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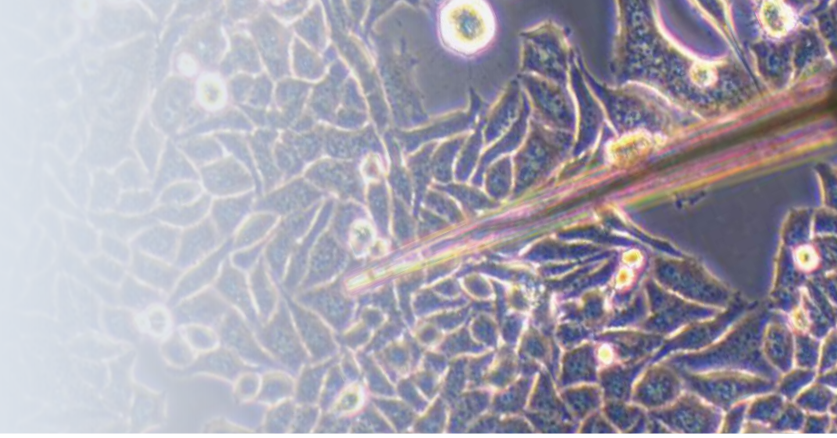


Using tissue oxygen levels to assess ex vivo brain slice quality

Measurement of tissue oxygen partial pressure provides an easy, quick and reliable method for screening and controlling for variation in ex vivo acute brain slice viability

The application note is based on the research and article by:

Voss et al.

The application note is written by:

Sandfeld et al., Unisense

Introduction

The acute ex vivo brain slice model is a versatile tool for investigating neurophysiological processes, allowing experimental conditions to be tightly controlled. However, the utility of the method can be compromised by variation in tissue quality, which can be difficult to reliably assess using simple electrophysiological approaches.

We all know that animals rely on oxygen to fuel the production of energy to sustain living tissue. Intuitively, it is also well understood that the more active the tissue, the greater the oxygen requirement to maintain that activity. In this study, we utilised this simple relationship to develop a straightforward method for reliably assessing the quality of acute tissue slices, following the rationale that healthier tissue will consume more oxygen.

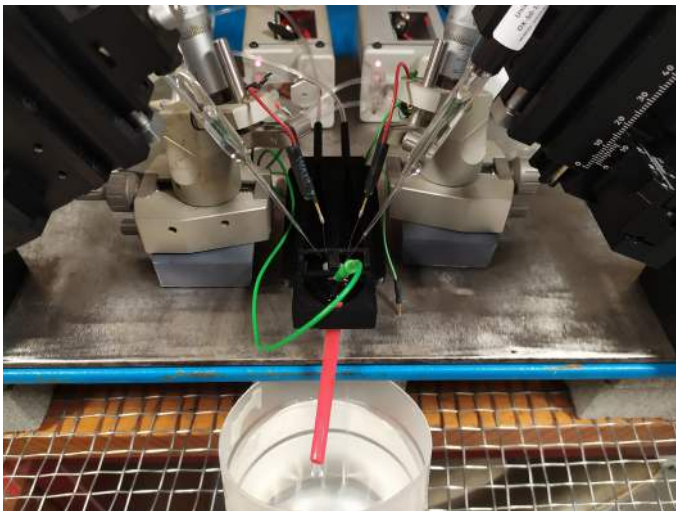
If one knows the tissue oxygen solubility and diffusion characteristics (the "Krogh" coefficient), oxygen consumption can be accurately quantified from the curvature of the tissue depth versus oxygen partial pressure profile. However, accurate tissue oxygen profiling is time consuming and requires offline calculation. We hypothesised that the tissue oxygen minimum level (pO_2min) would provide a more accessible method.

"The Unisense hardware, software and electrodes work flawlessly for the applications I use in the laboratory and the customer service is top-drawer."

Dr. Logan Voss, Dept Anaesthesia, Waikato DHB

Laboratory setup

The appeal of this method is its simplicity. Using a Unisense oxygen electrode attached to a standard micromanipulator, the electrode is advanced through the tissue until the oxygen partial pressure reaches pO2min. The electrodes can be retracted and advanced two or three times to confirm the true nadir in oxygen level has been identified.



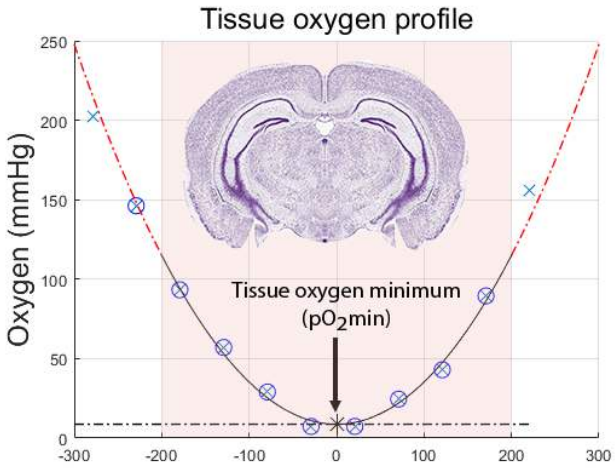
Laboratory setup: Tissue pO_2 measurement setup showing two oxygen microsensors inserted into a brain slice submerged in a perfusion bath.

Results and conclusion

We have shown that pO_2min correlates with oxygen consumption rate and tissue viability – the lower pO_2min, the higher the tissue oxygen consumption and the healthier the tissue. If pO_2min is zero, oxygen supply is not meeting tissue demand and the flow rate of the perfusate should be increased. The pO_2min value can be used to discard unhealthy tissue or to control for variation in tissue health from one experiment to another. For the experimental parameters in this study (mouse cerebro-cortical slices perfused at room temperature at a flow rate of 6 mL/min), strong viable tissue was reflected in pO_2min values of 0-50 mmHg in population-active tissue – and 150-200 mmHg in quiescent tissue.

Tissue oxygen minimum is simple to measure and provides a robust estimate of ex vivo tissue viability status. While the specific pO_2min values will vary with preparation and experimental parameters, the principle is widely applicable across tissue types and perfusion platforms.

You can read more in the article by Voss et al. "Tissue oxygen partial pressure as a viability metric for ex vivo brain tissue slices", Journal of Neuroscience Methods 396 (2023) 109932 and in the article by Steyn-Ross et al. "Determination of Krogh Coefficient for oxygen consumption measurement from thin slices of rodent cortical tissue using a Fick's law model of diffusion", Int. J. Mol. Sci. 2023, 24, 6450.



Example of a pO_2 depth profile recorded throughout the depth of a brain slice. The pO_2min was identified at the bottom of the pO_2 depth profile.

Suggested products

- O_2 Micro sensors
- Microprofiling System
- SensorTrace Profiling

Related publications

Voss et al. "Microalgae-based photosynthetic strategy for oxygenating avascularized mouse brain tissue - An in vitro proof of concept study", Brain Research 1768 (2021) 147585.

Malle et al. "Teriflunomide Preserves Neuronal Activity and Protects Mitochondria in Brain Slices Exposed to Oxidative Stress", Int. J. Mol. Sci. 2022, 23, 1538.

Chausse et al. "Selective inhibition of mitochondrial respiratory complexes controls the transition of microglia into a neurotoxic phenotype in situ", Brain, Behavior, and Immunity, Vol 88, 2020, 802-814.

Hencz et al. "Mild hypoxia-induced structural and functional changes of the hippocampal network", Front. Cell. Neurosci. Vol 17, 2023.

Pospelov et al. Endogenous Brain-sparing responses in brain pH and PO2 in a rodent model of birth asphyxia", Acta Physiologica. 2020;229:e13467.

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