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Towards Single-Cell Control of Hypoxia in Microfluidic Cancer Assays

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Hypoxia has been repeatedly demonstrated to have an adverse prognostic impact in various types of tumors [1]. A growing body of evidence indicates its central role in both, malignant progression, as well as in resistance to cancer treatment. While diminishing the efficiency of some forms of therapy, hypoxia also provides an opportunity for a new class of drugs, so called bioreductive drugs, specifically engineered to require hypoxic conditions for activation [2]. The development and in-vitro evaluation of these compounds however requires precise control over the cellular micro-environment, something not easily accomplished with traditional well-based cell-culture assays performed in air (~21% O_2).

However, the use of microfluidics, a new fast-growing area of research and development, promises to overcome the limitations of open culture systems by relocating cells and reactions into enclosed microchannels on Lab-on-a-Chip devices. Recently we have introduced a novel optical oxygen sensor capable of resolving biologically relevant oxygen levels in such devices via fluorescence microscopy [3]. When combined with microfluidic flow control, cells cultured inside a parallel-plate microchamber could be exposed to custom transverse oxygen gradients with intermediate levels ranging between hypoxic (0 mg/L O_2) to hyperoxic (34 mg/L O_2, saturation) conditions [4].

In this paper we will demonstrate spatially-resolved visualization of oxygen dissolved in a liquid medium and introduce two microfluidic devices for cell-culture experiments with integrated oxygen control. We will further show how these devices can be used to retain clusters or even individual cells within larger populations under hypoxic conditions, a capability which will allow the evaluation of cancer drugs on a cell-to-cell basis. In general, the combination of the oxygen sensor system with microfluidic culture devices has the potential to significantly improve the relevance of current cancer drug assays.

References:

[1] P. Vaupel and A. Mayer, "Hypoxia in cancer: significance and impact on clinical outcome," *Cancer and Metastasis Reviews,* vol. 26, pp. 225-239, 2007.
[2] S. R. McKeown*, et al.*, "Bioreductive Drugs: from Concept to Clinic," *Clinical Oncology,* vol. 19, pp. 427-442, 2007.
[3] V. Nock*, et al.*, "Patterning, integration and characterisation of polymer optical oxygen sensors for microfluidic devices," *Lab on a Chip,* vol. 8, pp. 1300-1307, 2008.
[4] V. Nock and R. J. Blaikie, "Spatially Resolved Measurement of Dissolved Oxygen in Multistream Microfluidic Devices," IEEE *Sensors Journal,* vol. 10, pp. 1813-1819, 2010.