UWS UNIVERSITY OF THE WEST of SCOTLAND | Thin Film Centre Microscale Sensors

SUPA

Ultrasonic imaging, RNA splicing and nanoscale cell mechanotransduction

David Hughes and Peter Childs

High frequency ultrasound imaging for Life Sciences and Medicine

David Hughes, Katherine Kirk, David Hutson

The Microscale sensor group at UWS has fabricated a number of high frequency ultrasound transducers (>70MHz), for medical and biological imaging challenges.

Dental Imaging:

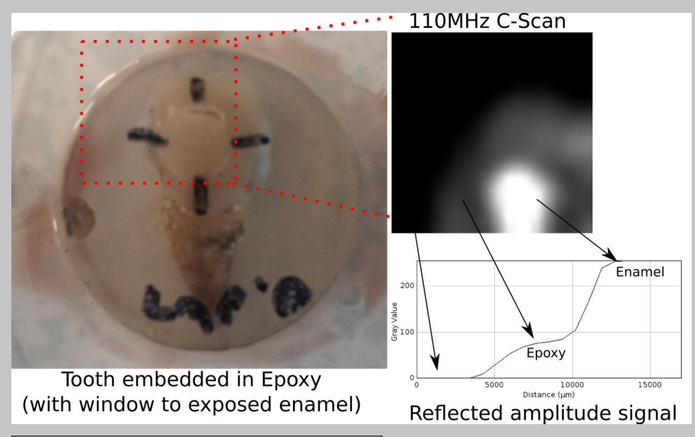
110MHz lithium niobate transducer are used to monitor the surface and thickness changes of tooth enamel during acid erosion. Tooth decay is a disease that affects around 80% of the population.

Breast Cancer Test Assay:

The group is working with an Edinburgh University spin-out company to use quantitative ultrasound imaging as a test for the efficacy of a breast cancer treatment on a novel 3D tissue assay.

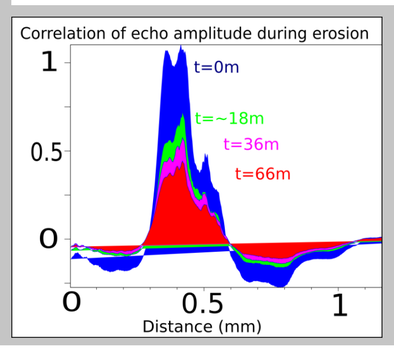
Acanthamoeba and Dictyostelium development:

Simple amoebas such as Acanthamoeba and Dictyostelium are very useful model organisms for investigating cell migration and multicellularity in cancer and embryo development. We are investigating the use of quantitiative ultrasound imaging to probe the mechanical properties and changes during these events.



Tooth embedded in Epoxy (with window to exposed enamel)

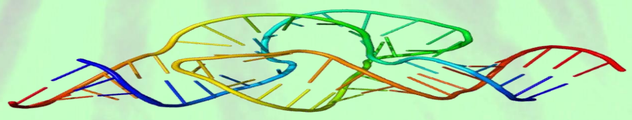
Reflected amplitude signal



Left: Reflected signal of ultrasound during the erosion of the tooth surface with 80mMol HCL, where a strongly detectable drop in reflection amplitude is observed as the surface becomes disrupted. Note that this change in surface is not detectable at such an early stage with current clinical tools. HCl erosion is biomedically relevant to studies of acid erosion through gastric reflux and bullimia.

RNA Splicing

Gregory V Morozov



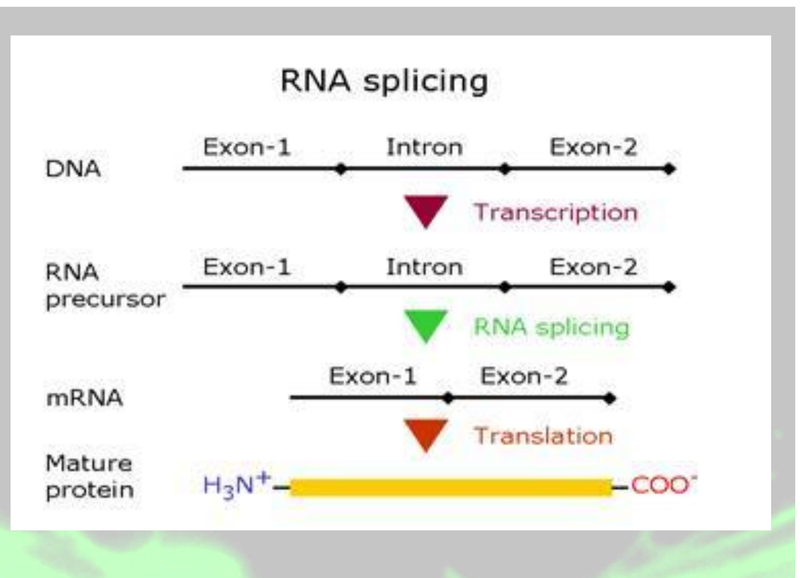
In plants and animals, most RNA molecules are made as long precursors that need to be trimmed and reassembled to create the final active molecule. This process called splicing.

Goal: to develop and elucidate the detailed mechanisms of RNA self-splicing, based on theoretical modeling of the molecular structure, charge distribution, possible intermediates and reaction routes.

Method: combination of Quantum Mechanics and Molecular Mechanics.

QM: accurate calculation of small reactive site (ground energy, energy barriers, transition states).

MM: to obtain global secondary and tertiary structure of molecule and approximate charge distribution.



Planned Activity

- **investigate the impact of the secondary and tertiary structure of the RNA chains that will involve, hydrogen bonding, explicit and implicit solvation and long range coulomb interactions**
- **charge distribution analysis and possibly partial charge re-parameterization will be combined with the calculation of the structural and thermodynamic properties of RNA complex**
- **analyze electronic and atomic charge distribution of the active site in order to reveal factors that would provide high selectivity of the guanosine binding site**
- **alternate the sequence of the base-paired P1 duplex in order to theoretically verify the impact of substrate structure on the docking process**

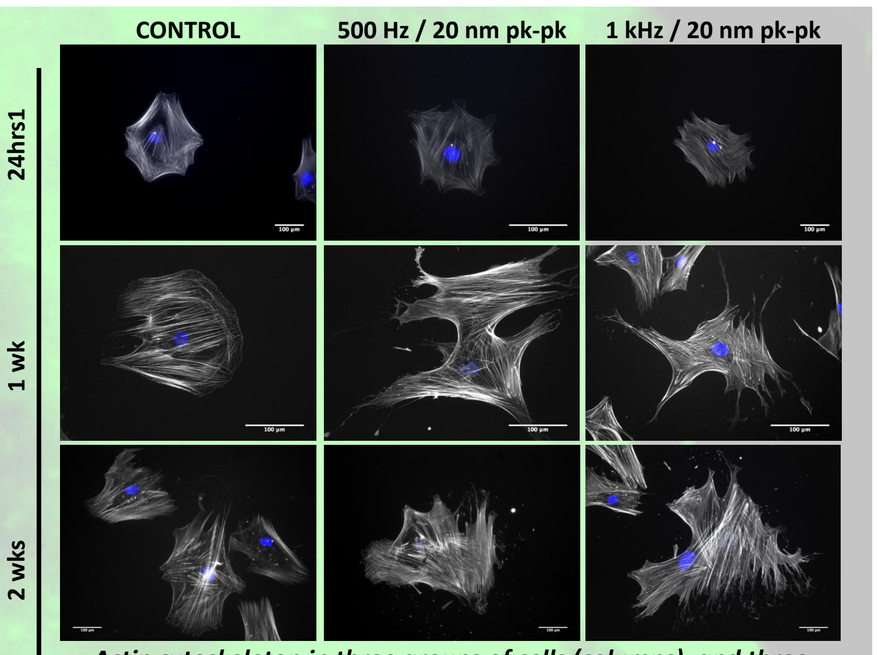
Cell mechanotransduction/stem cell differentiation

Peter Childs, Stuart Reid, Fiona Henriquez, with CCE colleagues at GU

In collaboration with the Centre for Cell Engineering and the Institute for Gravitational Research (Glasgow), we have demonstrated that cell behaviour and stem cell differentiation can be significantly modified through low-frequency nanoscale vibrations, with sub-pN forces per cell. Understanding the mechanisms responsible for cell mechanotransduction (how cell process mechanical signals), and how this can be used to control stem cell differentiation, could be used to significantly advance many aspects of tissue engineering and regenerative medicine. We plan to:

- **Study stochastic resonance within the cell responses**
- **Compare cell responses to nanopit arrays, where nano-features have been widely studied for manipulating stem cell differentiation**
- **Investigate applying sub-pN forces to cell nucleus by attached magnetic nanoparticles**

Right: first demonstration of promoting osteogenesis in mesenchymal stem cells using nanoscale vibrations (Nikukar & Reid et al., ACS Nanoletters, *in press*).



Actin cytoskeleton in three groups of cells (columns), and three periods of time (rows), reveals stress fibres caging the nucleus and polygonal spreading after stimulation.

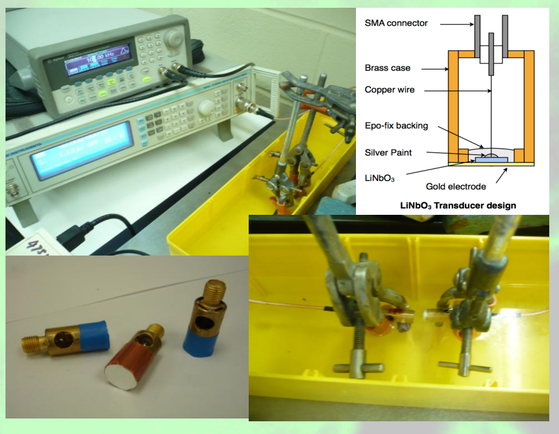
High frequency ultrasonic probe for mechanobiology

Michael Butler, Katherine Kirk, David Hutson

Mechanobiology (or mechanotransduction) is a growing and important area within biophysics, yet there are few techniques currently available that can probe cell response to mechanical signals with small and fast dynamics.

We have designed broadband high frequency ultrasonic transducers which are able to produce acoustic waves approaching the fast vibrational frequencies of larger cell assemblies (GHz).

With a range up to 1.5 GHz and a good response through water (fully characterised up to 150 MHz), our current design is being tested with actin polymerisation protocols *in vitro*. Future work hopes to extend to *in vivo* biophysics.



High frequency ultrasound testing in water (top left, bottom right) High frequency transducer design (top right) & devices (bottom left)

Planned research includes:

- **Collaborating with mechano-biologists to design ultrafast biophysical experiments, investigating *in vivo* cytoskeletal, mechano-sensory channel or focal adhesion response.**
- **Improving design to increase the max. frequency/reduce the size of transducers**
- **Improving the signal control and characterisation by using ultrafast signal generators/amplifiers and designing multiple frequency arrays.**

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