FOGALE nanotech

Application Note

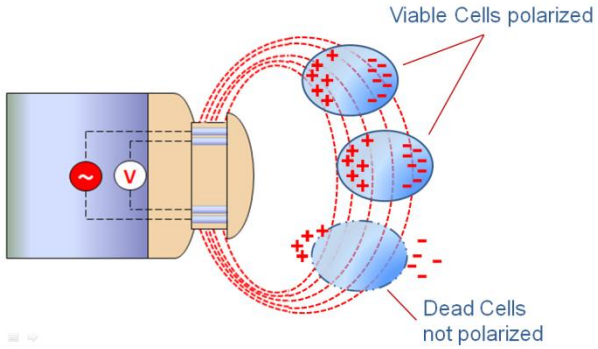
Online Capacitance Measurement – How Does It Work?

Benefits

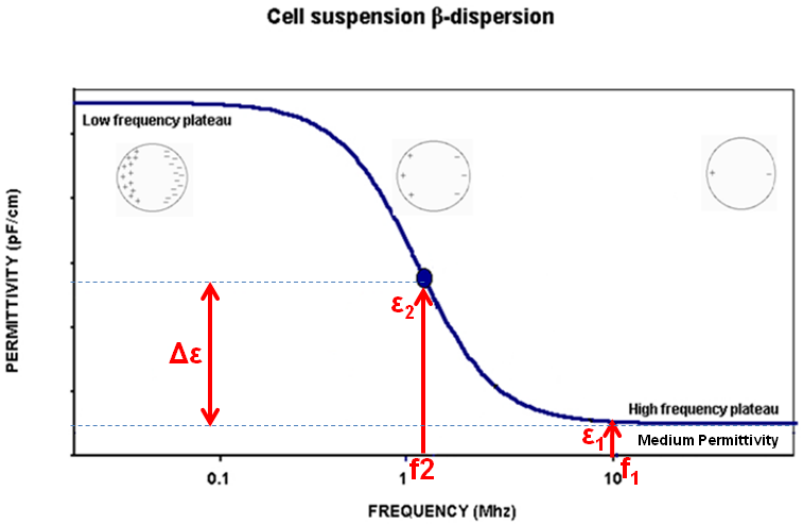
- Measure the viable cell concentration online and in real-time. The capacitance sensor is insensitive to cell debris, dead cells, micro-carriers or other non-cellular particles in suspension.
- Optimize cell growth, media, feeding strategies, induction time, harvesting time, or detect cell lysis or any process deviations
- Reduce your contamination risks and lab work with an online instrument

Principle

The capacitance sensor uses the dielectric properties of living cells to continuously monitor viable biovolume in reactors, from benchtop reactors up to large industrial scale reactors.



2 small electrodes located at the tip of the sensor are used to create an alternating electric field in the cell suspension. Within that field, cells with intact plasma membranes are polarized and behave like tiny capacitors. Dead cells have a leaky membrane and therefore do not contribute to the signal. When the electric field is released, the ions relaxation is measured by a second pair of electrodes resulting in a permittivity signal that is accurately correlated with the viable biomass concentration.



The polarization rate of the cells is a function of the frequency at which the electric field is reversed. As frequency increases, the permittivity of the cell suspension falls from a low-frequency plateau (maximum polarization) to a high-frequency plateau (minimum cell polarization). This frequency-dependent phenomenon is known as the β–dispersion. The sensor uses a dual-frequency measurement mode: the medium baseline is obtained around 10MHz, while the signal from the cells is measured around the critical frequency region, at the inflection of the curve (1 MHz for animal cells and bacteria, 2MHz for yeast) where we obtain the best signal linearity.

Application Note

Applications and References

The technology works on a large variety of cell culture and fermentation applications.
For example, we have had great success with the following cells and micro-organisms in the past few years:
Animal cells: CHO, BHK, MDCK, PERC6, NSO, HEK, Hela, Hybridoma, Vero
Insect cells: sf9, Hi-5
Bacteria: E.Coli, Bacillus Thuringensis, Salmonella, Streptomyces, Lactic Bacteria
Yeasts: Pichia Pastoris, Saccharomyces Cervisiae, Polymorpha Hasenula
Fungi: Absidia

The concentration range of the sensor is the following:
2.10^5 – 1.10^9 Cells/ml (cell culture)
1 – 200 g/l dry weight (fermentation)
5 – 200 g/l dry weight (fermentation - highly aerated culture)

You can further read about the technology, its applications and results in the following literature:

- Monitoring nutrient limitations by online capacitance measurements in batch and fed-batch CHO fermentations. Sven Ansorge. ESACT 2005 Poster; CCEX 2006 Poster
- Capacitance Sensor as a Robust Tool for Cell Culture Monitoring in Process Development and Manufacturing. Damien Voisard. Biochemical Engineering XV 2007 Poster; CCE XI 2008 Poster
- Online Measurement of Viable Cell Density in Animal Cell Culture Processes. Georg Schmid. CCE IX 2003 Poster.
- Evaluation of a Novel Capacitance Probe for On-Line Monitoring of Viable Cell Densities in Batch and Fed-Batch Animal Cell Culture Processes. Georg Schmid. ESACT 2003 Poster
- On-line viable cell density and physiological states monitoring by dielectric spectroscopy sf9 growth and infection process. G.Esteban. CCEX 2006 Poster.
- On-line monitoring of infected Sf-9 insect cell cultures by scanning permittivity measurements and comparison with off-line biovolume measurements. Sven Ansorge. Cytotechnology (2007) 55:115–124
- Process optimization of large-scale production of recombinant adeno-associated vectors using dielectric spectroscopy. Alejandro Negrete. Appl Microbiol Biotechnol (2007) 76:761–772.
- Online monitoring of vero cells cultures during the growth and rabies virus process using biomass spectrometer. Samia Rourou. ESACT 2007 Poster
- On-Line Monitoring of Lentiviral Vector Production for Characterization of Viral Production and Release Kinetics. Sven Ansorge. ESACT 2009 Poster
- On-line Pichia pastoris physiological state monitoring by dielectric spectroscopy. L. PREZIOSI-BELLOY. ECB12 2005 Poster
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