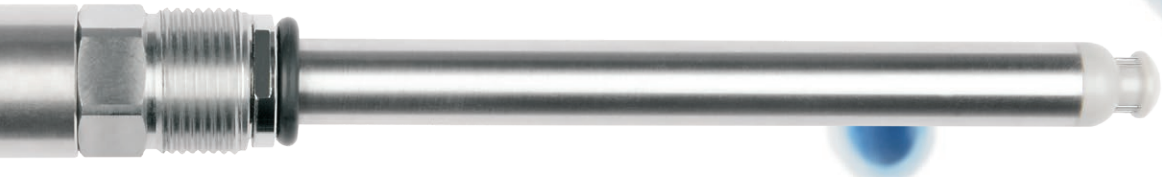
Human Platelet Protein Production from Human Cell Culture using an Advanced Bioreactor



Online viable cell density monitoring in a platelet bioprocess production

Industry: Bioreactor Manufacturing
Application field: Production of Platelets
Hamilton products: Incyte Arc, ArcAir Software

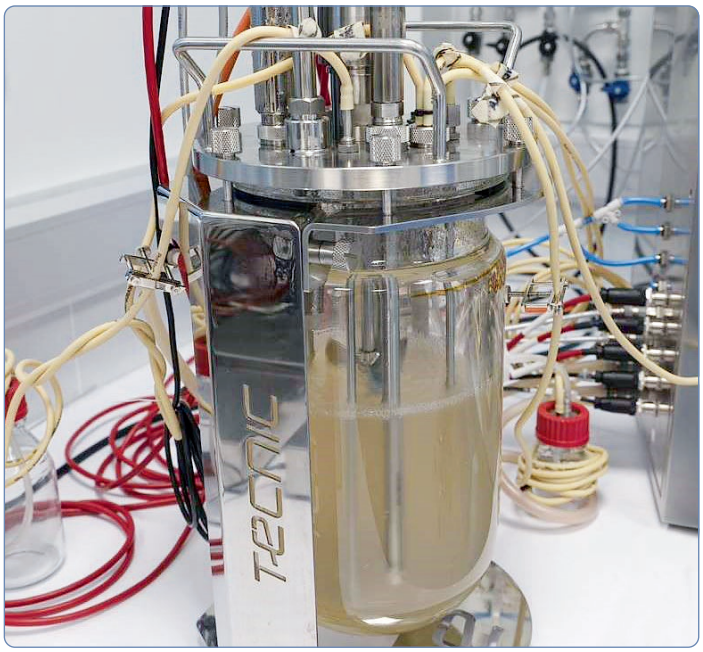


Figure 1: Incyte Arc sensor in a 5 liter bioreactor in order to determine cell density in megakaryoblastic cell type.

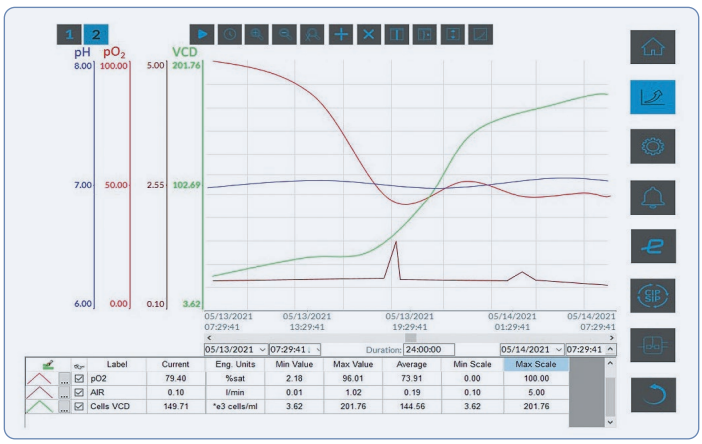


Figure 2: Embedded Graphs – also for VCD of the Incyte Arc Sensor.

Introduction

In the formation of platelets – which play an important role in wound healing – two phases can be roughly distinguished. The first phase consists of the maturation and development of megakaryocytes, where these cells increase the size of the cytoplasm and the number of nuclei, in addition to an increase in cytoskeletal proteins and specific platelet granules. In the second phase, the megakaryocytes generate platelets by remodeling their cytoplasm and forming proplatelets, which undergo subsequent fission events to generate platelets in their final form.

This physiological process is simulated in a customized bioreactor designed and manufactured by TECNIC in order to obtain a large number of cells capable of generating platelets. These platelets are used by biotech companies as a source for the production of specific human proteins.

Platelet-derived human proteins can be used as a cell growth factor for multiple cell lineages. In an effort to avoid the use of fetal bovine serum whenever possible, several studies have already described the use of platelet lysate as a substitute.

TECNIC's bioreactor consists of a multi-layered fixed-bed matrix that rotates around a vertical axis, providing optimal conditions for cell adhesion and growth. The upper side of each layer provides an increased surface area optimized for colonization by adherent cells. The geometry of the bottom of each plane is designed to create a permanent radial fluid flow.

"Rotation of a solid structure for adherent cells is an intelligent and innovative solution to provide a homogeneous mixing of the culture medium to all cells."

Optimum fluid turbulence is achieved through the rotary shaft structure and the fixed elements of the bioreactor. This turbulence is necessary to obtain sufficient energy transfer to achieve the maximum number of cells with the highest volumetric productivity.

Furthermore, the standard sensors such as pH, dissolved Oxygen (DO) and VCD (Viable Cell Density) are integrated in TECNIC advanced bioreactors for cell culture.

Critical Process Parameter in cell culture is the VCD in order to ensure an optimal cells growth and its reproducibility among iterative batches. This is achieved by using the Incyte Arc sensor to determine the online cell density in real time. The determination of the viable cell density is based on a capacitive measurement which is not influenced by dead cells, debris or air bubbles and ensures a robust measurement resolution.

Additionally, the off-line measurement based on sampling and cell counting may hide very valuable information between two consecutive samples. Off-line sampling can lead to a loss of culture volume and could be a source of contamination.

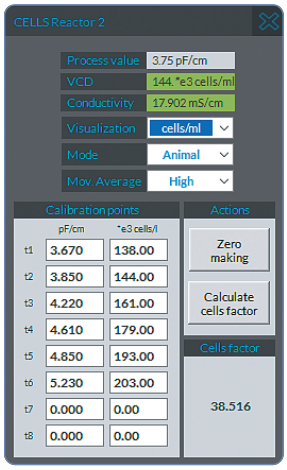


Figure 3: Display of the completely integrated data of the Incyte VCD sensor and correlation of the values.

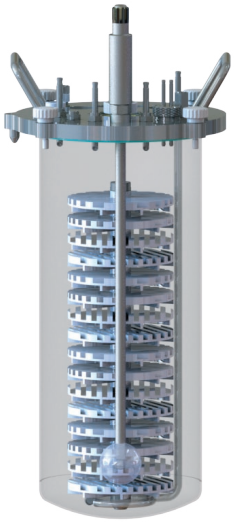


Figure 4: Incyte Arc Sensor in a TECNIC bioreactor with adherent cells attached to a rotating scaffold.

The eSCADA software used in TECNIC bioreactors converts the Incyte Arc raw data (pF/cm) to cells/ml by introducing a minimum of 3 different offline cell density values obtained in exponential phase at the laboratory.

The aim is to increase the biomass and consequently its volumetric productivity by scaling-up the working volume from 5 to 20L with reproducible conditions. In the 20L bioreactor the Incyte Arc sensor used is placed in the bottom side of it with a fixed TriClamp fitting.

"The Incyte Arc sensor provides a much better understanding of the bioprocess, avoiding associated risks due to the off-line sampling like contamination, human errors or inconsistent data."

TECNIC
BIOPROCESS EQUIPMENT MANUFACTURING

Author

Natalia Serrano Morillas PhD, *Cell Culture Researcher at TECNIC Bioprocess Equipment Manufacturing*

C/ Ponent, 10 – no. 1,2,3
Pol. Ind. Can Pruna 17421
Riudarenes Girona, Spain
www.tecnic.eu

REF 111004661/00 — 03/2022

HAMILTON

Web: www.hamiltoncompany.com
USA: 800-648-5950
Europe: +41-58-610-10-10

Hamilton Americas & Pacific Rim
4970 Energy Way
Reno, Nevada 89502 USA
Tel: +1-775-858-3000
Fax: +1-775-856-7259
sales@hamiltoncompany.com

Hamilton Europe, Asia & Africa
Via Crusch 8
CH-7402 Bonaduz, Switzerland
Tel: +41-58-610-10-10
contact.pa.ch@hamilton.ch

To find a representative in your area, please visit www.hamiltoncompany.com.