



New Applications for In-situ Microscopy: Inline Monitoring of Cultivations and Crystallisation Processes

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Aim of this Project

The In-situ microscope is a sterilizable and non-invasive image analysis system. A connected PC contains control and analysis software. The microscope is placed through a 25 mm standard bioreactor side-port. During biotechnological processes (cultivation, crystallisation) the microscope's sampling zone is directly immersed in the medium. The system can be easily cleaned and serviced without process interruption and contamination risk. During the process a defined medium volume is enclosed by the sampling zone and image series are taken in intervals automatically. Process relevant information is extracted from the images by image processing algorithms.

Applications

Inline monitoring of crystals

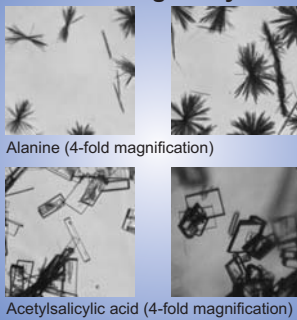


Figure 1: Images of crystals.

In-situ microscope

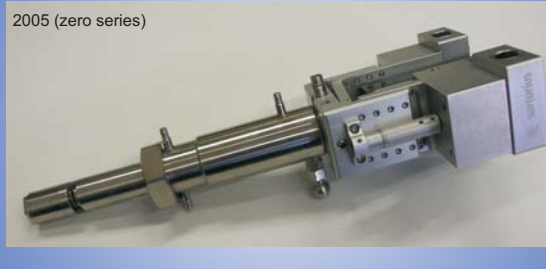


Figure 2: In-situ microscope system.

Inline monitoring of NIH-3T3/ Cytodex 1 microcarriers

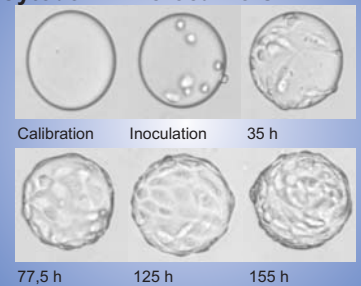


Figure 3: Batch cultivation of NIH-3T3.

Object sampling principle

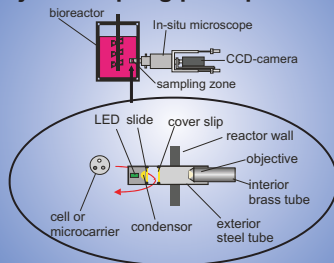


Figure 4: Flow-through sampling zone.

Image analysis principle of CHO

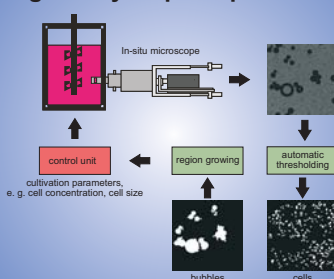


Figure 5: Image analysis embedded in the process control.

DVD

Image analysis principle of yeasts

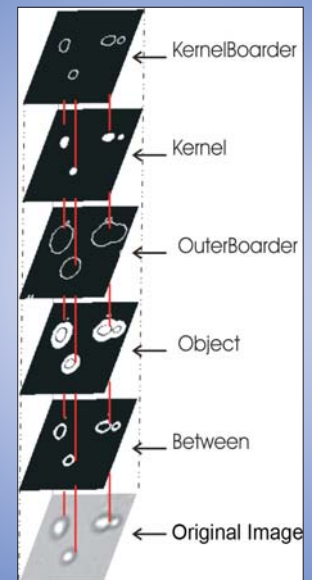


Figure 6: Procedure of image analysis.

Hardware Features

- Brightfield transmitted light microscopy (LED illumination)
- High resolution Fire-Wire CCD-camera (1280 x 960)
- Finity corrected objectives
- 4-fold, 10-fold and 20-fold optical magnification
- Total magnification up to 1000-fold
- Field of view: 200 μm^2 to 1 mm^2
- Full autoclavable
- Cleaning of sampling zone by retract system
- Robust, for long-term operation
- Use in bioreactors with 25 mm standard side-port

Software Features

- Image analysis
- Yeasts:
 - Cell number and concentration
 - Cell size distribution
 - Cell volume (biomass)
 - Differentiation (single cells, double cells, clusters)
 - CHO, BHK:
 - Cell number and concentration
 - Cell size distribution
 - Detection of air bubbles
 - Detection of sticking cells
 - Graphical user interface