Acoustic neuromodulation in cortical neurons and retinal tissue

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Introduction

Neurological diseases such as Alzheimer's disease, pain syndromes, and epilepsy affects 1 in 7 people. These disorders are caused by malfunctions in neurons and there is a high demand for effective and personalized therapies. Pharmaceutical treatments require large volumes of drugs and currently non-pharmaceutical techniques for this purpose, including electrical and optical simulation. However, the last two are too invasive and ineffective to justify their widespread use. Acoustic neurostimulation is an emerging and promising method for treatment of neuronal disorders (Sassaroli et al. 2016) and positive interactions of cells and tissue with acoustic waves and streaming has been observed for many years (Izadifar et al. 2017). In this research, we present a novel approach for neuronal stimulation and enhanced drug uptake through acoustic actuation, applying surface acoustic waves. By developing a fundamental understanding of neuromodulation via mechano-acoustic stimulation, we will create a new mechanism to study neural signalling and to develop new therapies.

Aims

The aim of this research is to fabricate an acoustic life-on-chip platform to examine acoustic modulation in neural cell populations and tissue. We will create well-characterised SAW-based actuation platforms, where the precise substrate deformations and resultant pressure fields across a microfluidic device are known. Taking advantage of the ubiquity of Calcium signalling in neurons and the ability to use chemical indicators as a marker of its concentration, we will use Calcium imaging as a tool for monitoring the activity of individual neurons in vitro.

Methods

Chip fabrication: LiNbO3 128° Y-Cut, equipped with interdigital transducer (IDT) with wavelength λ=50µm by standard lithography was used for SAW excitation.

SAW characterisation: heat dissipation was measured via infrared microscopy under unloaded and water loaded conditions. Surface deflection, wave propagation and attenuation at liquid interfaces mimicking cells on the chip were measured applying laser-doppler interferometry. Shear rates of acoustic streaming were determined using scanning particle image velocimetry (SPIV).

Cell culture and tissue: p0 to p2 rat pups' primary cortical neurons were dissected and cultured directly on the chip.

R Retinas from adult pigmented Long Evans rats older than 3 months were used. 0.5µl of 20 mM Oregon Green 488 BAPTA-1 was injected directly into the optic nerve.

Monitoring: fluorescence imaging was applied for real-time monitoring of cell activity and particle uptake.

Results and Discussion

With an applied SAW of power level p=2dBm, a temperature increase of ΔT=10°C on air and ΔT=2.5°C in water was detected. The wave amplitude was determined with 2nm and the characteristic 1/e decay length l=490µm under load. The local shear rates at the side of the cells and tissue was measured with γ=4000 s-1 and an area of approximately 200µm^2.

After culturing for three days, cell viability could be confirmed when compared to reference samples with the SAW-chip. Further tests to examine cell morphology and toxicology will be conducted - first stimulation tests show positive reactions.

References

1. Izadifar, Zahra, Paul Babyn, and Dean Chapman. 2017. "Mechanical and Biological Effects of Ultrasound: A Review of Present Knowledge." *Ultrasound in Medicine & Biology* 43 (6):1085–1104. https://doi.org/10.1016/j.ultrasmedbio.2017.01.023.
2. Sassaroli, Elisabetta, and Natalia Vykhodtseva. 2016. "Acoustic Neuromodulation from a Basic Science Prospective." *Journal of Therapeutic Ultrasound* 4 (1). BioMed Central:17.