New Raising Power Measurement Devices for Advanced Tasks

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How all began . . .

Customer-Driven Development for

Centre de Recherche Nestlé (CRN) in Lausanne:

Low Temperature Inactive (LTI) Yeast Project
asks for a sensitive measuring device to detect
gassing activities of 100- to 1000-fold below
standard yeast dough conditions

Systems on the market did not fulfill these criteria!

We: A Spin-off Company from ETH-Zürich were already in collaboration
with Nestlé in the topic of

Advanced Bioprocess Technology
„Quality Control by Process Control“
Our concept from 1994 . . .

. . . becomes 10 years later a major demand of US-FDA‘s PAT-Initiative!

New Raising Power Measurement Devices for Advanced Tasks — 22nd VH Yeast Conference in Berlin, April 27-28, 2009
Roche Vitamins / DSM: Production Plant with 6 Bioreactors, each 140 m³
Monitoring of Product, Byproduct and Cell Density

On-line Monitoring of Industrial Fedbatch Process

![Graph showing the monitoring of Product, By-Product, and Optical Density over time.](image)

- **Product**
- **By-Product**
- **OD (660 nm)**

*New Raising Power Measurement Devices for Advanced Tasks — 22nd VH Yeast Conference in Berlin, April 27-28, 2009*
User Requirements (selection)

- Lower detection limit at about 1 ml gas per day
- Suitable system-volume for samples of about 30g dough
- Duration of experiments up to 3 weeks
- Ambient temperature range from 0°C to 40°C
- User-friendly concept
- Modular extendable system
Selection of Measuring Principle

1. Open Systems

1.1 Massflow Sensors
   not sensitive enough

1.2 „Classical“ Displacement principles

Automated evaluation of measuring requires additional sensors, complex handling
Selection of Measuring Principle

2. Closed Systems

Measurement of Pressure-Differences by

2.1 Absolute Pressure Sensors

2.2 Relative Pressure Sensors

reference measurement required

Disadvantage: Management of overpressure and security aspects
Realised System

Gasvolume-Monitor „Niesler“

(Name according to the Initiators Dr. Peter Niederberger and Dr. Christof Gysler from CRN)

Recording of absolute pressure over time, calculation of generated gas volumes according to

\[ p \times V = n \times R \times T \]
Gasvolume-Monitor „Niesler“

System Overview

Measuring Range: >4 Magnitudes
Lower Limit: 1 ml per day
Upper Limit: 3 L per hour
Resolution: 0.05 ml
Gasvolume-Monitor *Niesler*

**Windows-based Operation-Software**

- Automated and manual interactions with measuring units
- Units can be freely combined in experimental sets
- Multiple sets can be registered simultaneously
- Results are presented directly via online view on the screen
- Excel-readable files are generated for subsequent user-specific operations
- Generation of standardised reports in QA routine measurements is possible
Activity = f (Temperature)

- gassing activity increases with increasing temperature

Baker’s yeast in model dough

Data from Dr. Christof Gysler, Nestec Lausanne:

<table>
<thead>
<tr>
<th>Temperature</th>
<th>CO₂ Production (ml/35 g dough)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2°C</td>
<td>0</td>
</tr>
<tr>
<td>4°C</td>
<td>2.4 ul CO₂ / g *h</td>
</tr>
<tr>
<td>6°C</td>
<td></td>
</tr>
<tr>
<td>8°C</td>
<td></td>
</tr>
<tr>
<td>10°C</td>
<td></td>
</tr>
</tbody>
</table>

2.4 ul CO₂ / g *h
Activity = f (Recipe)

e.g.: NaCl concentration

Data from Dr. Christof Gysler, Nestec Lausanne:

Niesler® gas-monitor:
Data from Dr. Christof Gysler, Nestec Lausanne:

Activity = f (Yeast concentration)

Cumulative CO$_2$ development

Initial activity (5-35 hrs) vs. [conc.]
Data from Dr. Christof Gysler, Nestec Lausanne:

**Activity = f (Time)**

- At low temperatures and low yeast conc. the gassing activity is linear

« normal » dry Yeast / LTI Yeast

- Temperature-Profile of LTI-Yeast is not according Arrhenius

ROBUST AND PRECISE

• Fabricated completely in stainless steel
• Water protected measuring head
• User-friendly and efficient Tri-Clamp fastener
• „Plug and Work“-Layout
• Improved concept of components => improved gas-tightness
• Extended Security-Concept for Overpressure (Software, Firmware, Hardware)
Niesler 2009: Reproducibility

Gassing activity from 100g model dough at 30°C, measured in 3 different Units

ml CO₂ / g dough

hrs

rel. StdDev ≤ 1%

Comparison of Niesler with SJA Fermentograph

Experiments at VH-Berlin by Dipl. Biotechnol. Claus Decker were just started . . .

Exemplary first results: Gassing activity as a function of sample size
Future Perspectives:

Development of new Evaluation and Reporting Tools for Industrial Routine Applications

Development of other Vessel Formats adapted to Customer-specific Work-Flows

... to be continued ...

What are your specific needs?