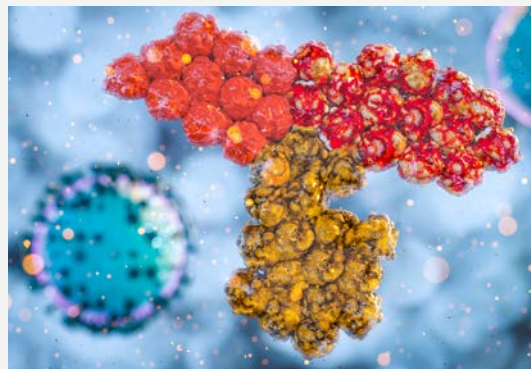




In-line qualification of monoclonal antibody production by cell culture

The production of monoclonal antibodies, derived mainly from culturing mammal cells, requires real-time in-situ monitoring for optimum quality control of the finished product.

A robust production method but improvements are possible

In the last few decades, the production of therapeutic monoclonal antibodies (mAbs) has developed significantly, becoming dominant on the worldwide biopharmaceutical market.

This commercial success is founded on robust, profitable production based on mammal cell culture systems.

One of the critical quality criteria for therapeutic mAbs is glycosylation, which is known to affect several key properties of the protein, such as solubility, stability, bioactivity, pharmacokinetics, etc.

Traditionally, this criterion was monitored by destructive chemical analysis for post-production quality control, which is why a real-time in-line analysis method is needed.



The advantage of checking in situ

Real-time in-situ measurement of the critical production criteria will make it possible to automate this analysis and thus improve quality.

The aim of the research work was initially to demonstrate Viserion's ability to check for the presence or absence of antibody glycosylation in complex cell culture media during CHO cell culture in the bioreactor in batch mode or by perfusion.

The second aim was to perform this monitoring in real time, according to the changing conditions of culture.

How?

Proteins have a Raman response which can be exploited:

- Proximity of the structure of the glycosylated antibodies and the different glycoforms : Considerable selectivity is necessary
- Advantage of combining Raman spectroscopy and chemometric techniques for real-time monitoring

It will be possible to monitor the mammal cell cultures in real time using Raman spectroscopy associated with an in-situ measuring probe: our Viserion solution!

Qualification and quantification of antibodies in a cell culture

The DG44 CHO cell line, which produces an anti-rhesus D antibody, was cultivated in a classic cell culture medium, completed with glutamine, at 37°C in a 2L bioreactor.

The Viserion solution can be used to monitor the evolution of antibody production and the macroheterogeneity of the antibodies, i.e. the glycosylation or otherwise of the mAbs. This heterogeneity can be monitored by targeting a part of the Raman spectrum (Figure 1).

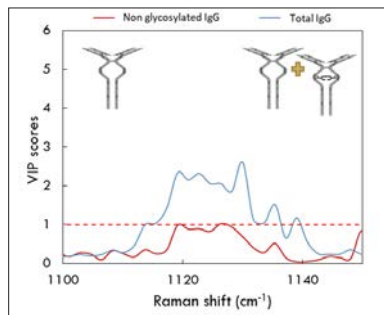


Figure 1:
Spectra of macroheterogeneity between 1100 and 1150 cm⁻¹

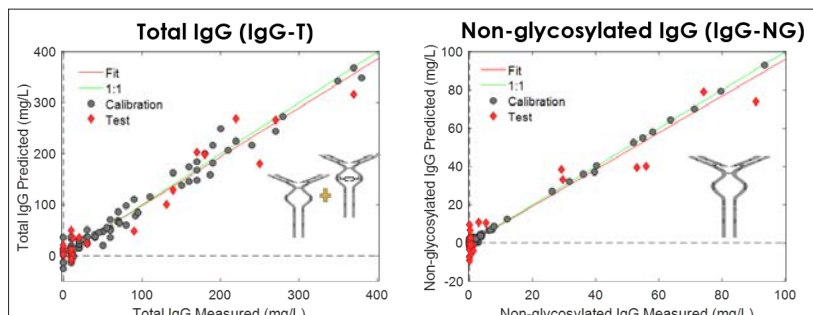


Figure 2:
Predictive models for non-glycosylated antibodies and total antibodies

The micro-zone of interest in the Raman spectrum for differentiating between antibodies will be used to draw up predictive models (Figure 2, PLS models) for the total antibodies and then for the non-glycosylated antibodies.

The integration of these chemometric models in Viserion then enables users to make a real-time prediction concerning the antibodies (Figure 3), as we can see, according to the culture time and the addition of media where culture is still under way.

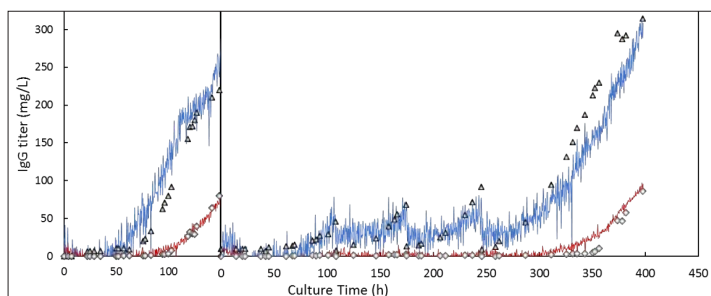


Figure 3:
Real-time prediction of non-glycosylated antibodies and total antibodies



Our teams at INDATECH will be delighted to answer your questions by telephone:
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Advantages of Viserion

Our Viserion solution offers sufficient selectivity and measurement accuracy to qualify microstructural differences in antibodies.

- A technology capable of monitoring the evolution of antibody production in situ in a complex cell culture
- Sufficient selectivity to distinguish macroheterogeneity
- Raman spectroscopy combined with chemometrics for real-time quantification of various molecules of interest characteristic of cell culture (antibodies, nutrients, etc.)

Viserion can be used to acquire as much information as possible in order to take decisions in real time.

