

## **22<sup>nd</sup> VH Yeast Conference**

**Berlin, April 27 – 28, 2009**

# **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**



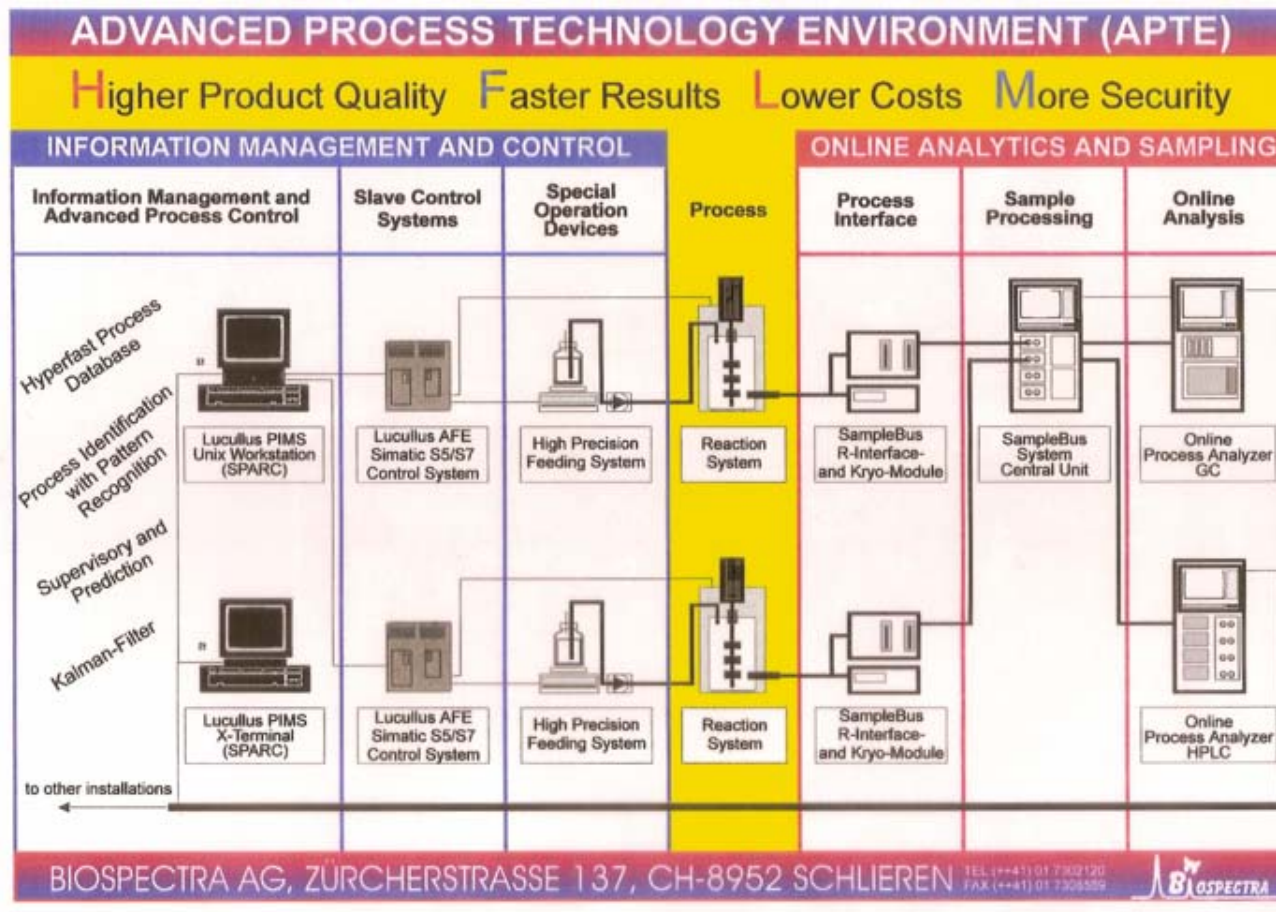
**Systems on the market did not fulfill these criteria!**

**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 . . .

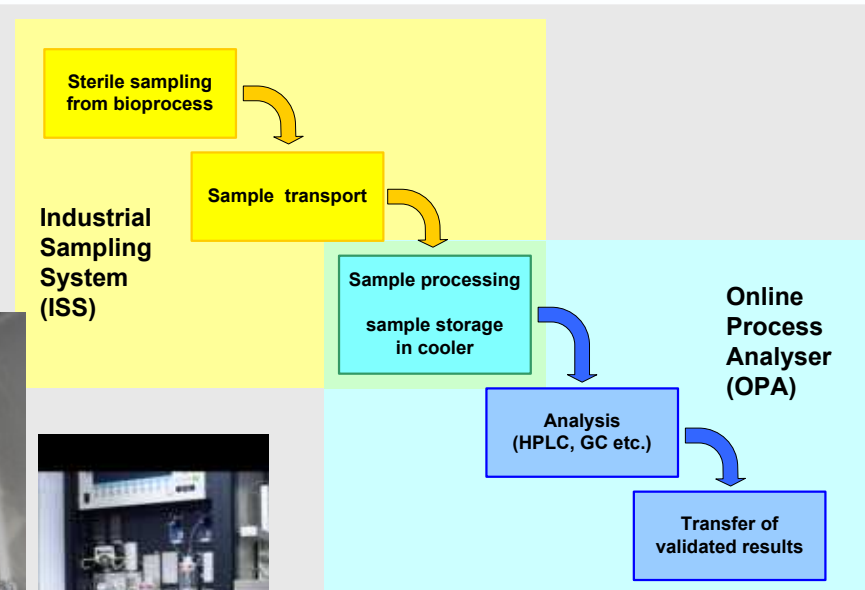


Presented at Hannover Trade Fair  
and at Biotechnica

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

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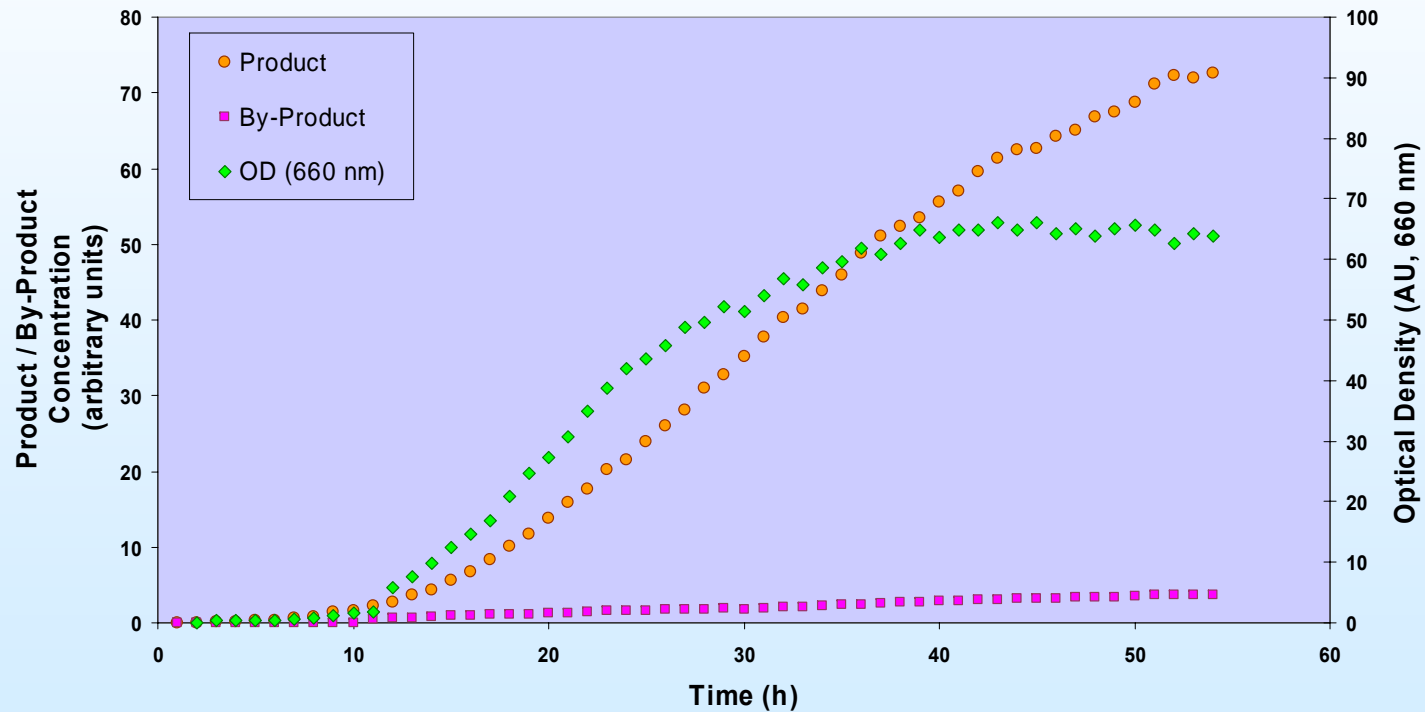
# Process Analytical Technology in „State of Routine“



**Roche Vitamins / DSM:  
Production Plant with  
6 Bioreactors, each 140 m<sup>3</sup>**

## Monitoring of Product, Byproduct and Cell Density

### On-line Monitoring of Industrial Fedbatch Process



## User Requirements (selection)

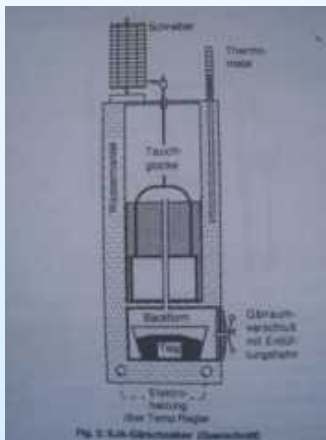
- Lower detection limit at about 1 ml gas per day
- Suitable system-volume for samples of about 30g dough
- Duration of experiments up to 3 weeks
- Ambient temperature range from 0°C to 40°C
- User-friendly concept
- Modular extendable system

## 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)



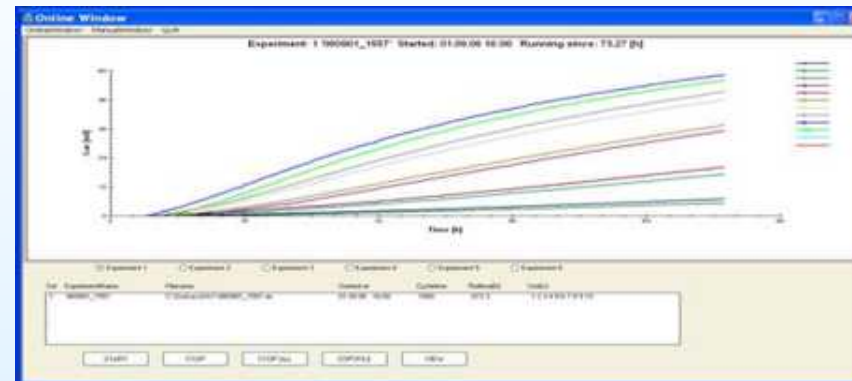
Recording of absolute pressure over time,  
calculation of generated gas volumes according to

*Ideal Gas Law*

$$p * V = n * R * T$$

## Gasvolume-Monitor „Niesler“

### System Overview

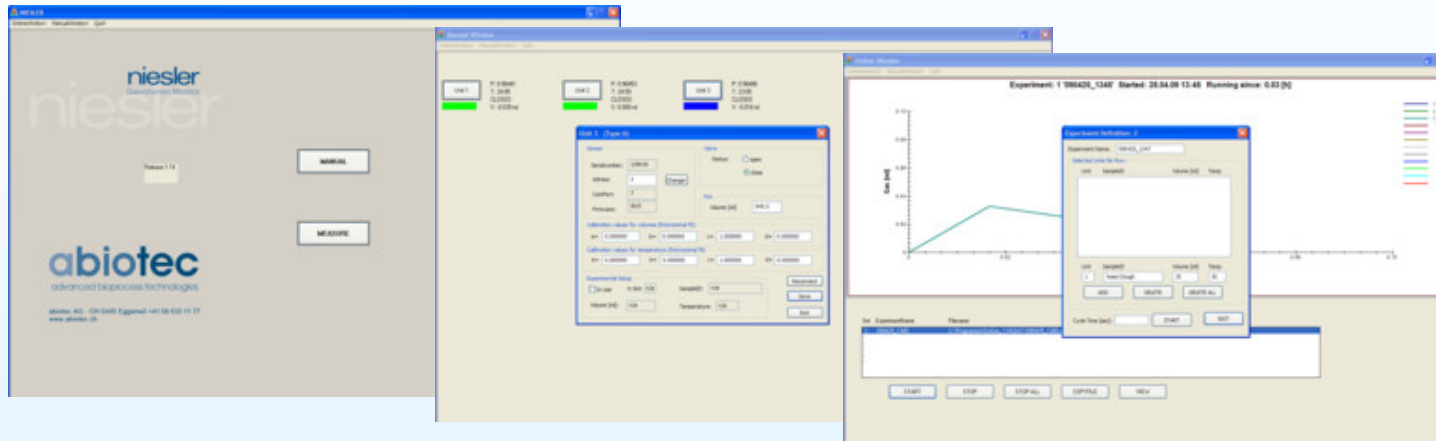


**Measuring Range: >4 Magnitudes**  
**Lower Limit: 1 ml per day**  
**Upper Limit: 3 L per hour**  
**Resolution: 0.05 ml**



## Gasvolume-Monitor *Niesler*

### Windows-based Operation-Software



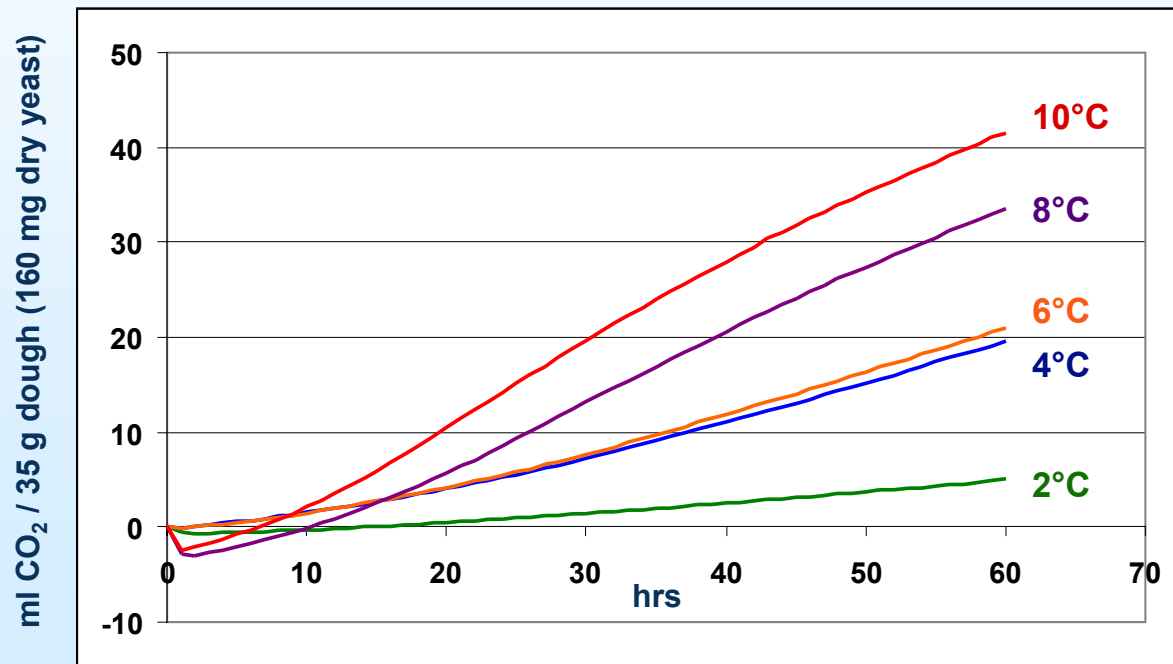
- Automated and manual interactions with measuring units
- Units can be freely combined in experimental sets
- Multiple sets can be registered simultaneously
- Results are presented directly via online view on the screen
- Excel-readable files are generated for subsequent user-specific operations
- Generation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

Data from Dr. Christof Gysler, Nestec Lausanne:

## Activity = f (Temperature)

- gassing activity increases with increasing temperature

Baker's yeast in model dough



Niesler<sup>®</sup> gas-monitor:

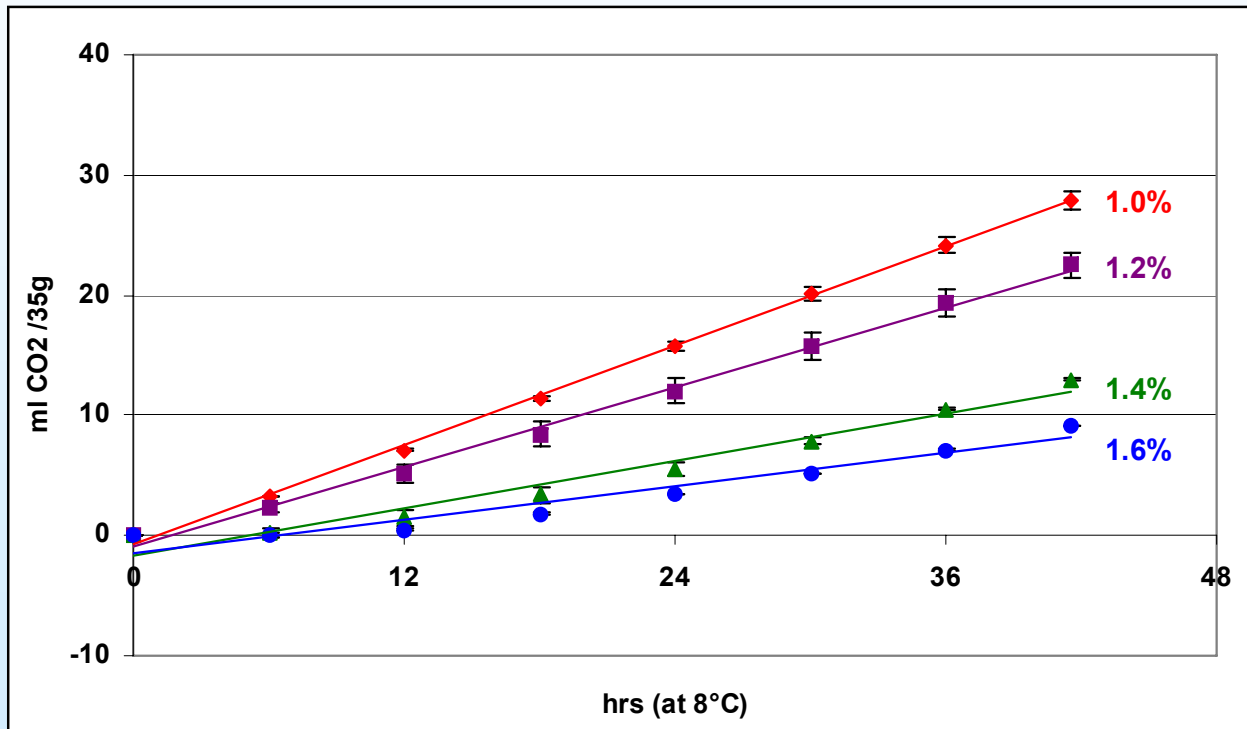


2.4 ul CO<sub>2</sub> / g \*h

Data from Dr. Christof Gysler, Nestec Lausanne:

# Activity = f (Recipe)

e.g.: NaCl concentration



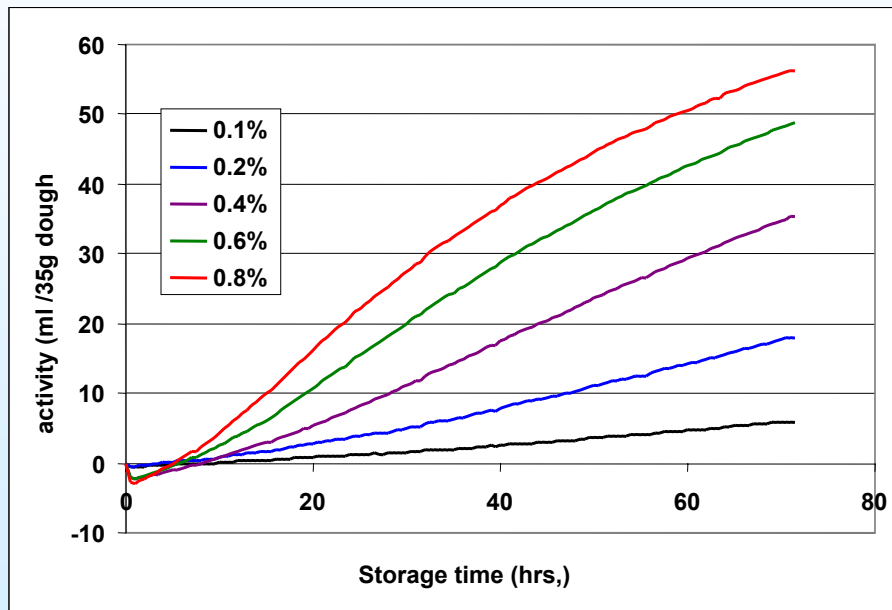
Niesler<sup>®</sup> gas-monitor:



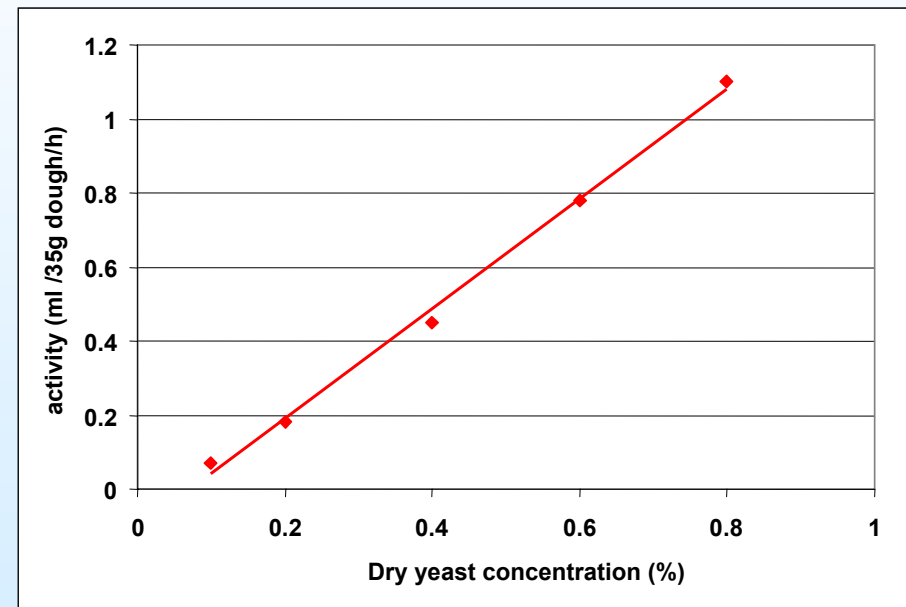
Data from Dr. Christof Gysler, Nestec Lausanne:

## Activity = f (Yeast concentration)

Cumulative CO<sub>2</sub> development



Initial activity (5-35 hrs) vs. [conc.]

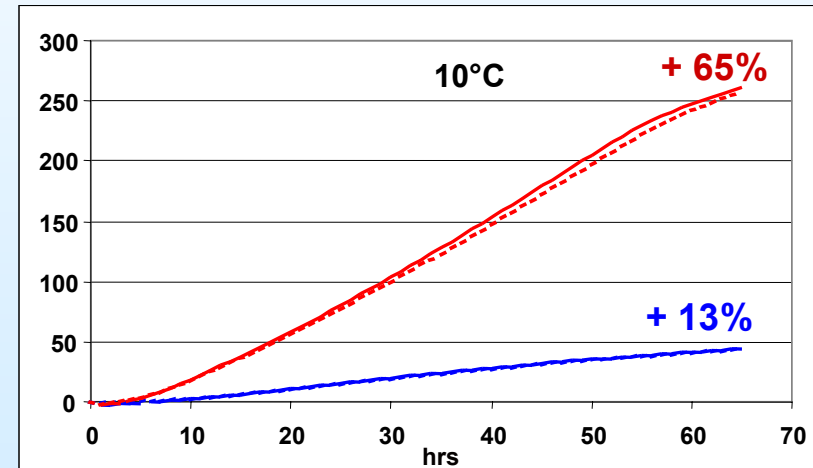
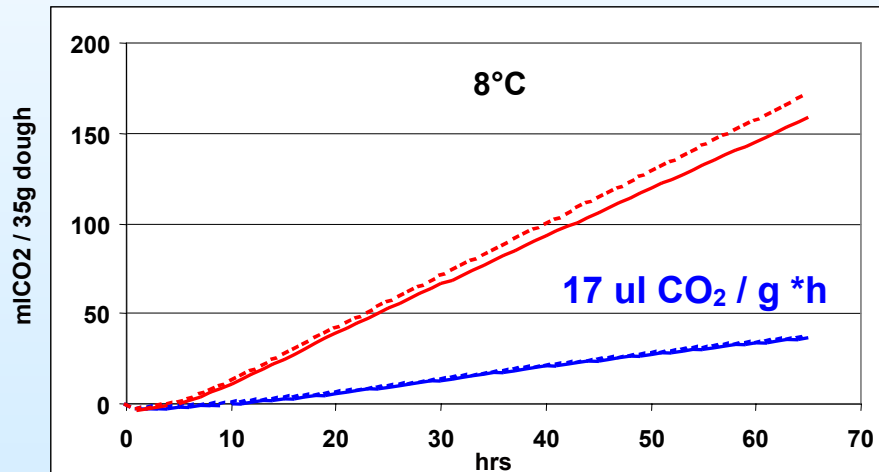


Data from Dr. Christof Gysler, Nestec Lausanne:

# 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

## Niesler: New Edition 2009



**abiotec**  
advanced bioprocess technologies



### **ROBUST AND PRECISE**

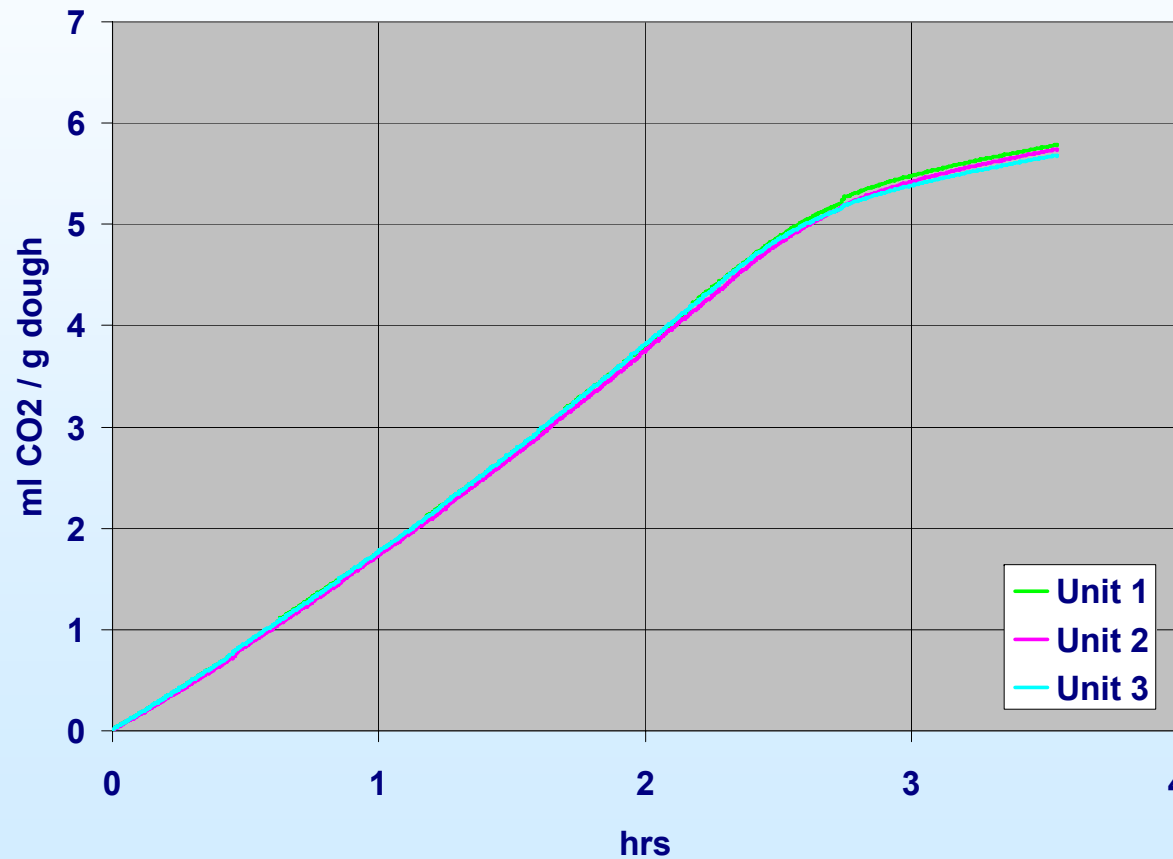
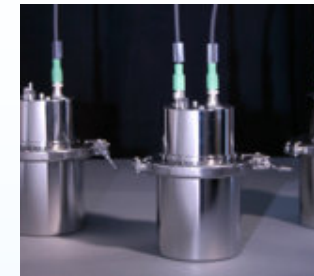
- Fabricated completely in stainless steel
- Water protected measuring head
- User-friendly and efficient Tri-Clamp fastener
- „Plug and Work“-Layout
- Improved concept of components => improved gas-tightness
- Extended Security-Concept for Overpressure (Software, Firmware, Hardware)

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## Niesler 2009: Reproducibility

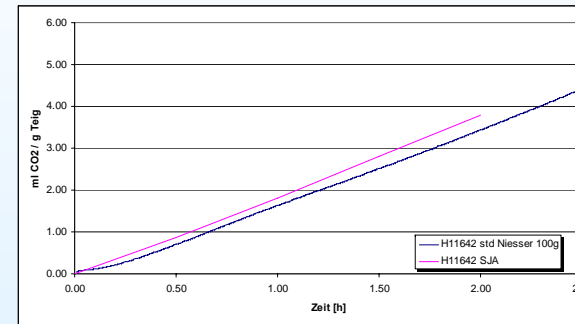
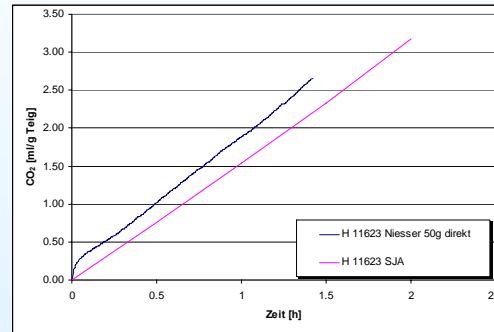
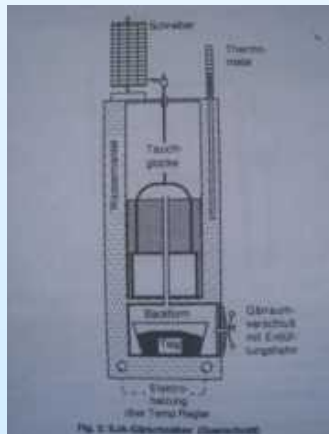
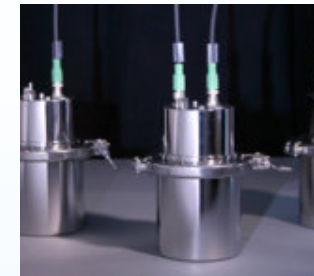
**Gassing activity from 100g model dough at 30°C,  
measured in 3 different Units**



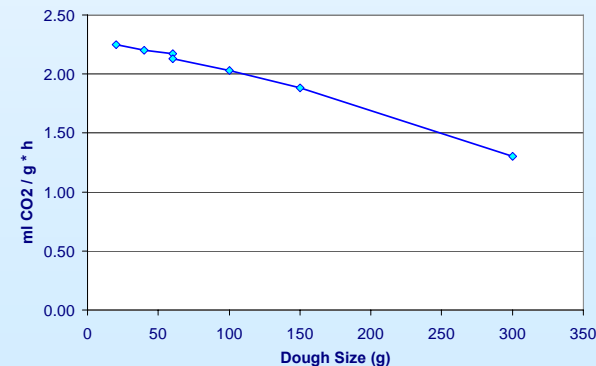
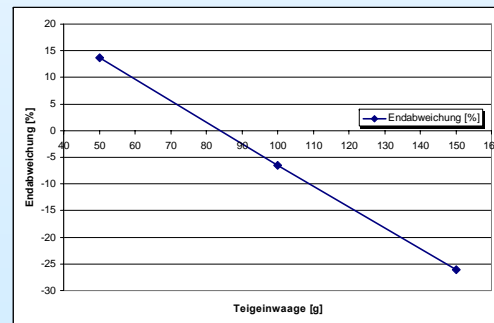
**rel. StdDev  $\leq$  1%**

# Comparison of Niesler with SJA Fermentograph

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



Spec. Gassing Activity Rates vs. Dough Size



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

**Niesler 2009:**

## **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 ?**

