Staying alive! Sensors used for monitoring cell health in bioreactors

P. O'Mara, A. Farrell, J. Bones, K. Twomey

www.elsevier.com/locate/talanta

PII: S0039-9140(17)30809-3
DOI: http://dx.doi.org/10.1016/j.talanta.2017.07.088
Reference: TAL17787

To appear in: *Talanta*

Received date: 6 June 2017
Revised date: 25 July 2017
Accepted date: 28 July 2017

Cite this article as: P. O'Mara, A. Farrell, J. Bones and K. Twomey, Staying alive! Sensors used for monitoring cell health in bioreactors, *Talanta* http://dx.doi.org/10.1016/j.talanta.2017.07.088

Staying alive! Sensors used for monitoring cell health in bioreactors

P.O'Mara[a],: A. Farrell[b],: J.Bones[b,c],: K.Twomey[a]

[a]Tyndall National Institute, Lee Maltings, Mardyke Parade, Cork, Ireland

[b]The National Institute for Bioprocessing Research and Training, Foster Avenue, Mount Merrion, Co. Dublin, A94 X099, Ireland

[c]School of Chemical and Bioprocess Engineering, University College Dublin, Belfield, Dublin 4, D04 V1W8, Ireland

Abstract

Current and next generation sensors such as pH, dissolved oxygen (dO) and temperature sensors that will help drive the use of single-use bioreactors in industry are reviewed. The current trend in bioreactor use is shifting from the traditional fixed bioreactors to the use of single-use bioreactors (SUBs). However as the shift in paradigm occurs there is now a greater need for sensor technology to play 'catch up' with the innovation of bioreactor technology. Many of the sensors still in use today rely on technology created in the 1960's such as the Clark-type dissolved oxygen sensor or glass pH electrodes. This is due to the strict requirements of sensors to monitor bioprocesses resulting in the use of traditional well understood methods, making it difficult to incorporate new sensor technology into industry. A number of advances in sensor technology have been achieved in recent years, a few of these advances and future research will also be discussed in this review.

Graphical Abstract

Cutting Edge Capsule Technology to be used in bioreactor environment monitoring

Keywords: Bioreactor, electrochemical sensors, optical sensors, capsule technology, pH, dissolved oxygen, temperature, microfabrication, Process analytical technology

1. Introduction

Bioprocesses have been used for thousands of years through fermentations to produce alcohol, cheese and more. However, it was not until Louis Pasteur's fermentation and germ theory in 1857, that this process was understood. Since 1916, with the first ever industrial production of acetone by Chaim Weizmann who is considered the father of Industrial fermentation, large scale stainless steel bioreactors have been the mainstay of the bioprocessing industry. One of the biggest milestones achieved in bioprocessing occurred in the 1980's with the first production of recombinant human insulin. The insulin was produced by splicing the human genomic sequence for Insulin into *Escherichia coli* bacterial cells. These cells are grown by fermentation in bioreactors to produce proinsulin, then my means of enzymatic cleaving human insulin was obtained [1]. These bioreactors can be seen in Figure 1.

High demand for these bioprocess derived products over the years led to using large stainless steel bioreactors to meet the demand, some of which reach volumes of around 10,000 L [2] and in some cases biopharmaceutical industries have used multiple 20,000 L bioreactors. [3].