Viral Vector Production

The insect cell baculovirus expression system has become one of the most widely used systems for the routine production of recombinant proteins. After infection with the baculovirus, cells undergo significant physiological changes resulting in cell enlargement, which is typically used as a parameter for successful infection.

Utilising Aber's Radio Frequency Impedance (RFI) measurements to not only measure the concentration of insect cells, but to also determine successful viral infection has allowed for better understanding and control of these processes. In a previous study, capacitance measurements were used to determine the most appropriate point of the Sf-9 growth curve where the baculovirus could be added for optimal recombinant protein production. Excellent correlation was observed between the viable cell count and capacitance measurement before the addition of the virus. Moreover, after the addition of baculovirus to Sf-9 insect cells, RFI was used to track the progress of infection. Interestingly, even though the offline viable cell numbers no longer increase, the capacitance continues to increase rapidly immediately after infection. It was concluded that this represents an increase in the diameter of the Sf-9 cells and therefore was used as a tool to determine a successful baculoviral infection (Ansorge et al., 2011).

Further demonstrating how capacitance signal reflects morphological changes in cells due to viral infection which are not reflected in offline cell counts is demonstrated in a study performed by Grein et al. (2018). Capacitance was used to track syncytia formation, virus release and cell lysis for measles virus harvest in vero cells which were grown on microcarriers. Detecting these events allowed for the prediction of the optimal harvest time despite variations in maxima time point between runs. The timing of harvest is critical due to the short life of the virus in the bioreactor after being released from the host cell. As a result of using capacitance probes to monitor measles virus production, the bioreactor volume required to manufacture 1 dose (10^{10}-10^{12}) of virus particles was reduced from 20 L to 500 mL.

There are an increasing number of applications which demonstrate how Aber's RFI acts as an effective tool to identify the infection point during viral vector production, another notable publication reports a study where capacitance was used to determine biovolume and in-turn the infection point in rVSV-ZEBOV production in HEK 293SF cells for a potential Ebola vaccine (Gélinas et al., 2019).

Summary of the benefits:

- Monitor growth of mammalian or insect cells in culture *
- Identify infection point *
- Use the Aber measurement as an indicator for successful infection
- Identify peak infection point *
- Identify virus release and optimum harvest point *
- Eliminates/reduces need for sampling
- Obtain fingerprint of the process in real time
- Troubleshoot the process
- Control critical events during the process *
- Improve productivity and process consistency

References:

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