DIELECTRIC MONITORING OF MAMMALIAN CELLS IN A BIOREACTOR

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Dielectric spectroscopy is an analytical technology with the potential to revolutionize the control of biopharmaceutical manufacturing. The frequency-dependent profile of ionic polarization of cells in response to an alternating electromagnetic field changes with respect to cell type, metabolism and media conductivity. The method has been adopted to measure the growth of cells through *in situ* capacitance measurements at a single frequency. However the power of such measurements can be enhanced through the use of a dielectrophoretic flow cytometer (DEP) that can measure the changing trajectory of single cells passing through a microbore tube subjected to an electromagnetic field controlled by a bank of electrodes. We have used this principle to analyze cells in a bioprocess to identify changing sub-populations of cells during apoptosis. This has led to the early detection of changes that lead to the eventual loss of productivity and viability.

The presentation will include comparative data from five alternative measurements of cell growth and viability. Each method provides a different profile which can be used to decipher changes in viability and metabolism of the cells during the production process. The value of these methods will be discussed in relation to the production of monoclonal antibodies from Chinese hamster ovary (CHO) cells. The data shows that dielectric cell monitoring provides unique information that can be related to more conventional methods of biochemical monitoring by fluorescent agents. At the on-set of apoptosis of cells in a bioreactor sub-populations were identified with characteristic dielectric properties that were quantified by a force index based upon their behavior in the electromagnetic field. The sub-populations were comparable to those of cells in early, mid and late apoptosis as identified by fluorescence staining. DEP offers a means of identifying cell characteristics without the use of markers and identifies loss of cell viability well before dye exclusion methods based upon membrane damage.