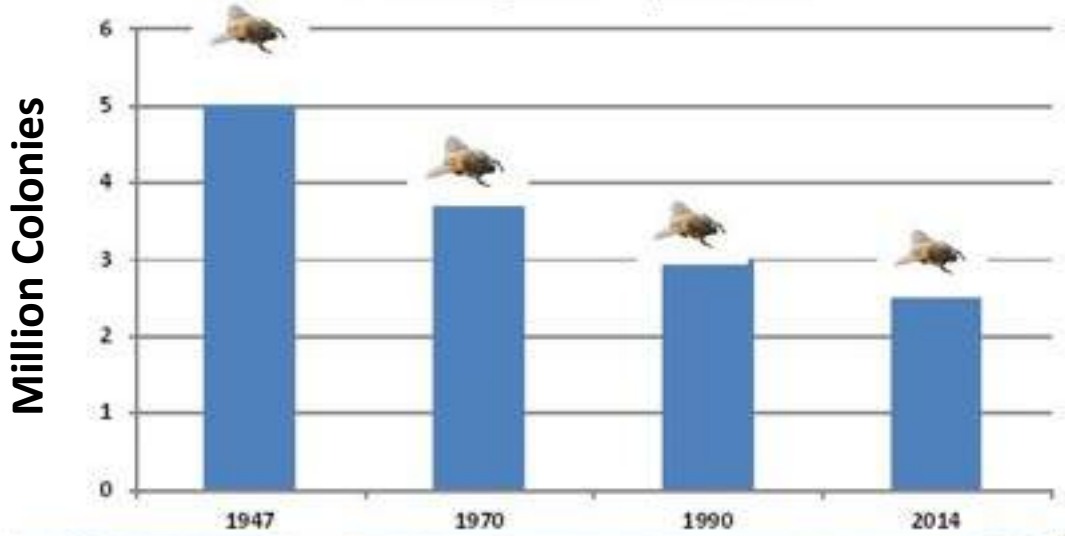
Igor Sikorsky, aircraft designer, aviation pioneer

Insect Tracking Projects

Motivation to bee tracking projects

Colony collapse disorder has ignited efforts to understand spatial interaction of bees with their environment






Your produce choices
without bees

Bee telemetry: state of the art

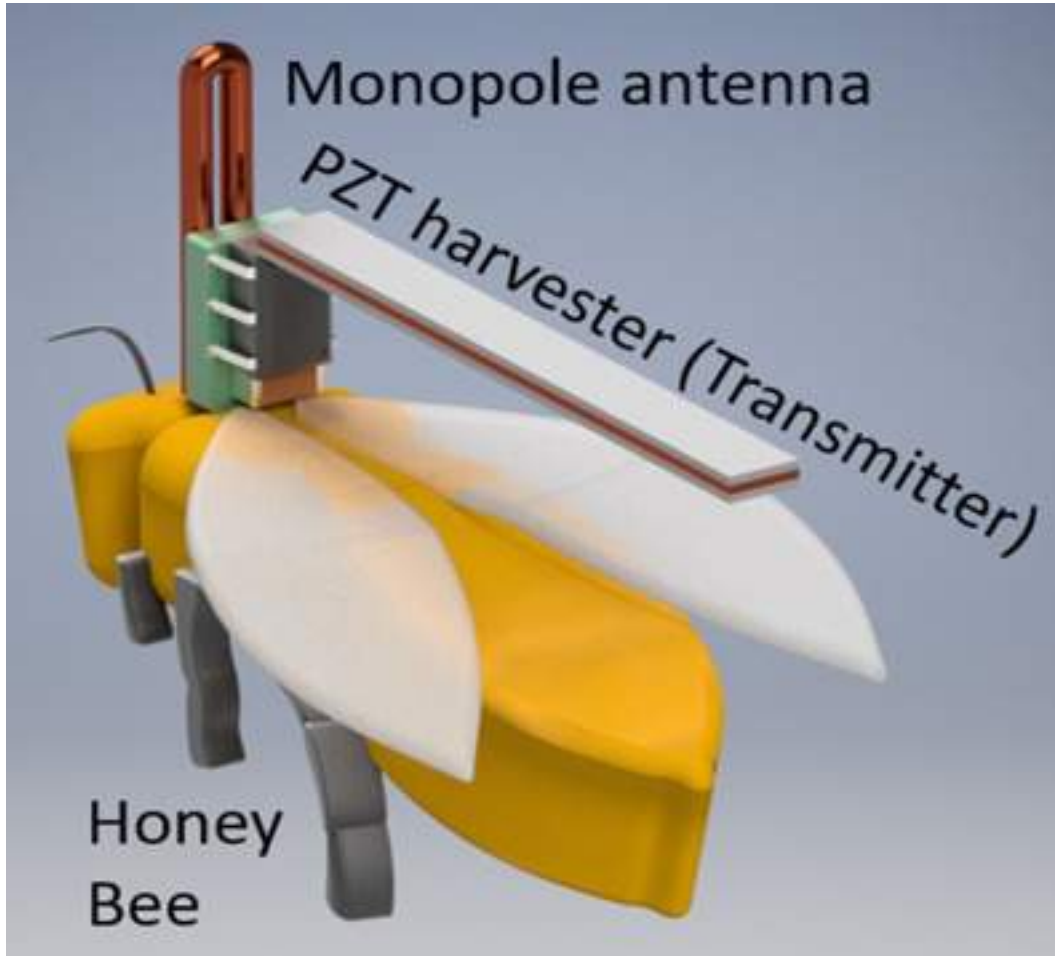
Current technologies cannot track bees across their entire foraging range

Harmonic radar tags

RFID

Radio telemetry

Bee tracking approach



- We are developing a battery-less radio telemetric approach, whilst pursuing significant weight and size reduction
- Honey bee location is determined by a compact portable scanning system analysing the received signal strength from a bee-wearable transmitter

2 distinct approaches and projects

Tracking drone:
Receiver

Tracking drone:
Transmitter and Receiver

A. Mellifera

Honey and bumble bee backpack:
Energy Harvester and Transmitter

V. Velutina

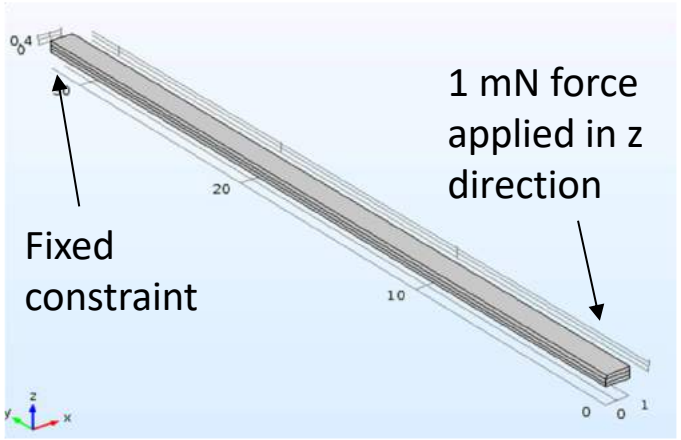
A. Mellifera

Asian hornet nanoparticle coating:
Passive scatterer

Energy Harvesting from bee flight

- Due to ease of device miniaturization, fabrication process and power generation at small sizes, piezoelectric energy harvesting was chosen
- By directly exciting the piezoelectric beam tip the generated power can be calculated:

$$P = \frac{V_{RMS}^2}{R_{LOAD}} = \frac{9}{64} \cdot \frac{E_p d_{31}^2}{\varepsilon} \cdot \omega_{ACT} \cdot K_{SPRING} \cdot Z_{PEAK}^2$$



Ambient source	Power density (μW/cm³)
Solar	Outdoor:15000 Indoor:10
Vibration	Electrostatic: 50~100 Electromagnetic:119 Piezoelectric: 250 Magnetostrictive:606
Thermal	60 (at 5°C gradient)

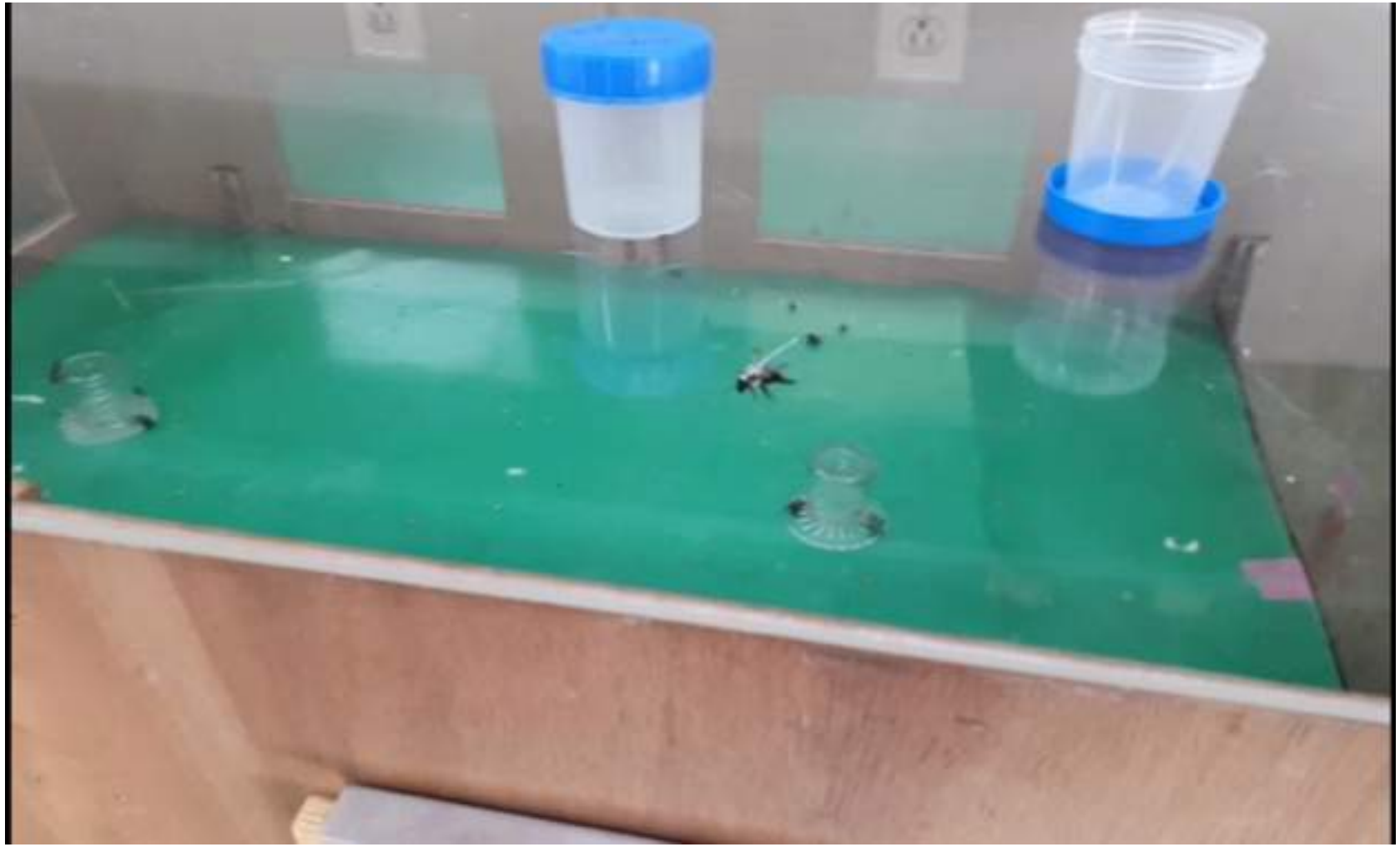
Demonstration of piezoelectric energy scavenging from insect flight

$$P = \frac{V_{RMS}^2}{R_{LOAD}}$$

Average force produced during flight is can be used to estimate a power output of 3.66 µW

Power measured across optimal load = 3.6 µW

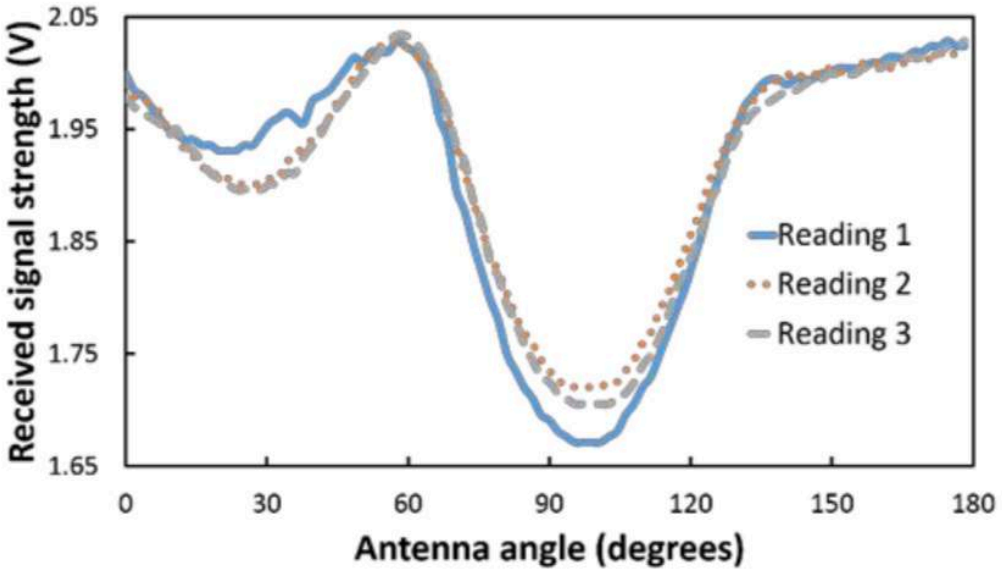
Demonstration that final weight is compatible with bumble bee flight



Validation of tracking approach through unmanned terrestrial vehicle

Tracking via unmanned aerial vehicle

- Angle of arrival determined using a RF detector, a µ-controller and a phase shifter driving antenna array attached to drone
- Relative Signal Strength information fed-back to drone control

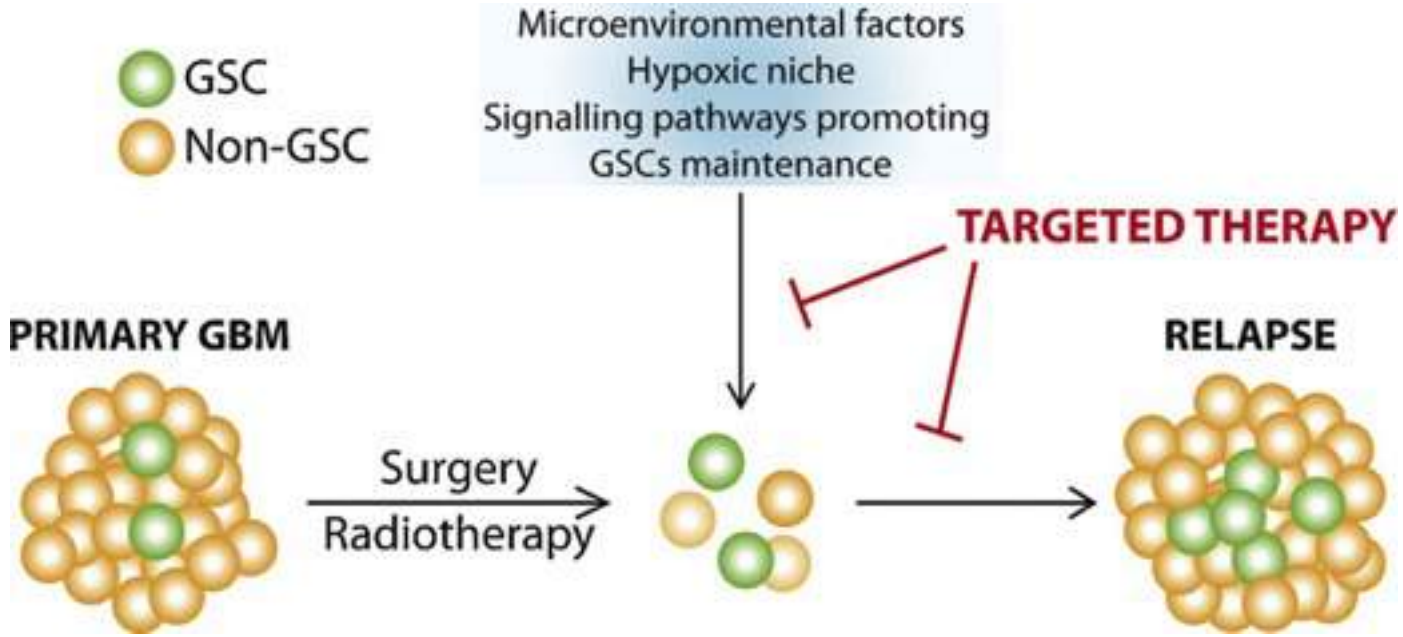


Results of experiments in China

- Bees can fly and and sustain 10m communication link!
- Bees left after 5 minutes, for 20-30 minutes at 40°C!
- Returned in good shape. No tag loss. Repeated the cycle twice.
- Exit/entry events monitored. Not much in between.

Lab on Chip (LOC) and cell tracking projects

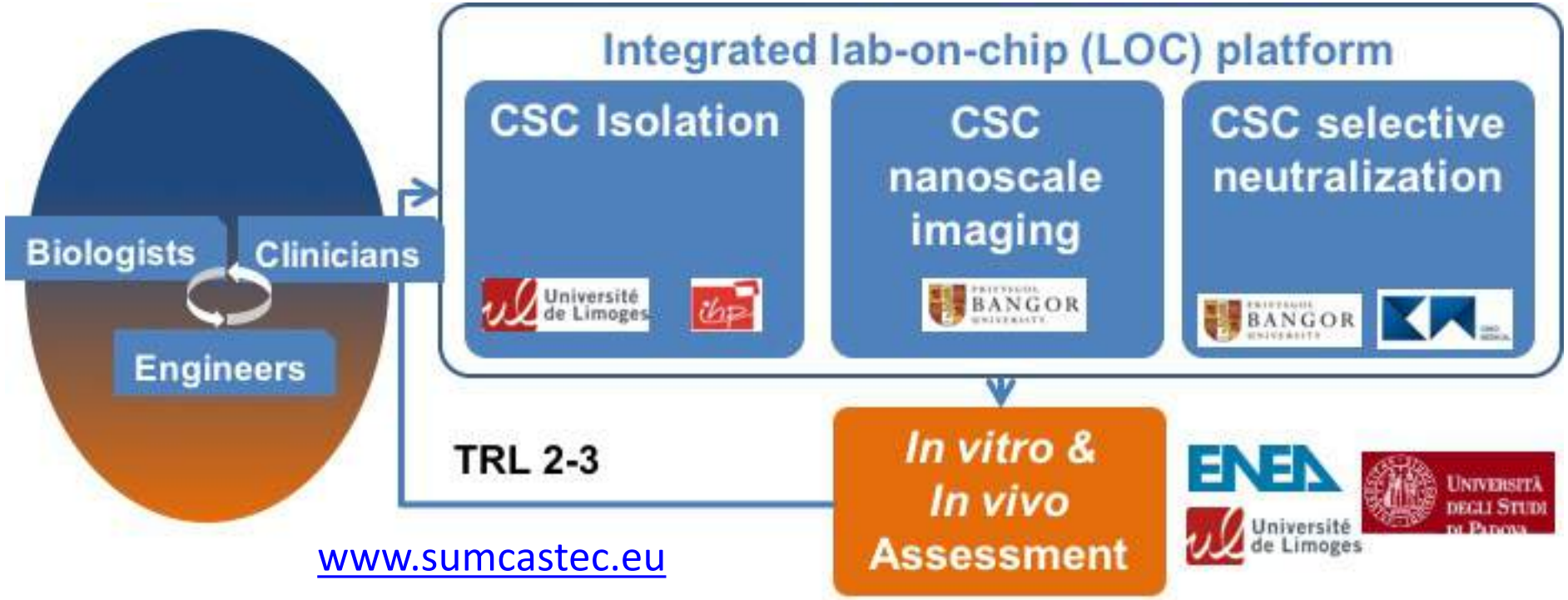
Context: Cancer stem cells (CSCs)



- Key to glioblastoma and medulloblastoma resistance and relapse
- Identification/isolation require 1+ month currently
- Evade state of the art treatments that target differentiated cells

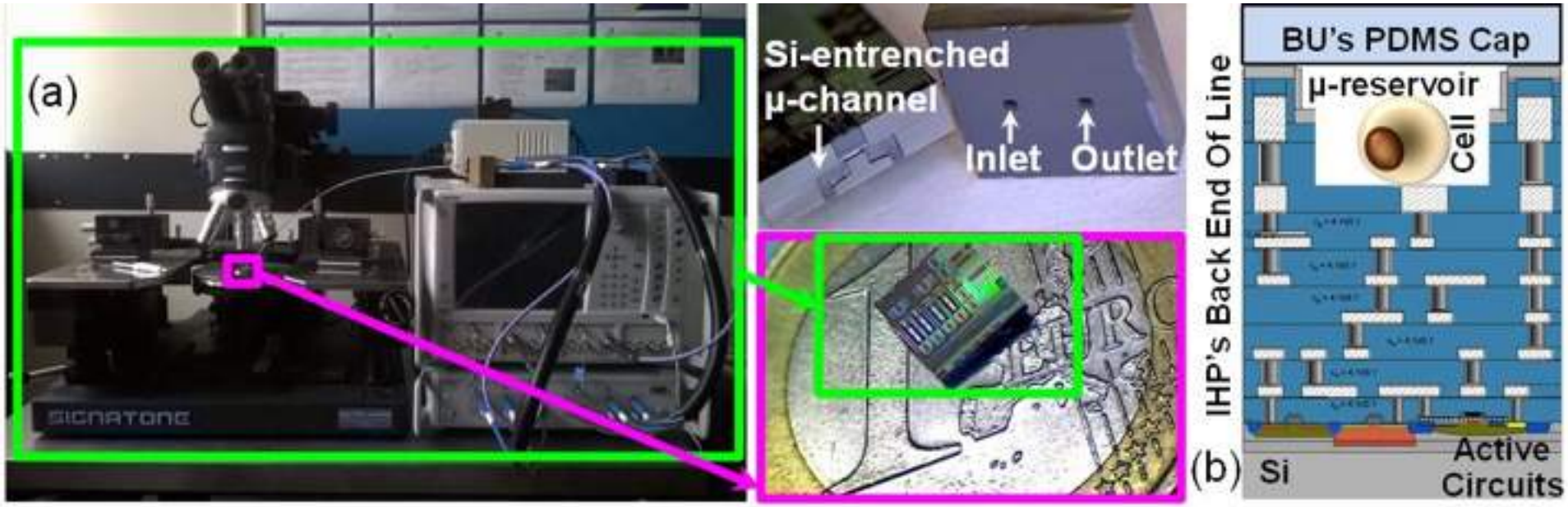
SUMCASTEC project purpose

Semiconductor-based **U**ltrawideband **M**icromanipulation of **CA**ncer **STE**m **C**ells (CSCs)



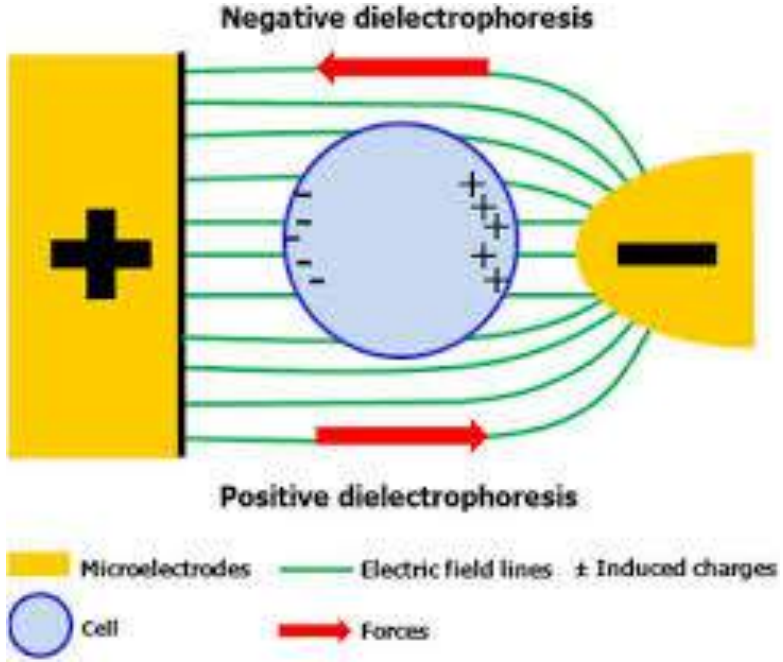
www.sumcastec.eu

Technology integration and miniaturization



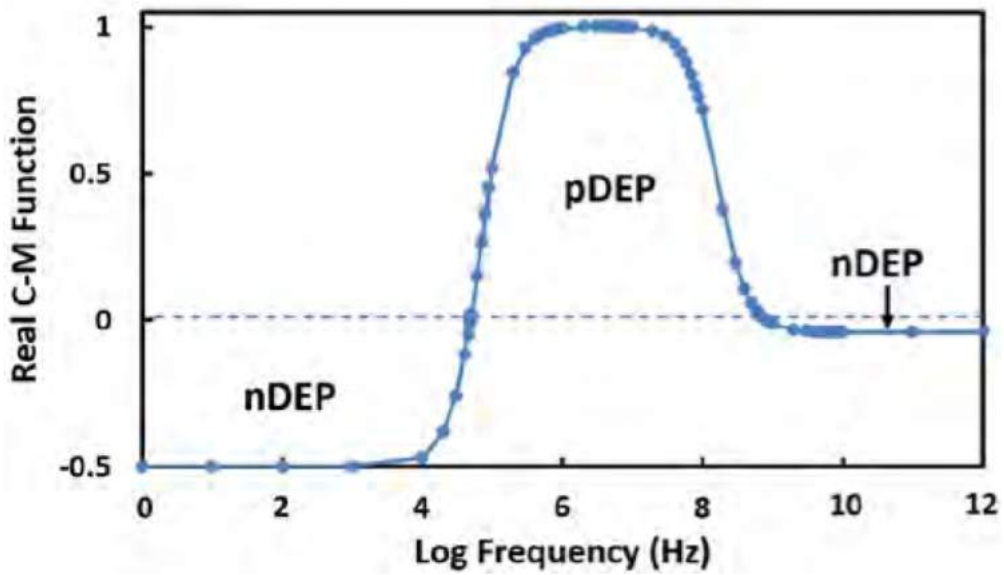
- Technology integration for fast, compact, high sensitivity performance. Uses very well established processes.
- Portable, autonomous chips for sensing and bioelectrics

Dielectrophoresis for cell control and spectroscopy



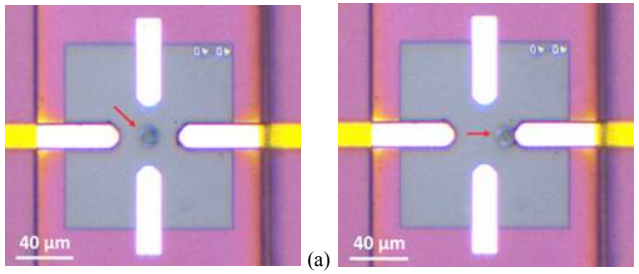
$$F_{\mathrm{DEP}} = 2\pi\varepsilon_m R^3 \mathrm{CM}(\nabla E^2)$$

$$\mathrm{CM} = \left(\frac{\varepsilon_p - \varepsilon_m}{\varepsilon_p + 2\varepsilon_m} \right)$$

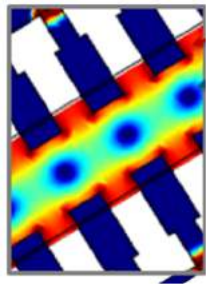


- The Clausius-Mossotti factor *CM* depends on the polarizability of the particle vs surrounding medium
- Assumes different signs at different frequencies

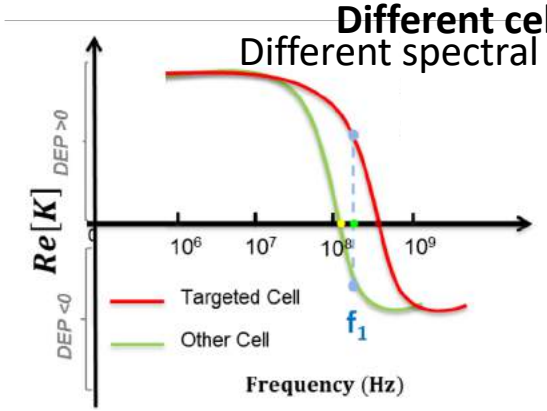
On-chip CSC sorting approach

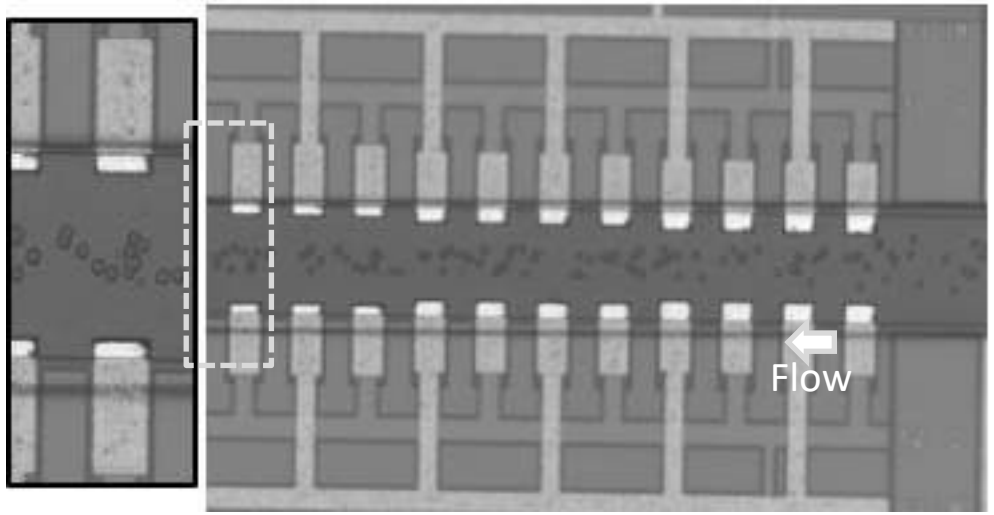


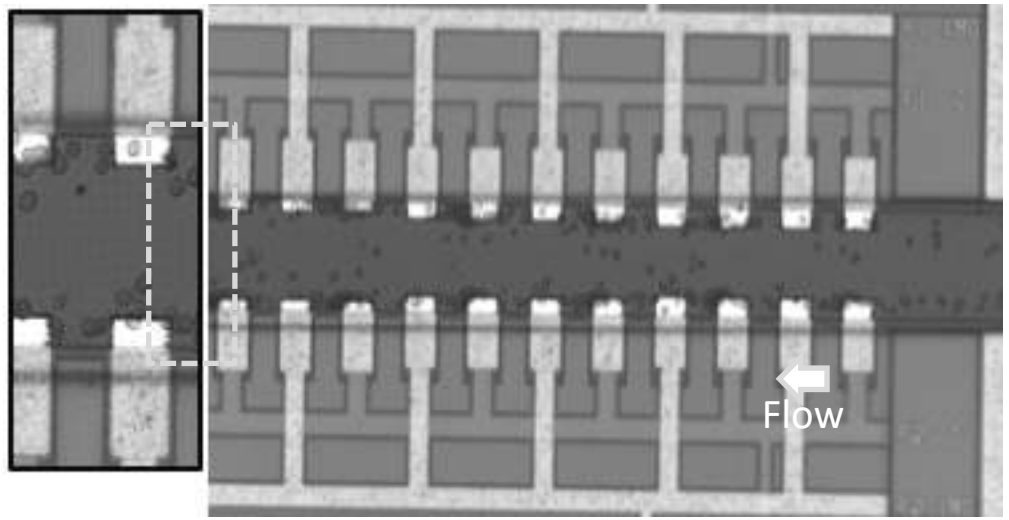
(a)



Different cells =
Different spectral signature



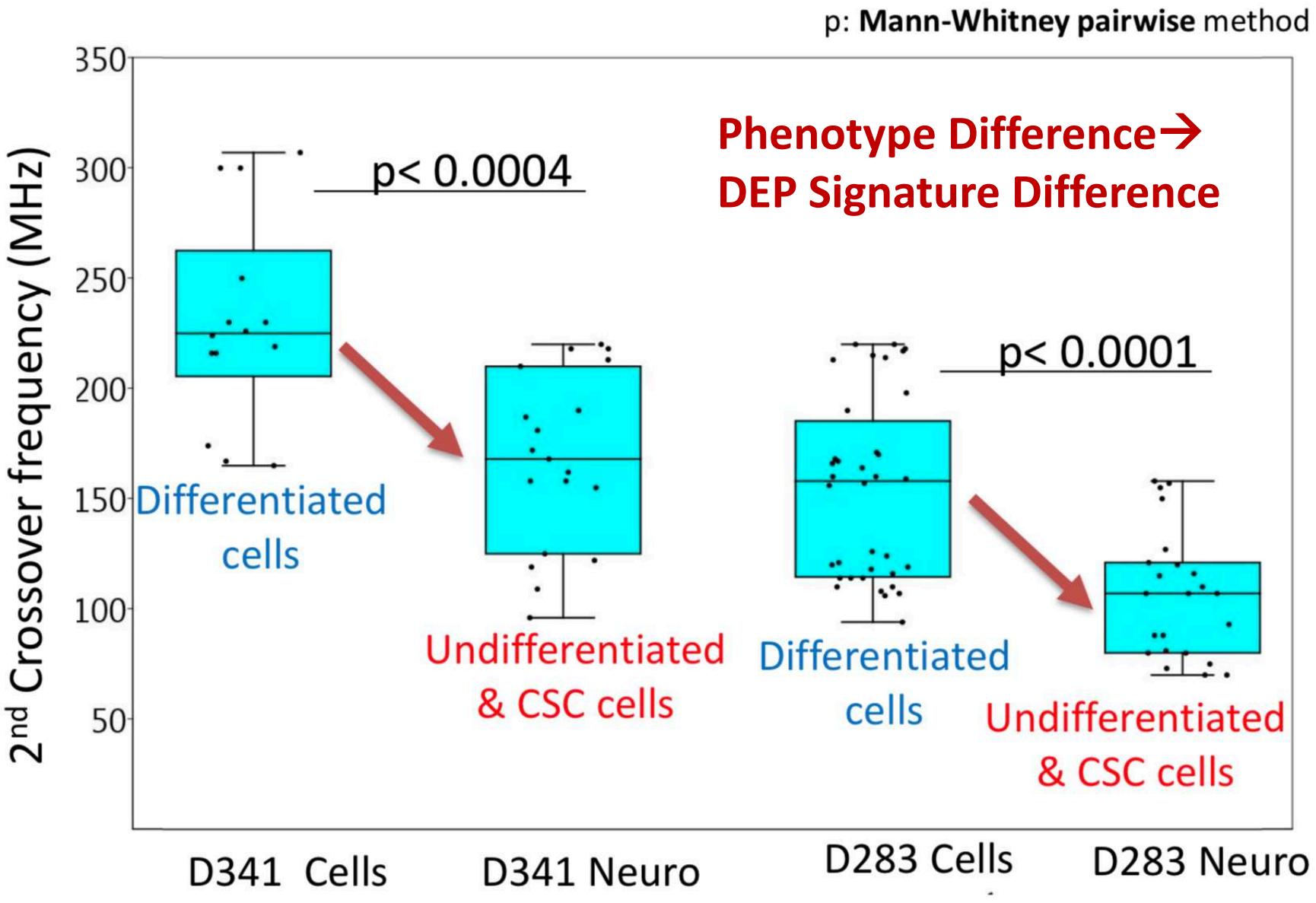




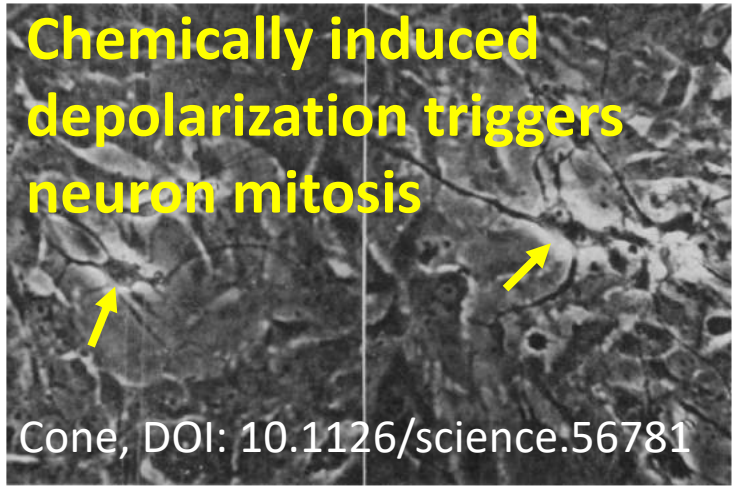
F_{DEP}> Fcross-over → Cells concentrate in micro-channel **center** seeking lowest E field intensity

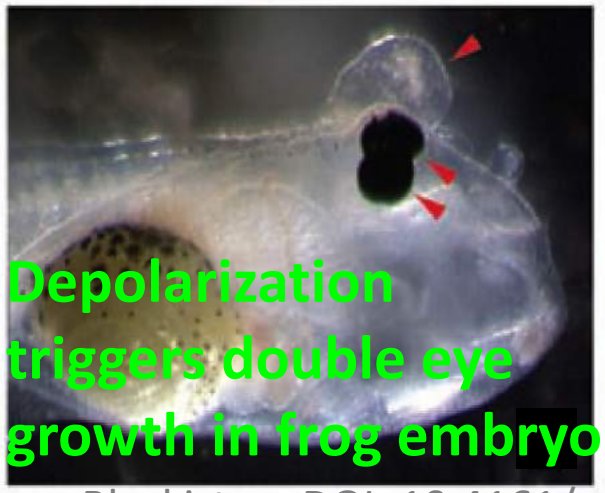
F_{DEP}< Fcross-over → Cells concentrate in micro-channel **edge** seeking highest E field intensity

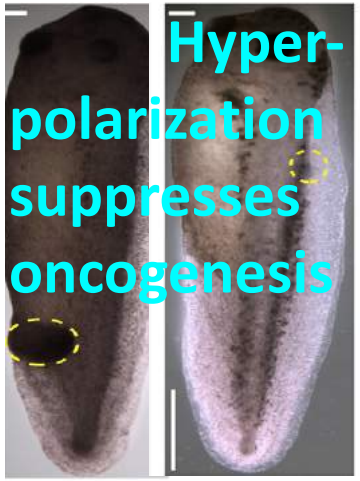
Results on MB cell lines



CSC selective neutralization: underpinning



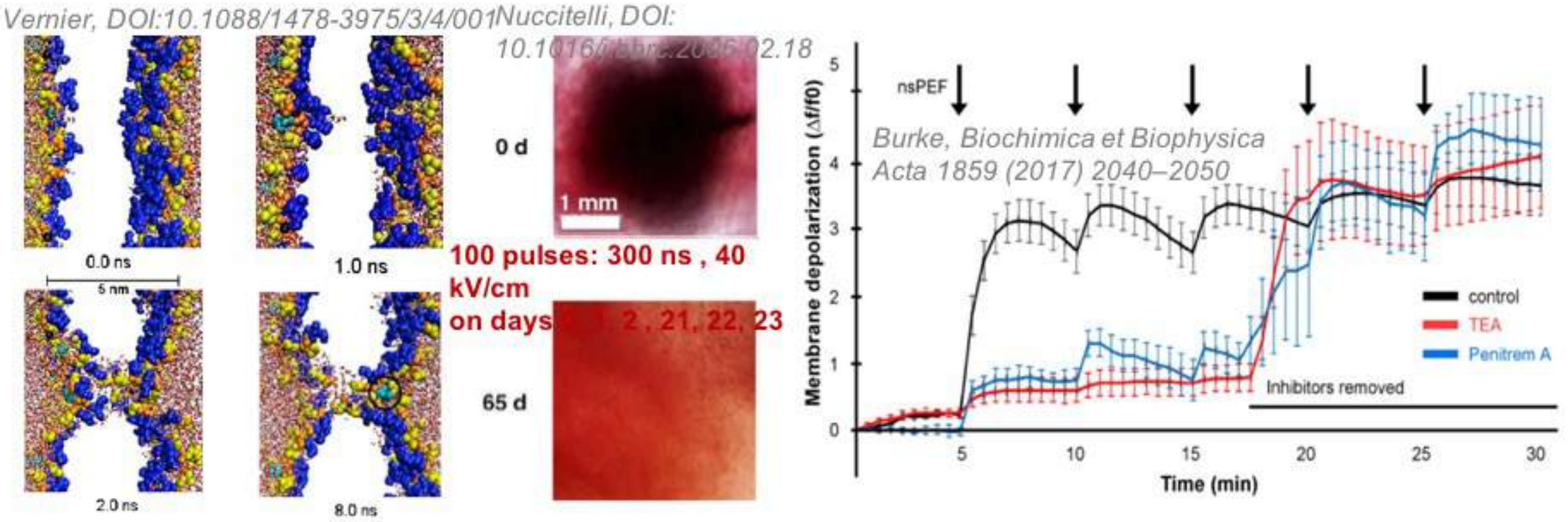




Blackiston, DOI: 10.4161/cc.8.21.9888
Brook: DOI:10.18632/oncotarget.1935

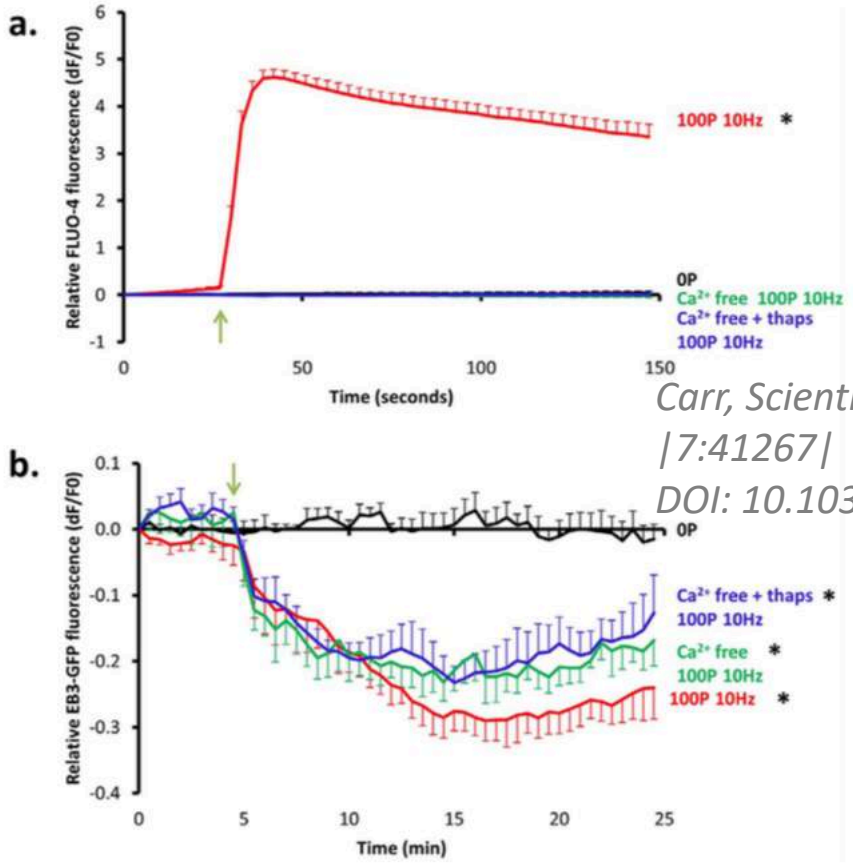
- Underpinning: connection btw membrane potential and proliferation
- Cells have relatively high (healthy), lower (cancer differentiated) and lowest (CSC) membrane potential
- Depolarization of tissue is associated to tumorigenesis and tumor growth
- Hyperpolarization suppresses oncogenesis

E-poration vs ion channel gating disruption

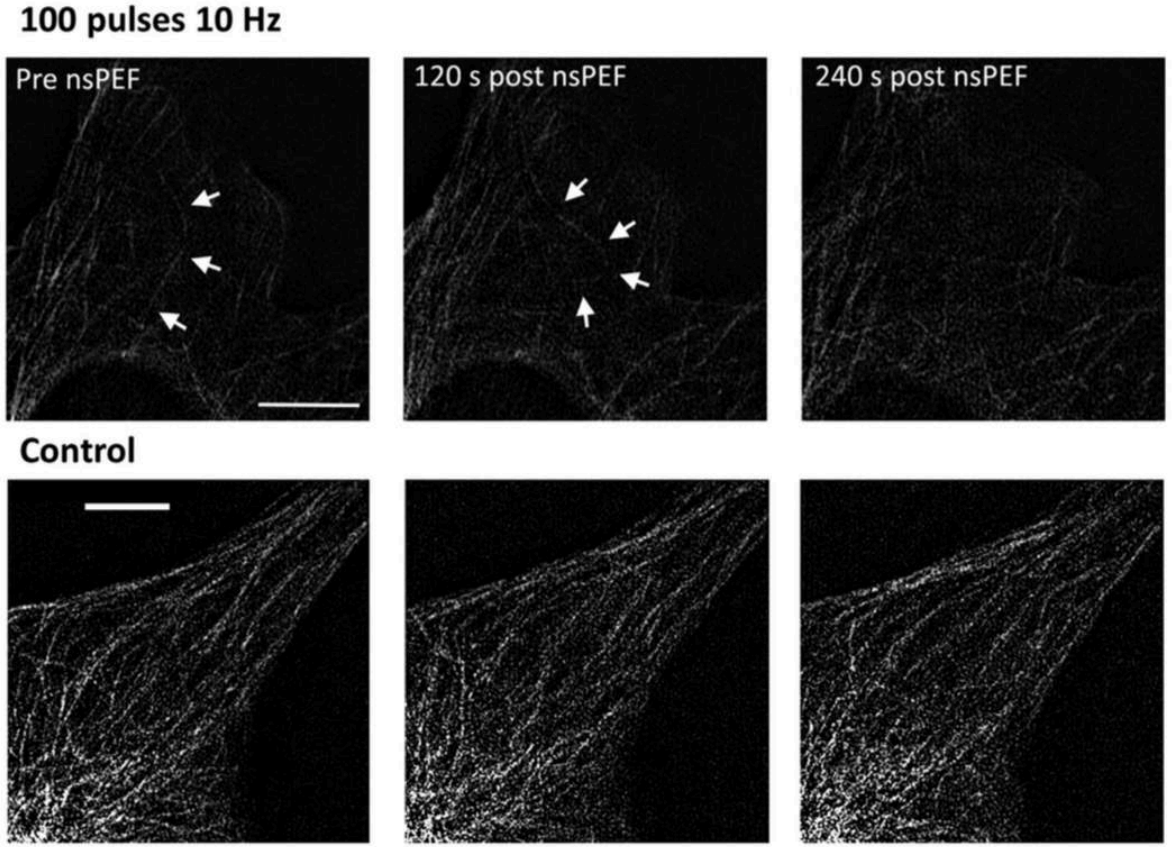


- Beyond electroporation: membrane depolarization demonstrated at lower field (34 kV/cm) than permeabilization threshold but high enough for ionic channel gating modulation
- No study has yet targeted Glioblastoma Multiforme or Medulloblastoma CSCs

Calcium independent micro-tubules disruption in U87



Carr, Scientific RepoRts |7:41267| DOI: 10.1038/srep41267

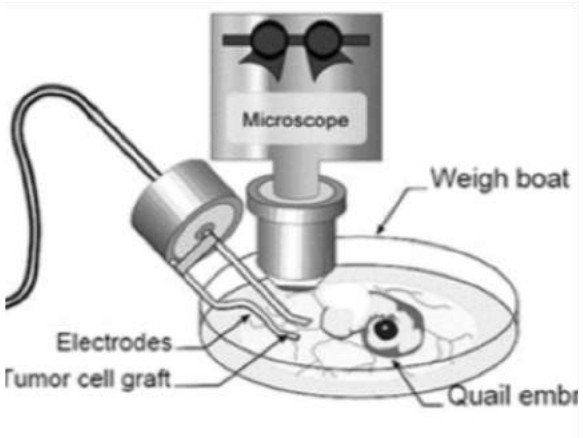


- Buckling and breaking of microtubule following 100, 10ns, 44kV/cm PEF application
- Microtubule network growth reduction even if intra/extracellular Ca^{2+} removed

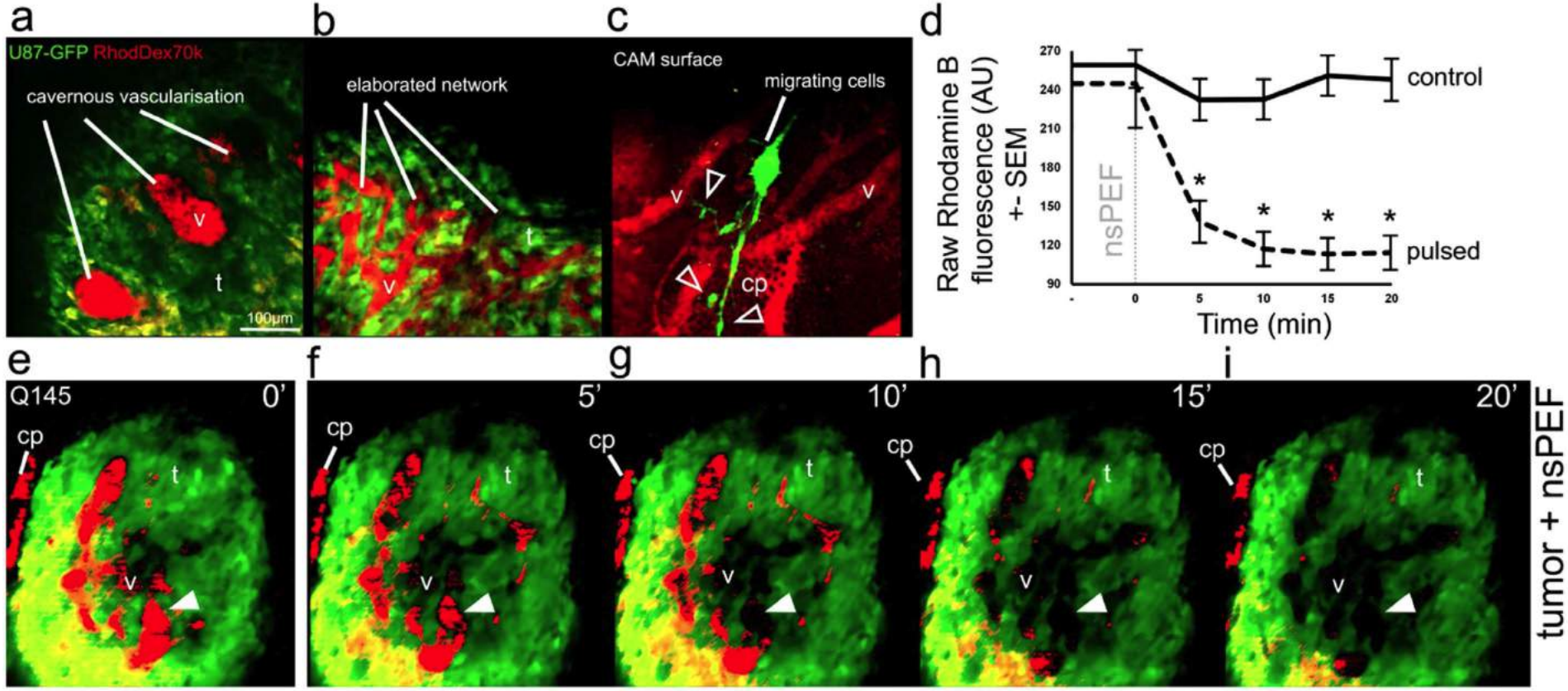
CSCs selective neutralization: results

- SUMCASTEC: first study specifically applying E-poration to CSCs
- Dielectric parameters for brain CSCs scarcely available
- Tests have been conducted off-chip while LOC developed
- Early results confirm strong interaction mechanism to modulate stemness and cell cycle status
- It would be interesting (but not ethically trivial) to test healthy stem cells

Tissue level application



Bardet, |634443|
DOI: 10.1038/srep 34333



- Collapse of vascular perfusion in GBM xenograft model demonstrated
- Application to GBM organelles planned to investigate 3-D dynamics

Thank you!

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