





Cell Mechanotransduction: Cell Responses To Nanoscale Vibrations

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Nano-scale patterns

- Nanoscale topographies being produced via electron beam lithography
- Mesenchymal stem cells (MSC's) differentiate into a variety of cell types – can control via pattern
- Applications for joint replacements and for stem cell transplant
- Can use osteogenic chemicals however not always in vivo

Image of cellular "nanopodeia" probing the nano scale landscape http://www.jwnc.gla.ac.uk/STEM.html



Nanoscale 'Kicks'

- Work by Anne Pierres shows cell membranes undulate at the nm scale (1/1000th of cell size)
- Piezos devices can allow this level of vibration resolution
 - Frequencies investigated, 1Hz 1kHz
 - 20nm pk-pk
 - 0.05 pN at 5Hz, 5 pN at 50Hz
- Stimulation in has shown changes in cell adhesion, cycle duration and gene expression in both MSC's and Le-2 endothelial cells







24hrs

<u>1 wk</u>

2 wks

500 Hz / 20 nm pk-pk

1 kHz / 20 nm pk-pk



Åctin cytoskeleton examples after set periods of stimulation at 500 and 1000Hz

First high-impact PaLS publication from this project: H Nikukar et al, ACS Nano Letters (In Press) Joint publication between Thin Film Centre (UWS) and CCE (GU)

Stochastic Resonance

- How do cells feel these vibrations over background seismic noise?
- At 1Hz seismic noise in the order of 1µm
 500 times larger than our vibration!
- Possible candidate Stochastic resonance
- Exhibited in many biological systems including neural networks and the human hearing
- Occurs when noise provides a signal processing benefit to a non linear system

Stochastic Resonance (2)

- Requirements for a stochastic resonance (SR)
 - Non linear output from system
 - Random noise
 - Coherent input signal





Stochastic Resonance:

From Suprathreshold Stochastic Resonance to Stochastic Signal Quantization McDonnell MD, et al., Cambridge University Press. (2008)

Ongoing Research

- This work has been identified as a spin-off from STFC funded research (gravitational waves) and is now partly supported by the STFC Futures program
- Determination if the criteria for SR are met
 - Remove background noise at these frequencies – seismic isolation via bungee
 - Observe if cells still respond to coherent signals



Ongoing Research

- Investigate the effect of frequency and acceleration separately
- Create physical models for cell behaviour which can explain fundamental responses to mechanical stimuli



