

INTRODUCTION

For cultivations of microorganisms and cell cultures, as well as for API screening and media optimization studies were often performed in parallel batches. Therefore multi-bioreactor-systems were used frequently (e.g. Biostat® Qplus from Sartorius, DASbox® from DASGIP, Sixfors® from Infors, etc.). Glucose is used as substrate for many microorganisms and cell lines. In microbial fermentations and in cell cultivations the glucose concentration has to be monitored permanently. High concentrations of lactate has to be avoided and a permanent determination of the actual concentration is advantageously.

TRACE C2 Control

TRACE C2 Control is an online analyzer for monitoring and controlling glucose and lactate concentrations (figure 1). Glucose can be controlled in a range between 0.1 g/L and 40 g/L. The parameter lactate can be additionally measured in a range between 0.05 g/L and 10 g/L.



Figure 1. TRACE C2 Control with tubing set

Measurements in four bioreactors in parallel are possible with the extension M4 or with another device MultiTRACE. The MultiTRACE is designed for cell culture applications, where the change of substrate and product is not too fast. For fast growing bacteria the combination TRACE C2/M4 (figure 2) was developed and better suited because of the fast measurement interval.

M4

The M4 is an extension of the TRACE C2 Control with the option to monitor up to four different bioreactors. The M4 integrates 4 additional pumps and four 3/2-way valves into the fluidics so that four sampling probes can be operated in parallel. The desired probe is then selected by means of the additional valves.

Advantages

- Fast measurements of Glucose and Lactate concentrations in up to four bioreactors
- Safe and economic operations
- Low installation size
- Less maintenance effort
- Disposable consumables
- Connection to different fermenter types

The sequence of the reactors and the number of measurements per reactor can be chosen by the user with the help of a time schedule. The appropriate probe will be selected by the valves and the measurement will be done automatically. Measurements are possible in the dialysis mode every two minutes. With the M4 it is possible to measure without the changing time period.



Figure 2. TRACE C2 Control with M4

Connecting to the Process

For connecting the device to the process, the patented dialysis probe (figure 3), the filtration probe, the bypass-module, or the single-use dialysis probe are optional available. Therefore the combination of TRACE C2 and M4 can be connected to common glass and stainless steel fermenters as well as to novel single-use bioreactors.

Michael Hartlep und Wolfgang Künnecke

TRACE Analytics GmbH
Richard-Wagner-Straße 1
38106 Braunschweig (Germany)
e-mail: mh@trace.de



Figure 3. Dialysis probe

The flow diagram of the TRACE C2/M4 for the dialysis mode is shown in figure 4.

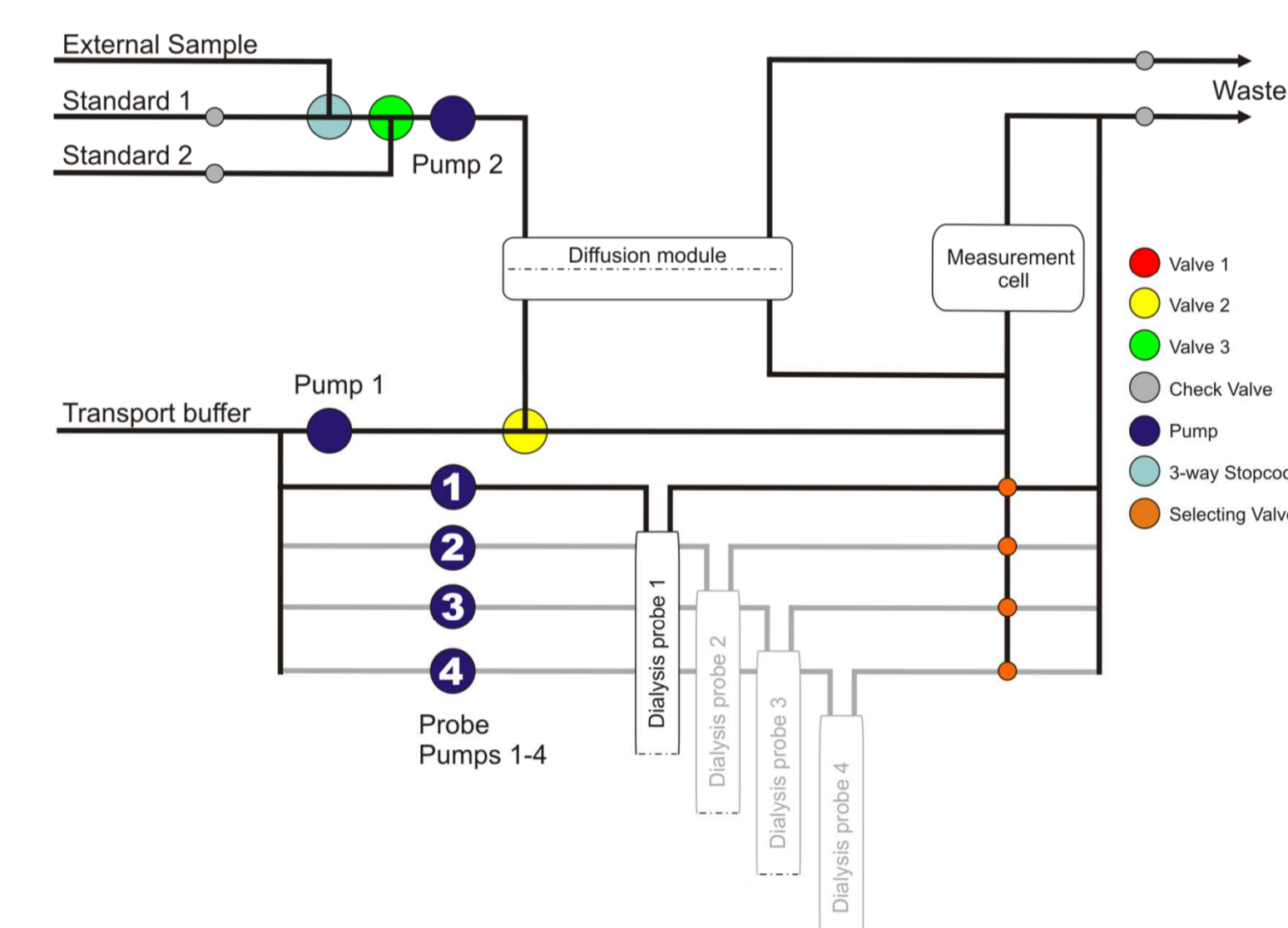


Figure 4. Flow diagram dialysis mode TRACE C2/M4

Glucose and Lactate monitoring

Four parallel cell cultivations were performed in 3L glass fermenters. Glucose and Lactate concentrations were monitored online. The measurements were compared with offline measurements using a Nova Biomedical Analyzer as reference (figure 5).

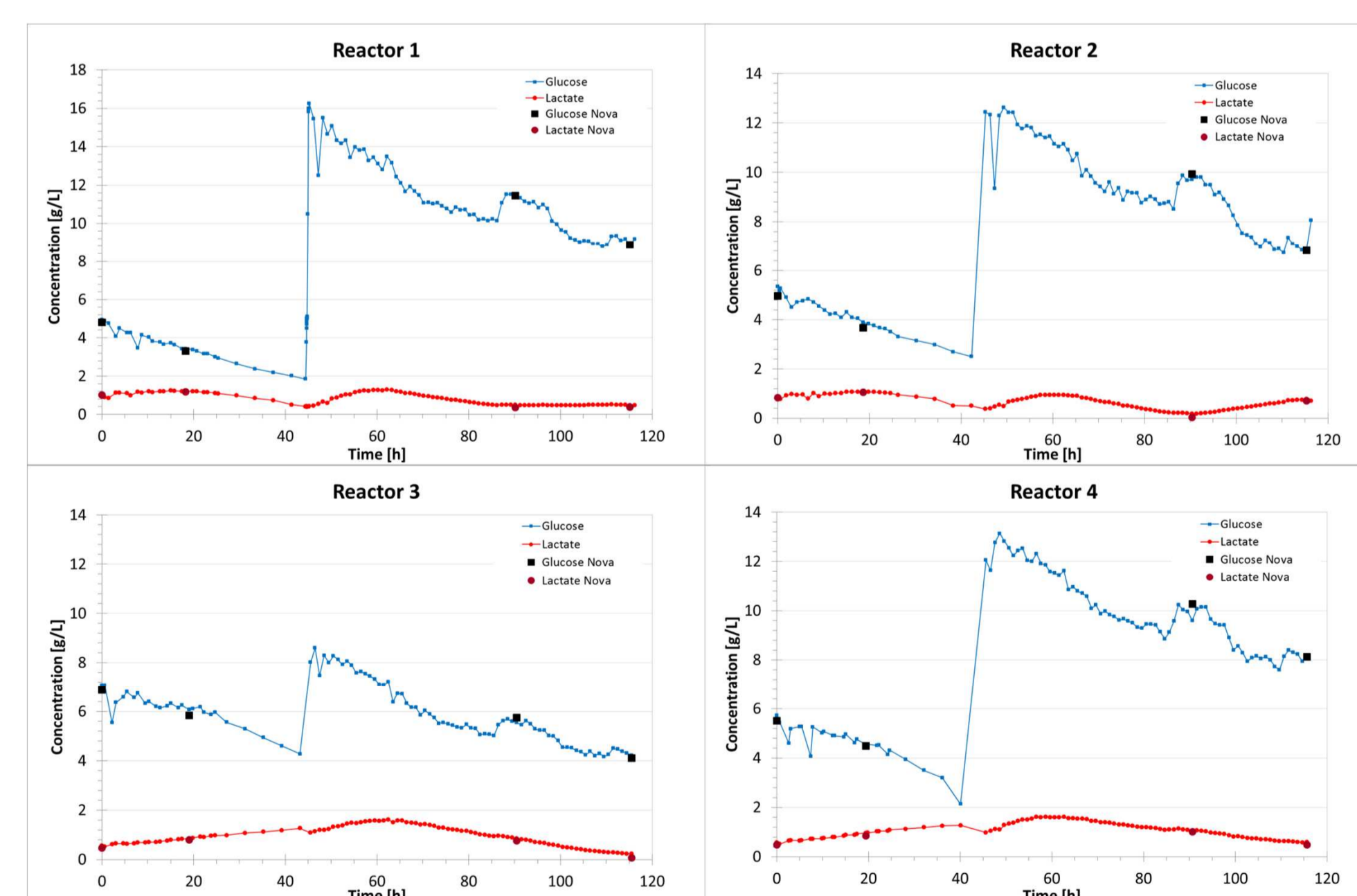


Figure 5. Glucose and Lactate measurements in four bioreactors

CONCLUSION

TRACE C2 is an online analyzer for monitoring and controlling Glucose and Lactate concentrations in bioreactors. With the extension M4 it is possible to monitor Glucose and Lactate in up to four simultaneous bioprocesses. Because of the fast measurement cycle the TRACE C2/M4 is specially designed for microbial cultivations.