

Immobilised Cells - Microcarriers

Measuring the cell density of immobilized animal cells grown on microcarriers can be very challenging. With microcarrier cultures, apart from the errors of sampling the heterogeneous suspension, the off-line method (usually based on a nuclear count) only provides a total cell count. Radio Frequency Impedance (RFI) provides a unique on-line method for estimating the live cell mass in real time.

Figure 1 shows the application of RFI to monitor CHO cells grown on microcarriers during long term culture runs at Genzyme Inc (USA) for both the growth and harvesting phases. The process has been scaled up and the RFI probes are used in cGMP production.

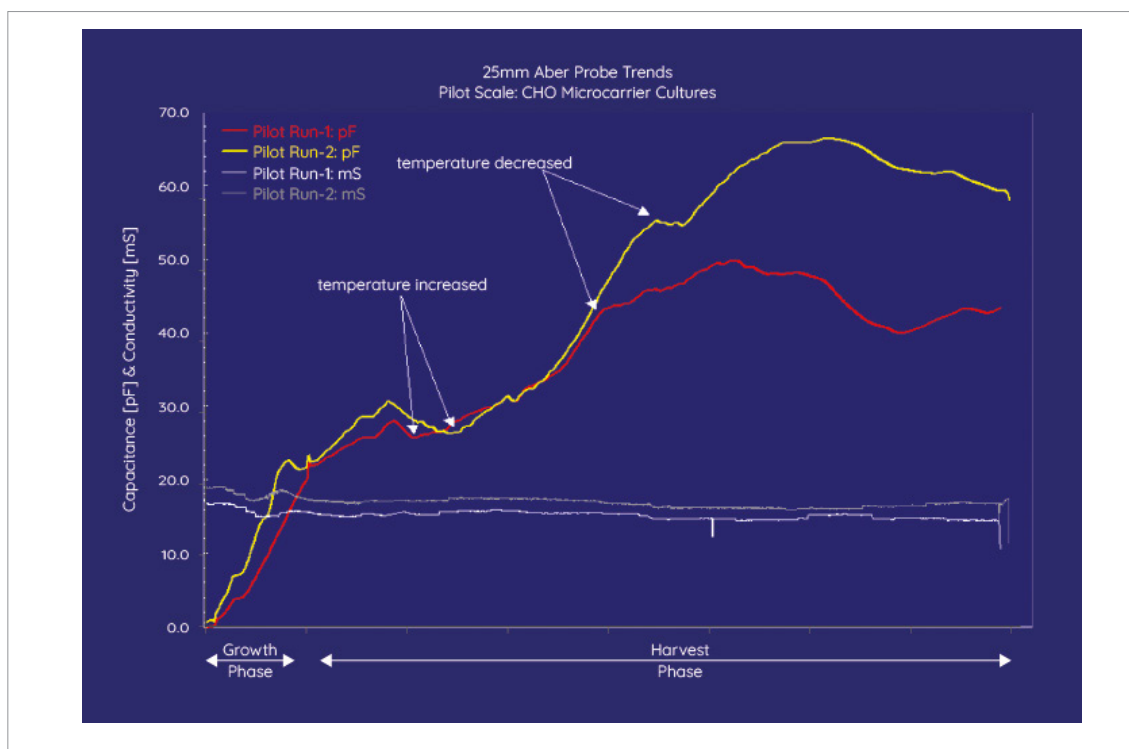


Figure 1 - Using RFI probes at Genzyme (USA) to monitor CHO cells grown on microcarriers

Figure 2 demonstrates the use of capacitance to monitor growth of Vero cells at Xenova (UK) on Cytodex 1 microcarriers, the drops in capacitance correlate with exchanges of media.

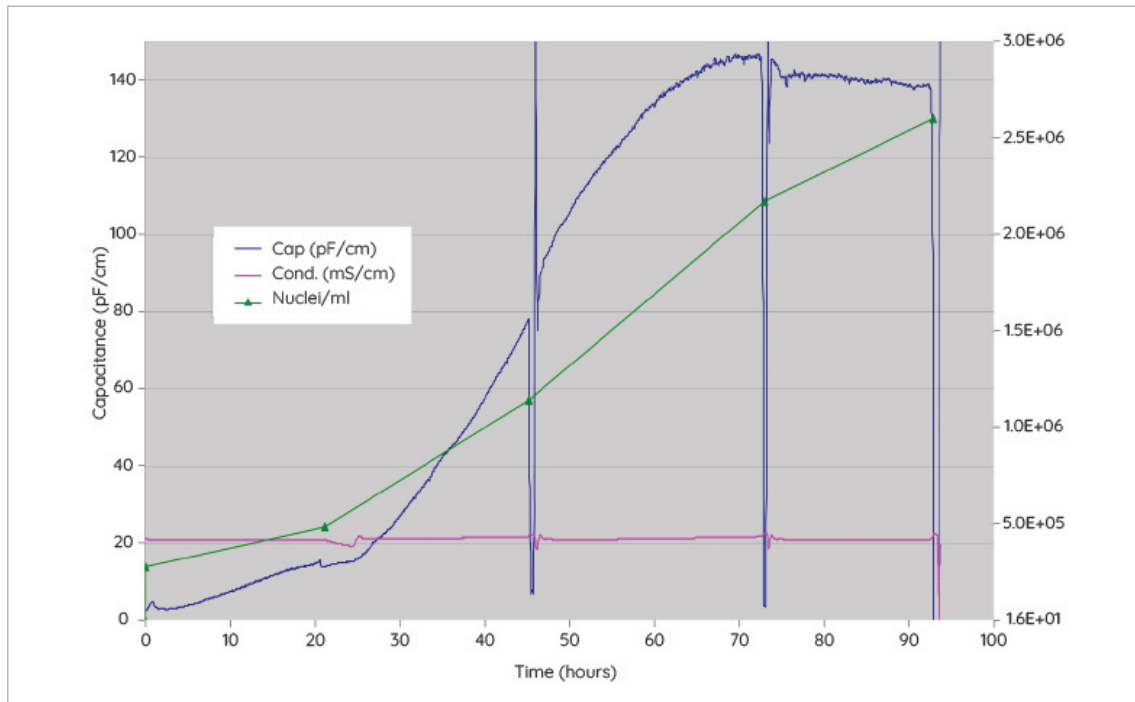


Figure 2 - Vero cells grown on surface microcarriers and monitored with a RFI probe (Courtesy of Xenova, UK)

Figure 3 presents data from a 20-day cultivation of baby hamster kidney (BHK) cells attached to macroporous microcarriers (courtesy of Novo, Denmark). Capacitance, conductivity, and the off-line cell counts are shown as a function of time. Samples were taken daily, and the cell counts were estimated by crystal violet staining followed by manual counting of released nuclei in a hemocytometer. Vertical lines shown in both capacitance and conductivity indicate the daily exchange of medium (the impeller is turned off to settle the cells). The off-line cell count on the macroporous carriers was unable to provide any meaningful data on the progression of the culture. By contrast, RFI provided valuable real-time information on the viable cell count. A small daily drop in capacitance signals indicates that essential nutrients are being depleted before the medium is exchanged.

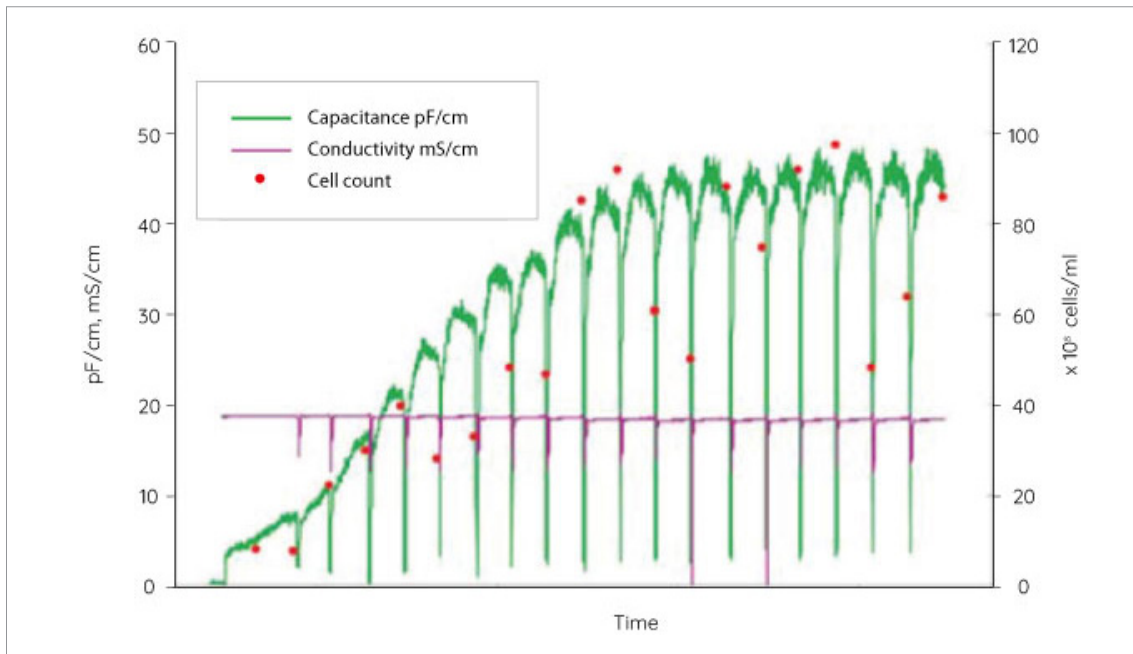


Figure 3 - Biomass of BHK cell cultivation, cells were attached to macroporous microcarriers and on-line monitoring commenced for 20 days in a 10 L fermentor (Data courtesy of Novo, Denmark)

Summary of the benefits:

- Monitor immobilized cells in situ and in real time.
- No influence on measurement from microcarriers.
- Eliminates/reduces need for sampling
- Perform cell density measurements non-disruptively
- Obtain fingerprint of the process in real time
- Troubleshooting the process
- Control critical events during the process

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