Microsaic Systems

Monitor and control your upstream bioprocessing using a deployable MS

Microsaic Systems plc, GMS House, Boundary Road, Woking, Surrey, GU21 5BX, United Kingdom

INTRODUCTION

The applications of mass spectrometry in the pharmaceutical industry have long been established. Mass spectrometers are highly versatile and commonly used to identify reagents, products, contaminants, and impurities from samples in drug research and development, scale-up, and high volume manufacturing lines. However, the instruments are normally large, power hungry, and expensive pieces of equipment operated in centralized laboratories by MS specialists. The new demands of bioprocessing, used to make biologics, means that there is a need for analytical instruments, such as mass spectrometers, to provide real-time information (on-line and at-line) at the point-of-need. The information-rich data provided by MS also helps to address the increased complexities of bioprocessing.

We show how our deployable, and compact mass spectrometer sampling the media from a bioreactor in real-time could provide important process monitoring, and critical quality attributes of the product. This information can then be used to maximize yields of biologics by optimising the cell media, feeding, and harvesting strategies of the target biologic being produced. In addition, MS point-of-need analysis provides timely safety assurance as any harmful PTMs of the product, and other dangerous host cell proteins can be controlled and minimized upstream.

FIGURE 1. *Prototype mass spectrometer based on the Microsaic 4000 MiD® and MiDas sampling interface unit.*

EXPERIMENTAL

This work used a prototype system, which is based on our Microsaic 4000 MiD® mass spectrometer and MiDas sampling interface unit, and is shown in Figure 1. The mass spectrometer has an adjustable mass range between 50 and 3200 m/z, which allows both proteins, and small molecules to be accurately identified.

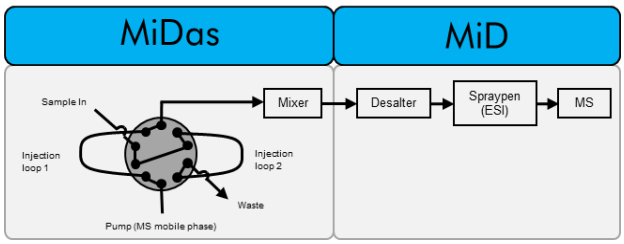

FIGURE 2. *Experimental setup showing the various steps and functions of the MiDas and MiD to analyse cell media and proteins.*

The prototype interface unit would allow biological liquids from bioreactors to be sampled, prepared, and separated into an easily ionizable electrospray, and mass spectrometer compatible mobile phase. The details of the experimental setup are shown in Figure 2, and representative work-flows of both biologic CQAs, and cell media monitoring are shown in Figures 3 and 4.

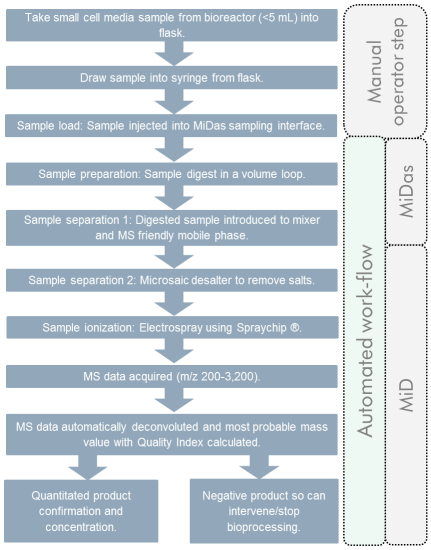

FIGURE 3. *Work-flow of biologic products monitoring in upstream bioprocessing.*

Microsaic Systems

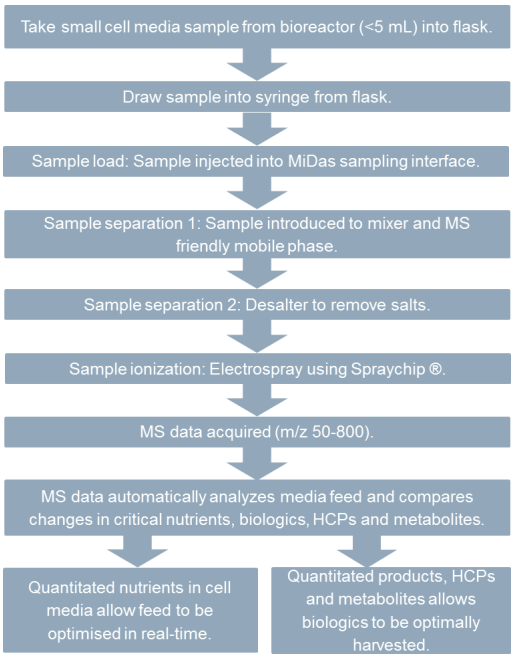

FIGURE 4. *Work-flow of cell media monitoring in upstream bioprocessing.*

RESULTS AND DISCUSSION

Representative proteins were sampled and tested using the same set-up for the cell media testing. Figure 5 shows the mass spectra of different proteins where important CQAs can be easily obtained using our real-time analysis tool. One example, also shown in Figure 5, is the automatic protein mass finder. This tool translates the information-rich data provided by the MS into an easy to understand data set, consisting of the most prominent protein mass and a 'Quality Index' for each mass. The index providing an easy to understand certainty of the protein's mass, and the quality of the input data. This data reduction allows data from the MS to be easily understood and allows operation of the MS close to the point of need by the non-expert.

A representative sample of cell media was sampled and analyzed. A typical mass spectrum is shown in Figure 6, clearly identifying 5 components of the media mix. The chemical information can then be used to control the bioprocess by optimizing the media, feeding, and harvesting strategies.

CONCLUSION

Microsaic has demonstrated that deployable mass spectrometry has the potential to be used for real-time point-of-need applications in upstream bioprocessing:

Cell media make-up optimization.

- Cell media monitoring and feeding.
- Biologic product CQA monitoring.

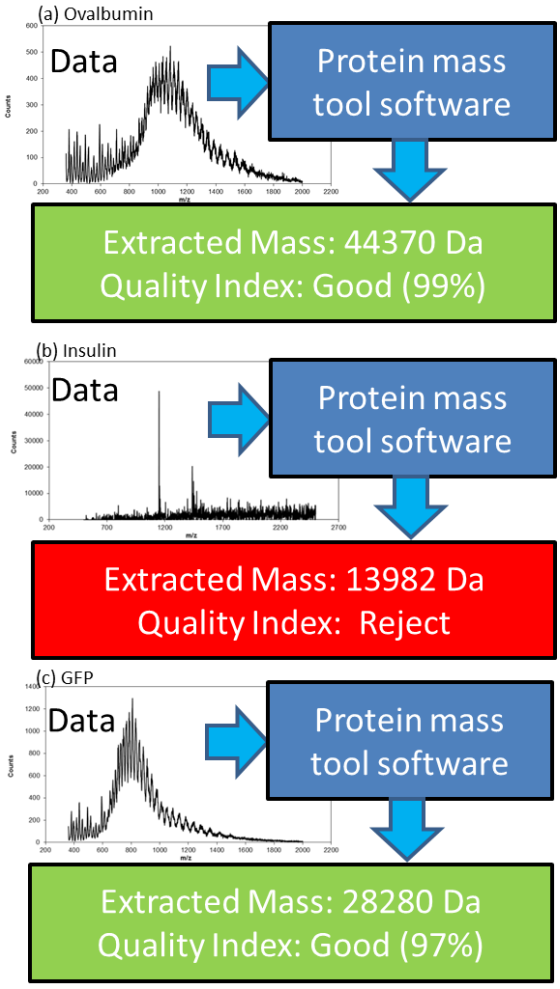

FIGURE 5. *At-line biologic product CQA monitoring in upstream bioprocessing (a) Ovalbumin (b) Insulin and (c) GFP his-tagged. bioprocessing (a) Ovalbumin (b) Insulin and (c) GFP his-tagged.*

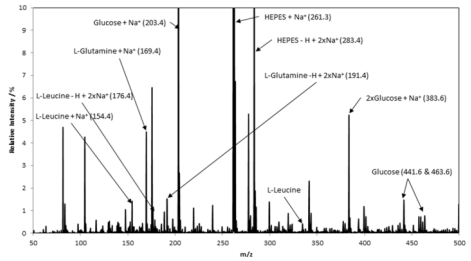

FIGURE 6. *At-line biologic product CQA monitoring in upstream*

The Microsaic product solution provides biopharma with a valuable tool to help the industry make cheaper, and safer biologics.

UNLEASH THE POWER OF MS INTO YOUR BIOPROCESS

Microsaic welcomes approaches from biopharma, and OEM partners to discuss their particular requirements.

microsaic.com +44 (0)1483 751 577 info@microsaic.com