Theory 4

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Theory 4:

Process engineering tools (sensor technology)

- thermal resistance measurement
- pressure and vacuum measurement
- barometric pressure measurement
- metric pressure measurement
- wireless temperature measurement (Amphenol)
- conductometry
- camera systems

Thermal resistance measurement (platinum temperature sensor)

Platinum temperature sensors use the effect of temperature dependence of the electric resistance of the precious metal platinum. The resistance increases at higher temperatures, it is a positive temperature coefficient, such sensors are named PTC (positive temperature coefficient).

Abbildung 6: Temperatursensorproduktion unter Reinraumbedingungen

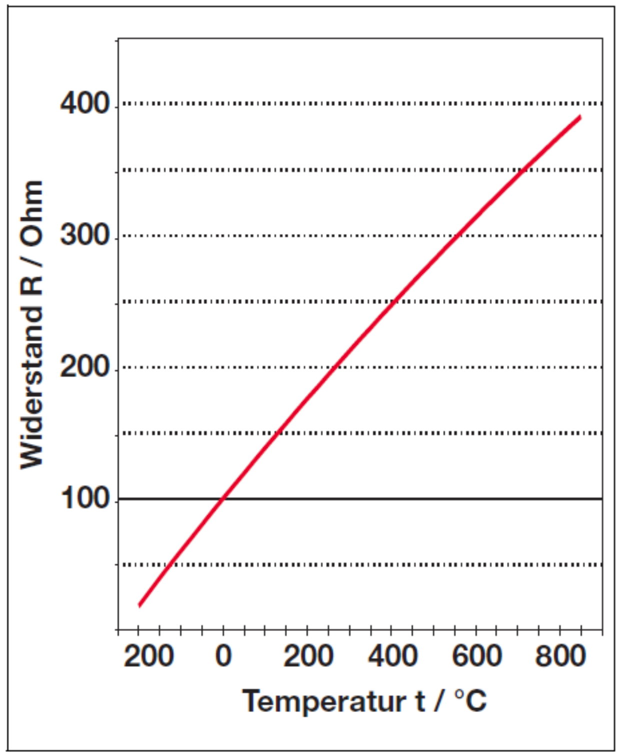


Abbildung 1: Pt100-Kennlinie

Thermal resistance measurement (platinum temperature sensor)

Besides the “standard” PT100 there are temperature sensors with higher nominal values for instance PT500, PT1000.

They have a higher sensitivity, because the increase factor of characteristic curve is directly proportional to the par value R_0.

Their advantage is a larger variation of their resistance depending on the temperature.

Resistance changes (temperature range up to 100 °C)

- 0,4Ω /K at PT100 temperature sensor
- 2,0Ω /K at PT500 temperature sensor
- 4,0Ω /K at PT1000 temperature sensor

Abbildung 12: Laserabgleich der Platin-Chip-Temperatursensoren

Thermal resistance measurement (platinum temperature sensor)

The long-time behavior is another important factor apart from tolerance of temperature sensors. It is responsible for the compliance of measurement uncertainty. The values listed in the data sheets are guide values. They were determined into an oven with normal atmosphere by temperature sensors.

The processing of temperature sensors and the materials with which it comes into contact can influence the long-term stability. In order to determine the long-term stability in each case of the existing construction a regular calibration in their intended conditions of use is necessary.

Abbildung 9: Automatisierte Produktion drahtgewickelter Platin-Glas-Temperatur-sensoren

Thermal resistance measurement (platinum temperature sensor)

Tolerance classes

Toleranzklasse	Sensor-Kategorie	Temperaturbereich in °C	Toleranz in K
Klasse AA	Dünnschicht Draht	-50 ... +200 -70 ... +250	± (0,10 K + 0,0017 × |t|
Klasse A	Dünnschicht Draht	-70 ... +300 -200 ... +600	± (0,15 K + 0,002 × |t|
Klasse B	Dünnschicht Draht	-70 ... +600 -200 ... +850	± (0,30 K + 0,005 × |t|
Klasse 0,5	Dünnschicht Draht	-70 ... +600 -200 ... +850	± (0,50 K + 0,006 × |t|
			|t| = Messtemperatur in °C (ohne Vorzeichen)

Tabelle 1: Toleranzklassen - Temperaturgültigkeitsbereich

Temperatur in °C	Klasse AA in K	Klasse A in K	Klasse B in K	Klasse 0,5 in K
-200		0,55	1,30	1,70
-70	0,22	0,29	0,65	0,92
0	0,10	0,15	0,30	0,50
100	0,27	0,35	0,80	1,10
250	0,53	0,65	1,55	2,00
350		0,85	2,05	2,60
600		1,35	3,30	4,10
850			4,55	5,60

Tabelle 2: ±-Toleranz in K je Klasse

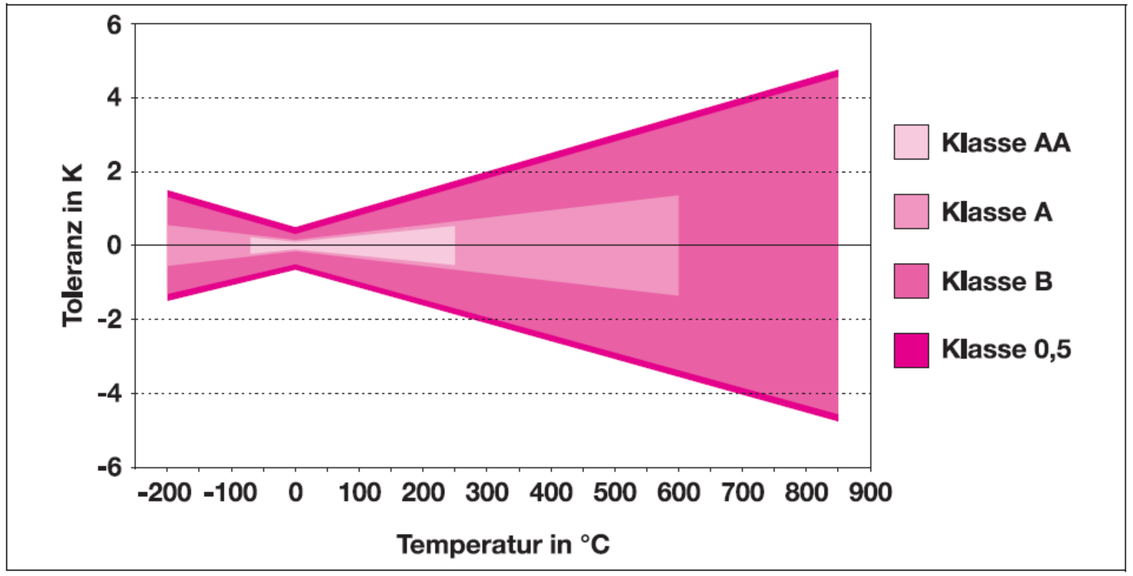


Abbildung 2: Toleranzverlauf in Abhängigkeit von der Temperatur

Thermal resistance measurement (platinum temperature sensor)

Construction PT-sensor

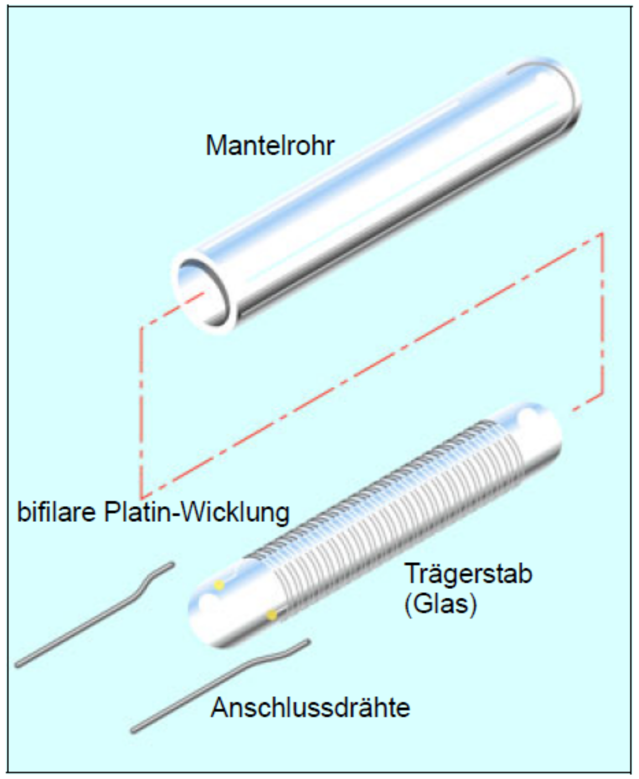


Abbildung 7: Prinzipieller Aufbau von Platin-Glas-Temperatursensoren

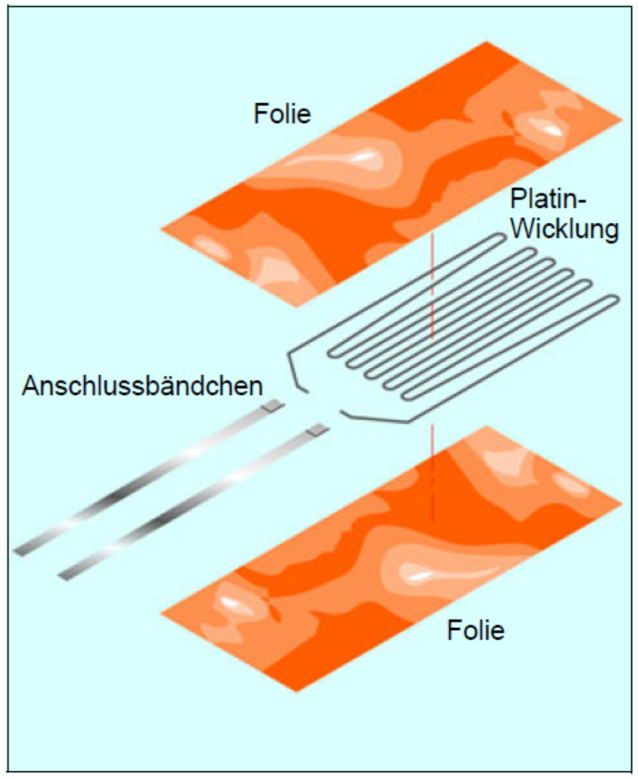


Abbildung 11: Prinzipieller Aufbau von Platin-Folien-Temperatursensoren

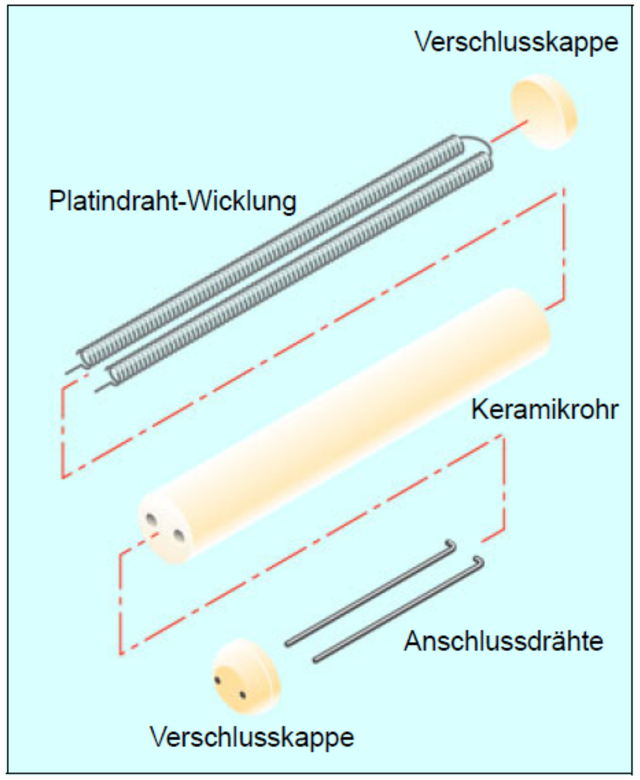


Abbildung 10: Prinzipieller Aufbau von Platin-Keramik-Temperatursensoren

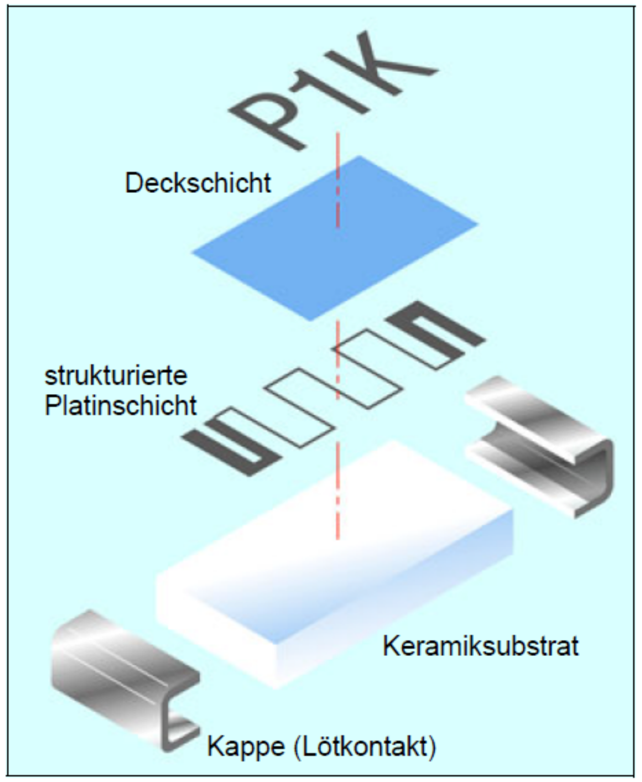


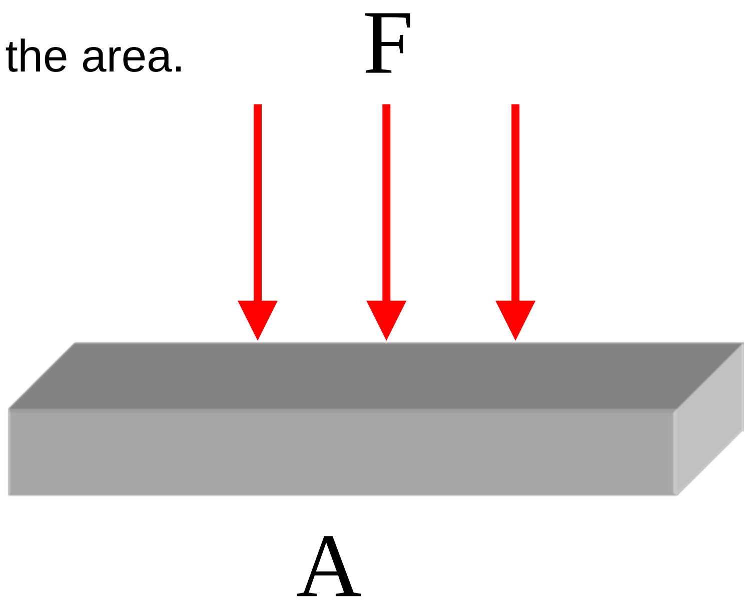
Abbildung 16: Prinzipieller Aufbau von Platin-Chip-Temperatursensoren in SMD-Bauform

Definition

How is pressure defined?

Pressure p is defined as the **force F** exerted on an **area A** divided by the size of the area.

$$p = \frac{F}{A}$$



Separate technical units of pressure:

newtons per square (*n/m2*), **Pascal** (*Pa*), **bar** (*bar*) und **Pound-Force per square inch** (*Psi*).

Furthermore **outdated units** are still in use: **technical atmosphere** (at) and **physical atmosphere** (atm) and **Torr.**

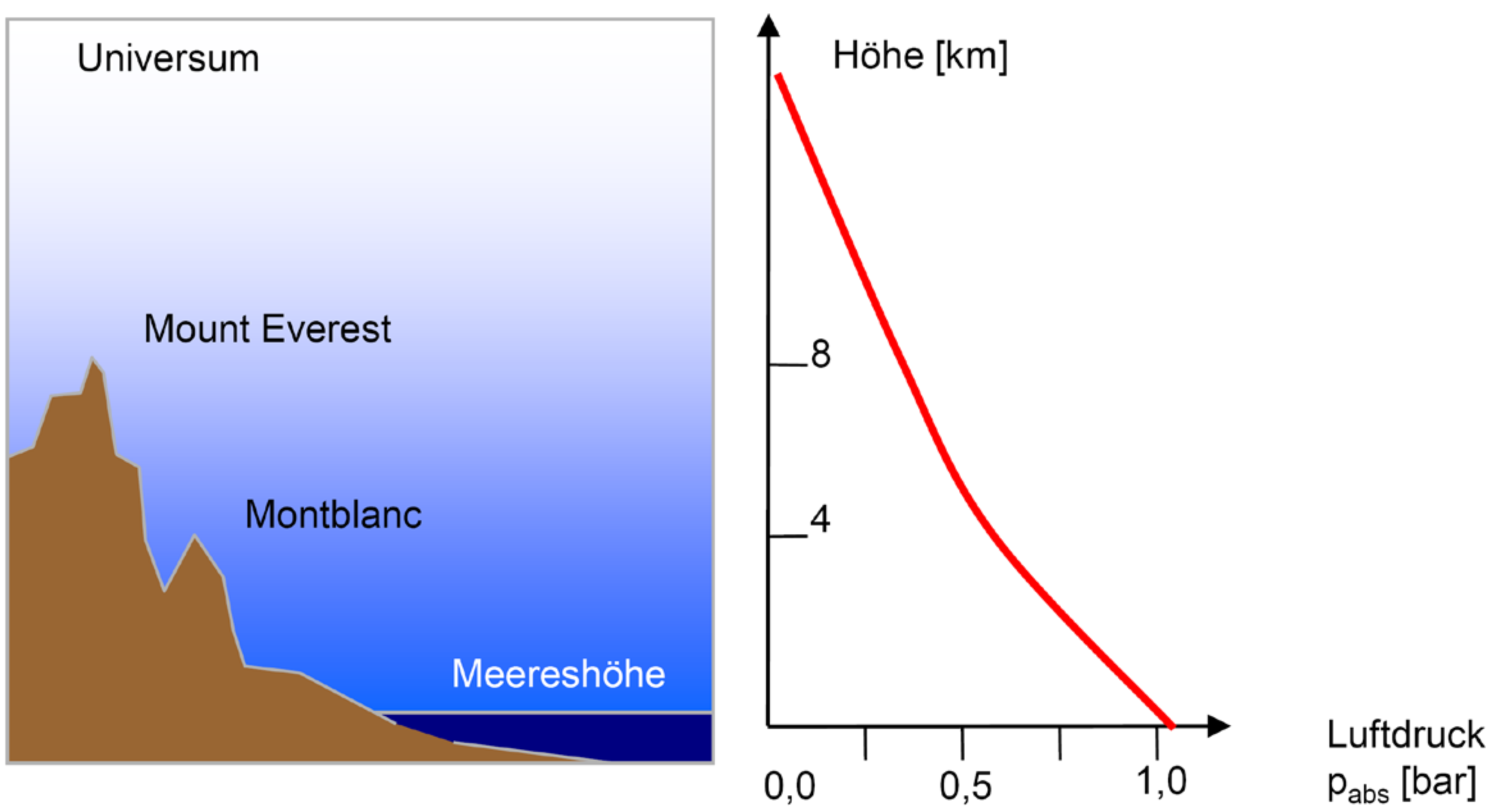
Each unit can be transferred to another:

1 bar = 100 000 pa ~ 14,504 psi ~ 1,0197 at ~ 0,98692 atm ~ 750,06 Torr.

Definition

P_{abs}

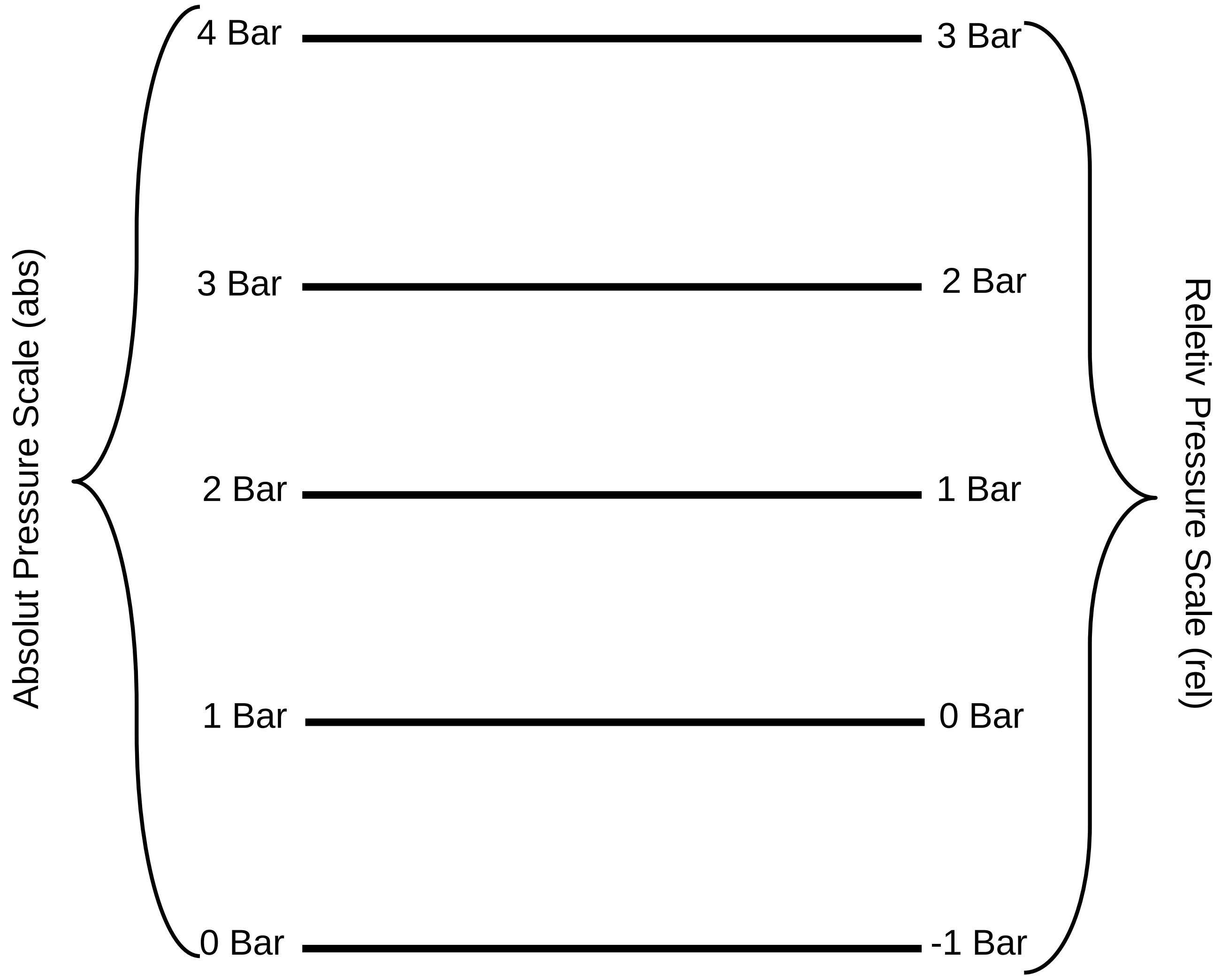
Referenz Pressure (Universe)



The Referenz Pressure will be generaded by Vacuumpumps

Process engineering tools (sensor technology)

Pressure scale



Process engineering tools (sensor technology)

Druckbereich	Druck in hPa (mbar)	Moleküle pro cm³	mittlere freie Weglänge
Umgebungsdruck	1013,25	$2,7 \times 10^{19}$	68 nm
Grobvakuum	300…1	$10^{19}…10^{16}$	0,01…100 µm
Feinvakuum	$1…10^{-3}$	$10^{16}…10^{13}$	0,1…100 mm
Hochvakuum (HV)	$10^{-3}…10^{-7}$	$10^{13}…10^{9}$	100 mm…1 km
Ultrahochvakuum (UHV)	$10^{-7}…10^{-12}$	$10^{9}…10^{4}$	$1…10^{5}$ km
extrem hohes Vakuum (XHV)	$<10^{-12}$	$<10^{4}$	$>10^{5}$ km

- rough vacuum: vacuum cleaner (> 0,5 bar)
- fine vacuum: low-pressure gas discharge lamps
- high vacuum: electron tubes, particle accelerator
- ultra-high vacuum: particle accelerator, near-earth space, frequent at equipment in the semiconductor industry
- extremely high vacuum: space, semiconductor industry

Pressure measurement (vacuum and overpressure)

One of the most important parameters is the pressure measurement

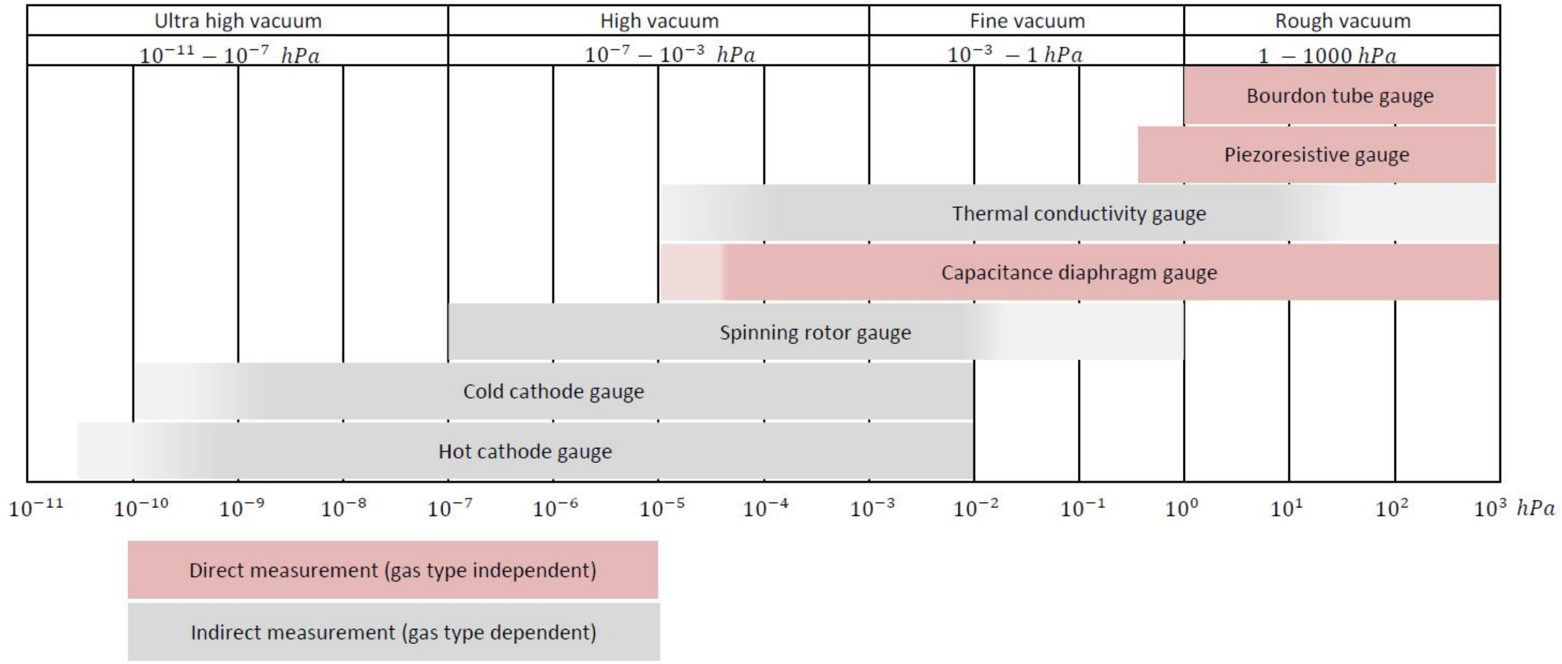
- during a running process the pressure measuring device must have a high accuracy (freeze-drying and sterilisation)
- during a freeze-drying the pressure measurement may be used for comparative pressure measurement (capacitive sensor / Pirani)
- during a sterilisation process the pressure measurement may be used for determining saturated steam conditions

Process engineering tools (sensor technology)

Pressure measurement (vacuum and overpressure)

The most common vacuum sensors at freeze-drying are:

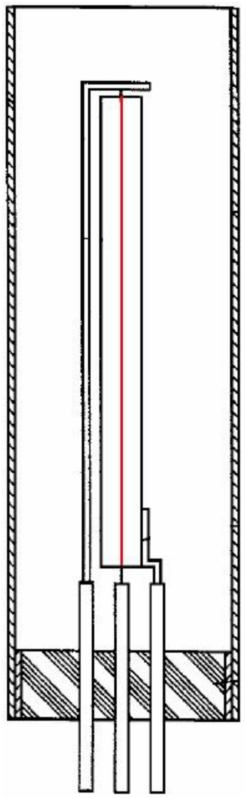
- conductive pressure measurement systems (Pirani)
- capacitive pressure measurement systems



Pressure measurement (vacuum and overpressure)

Construction of conductive pressure measurement systems (Pirani)

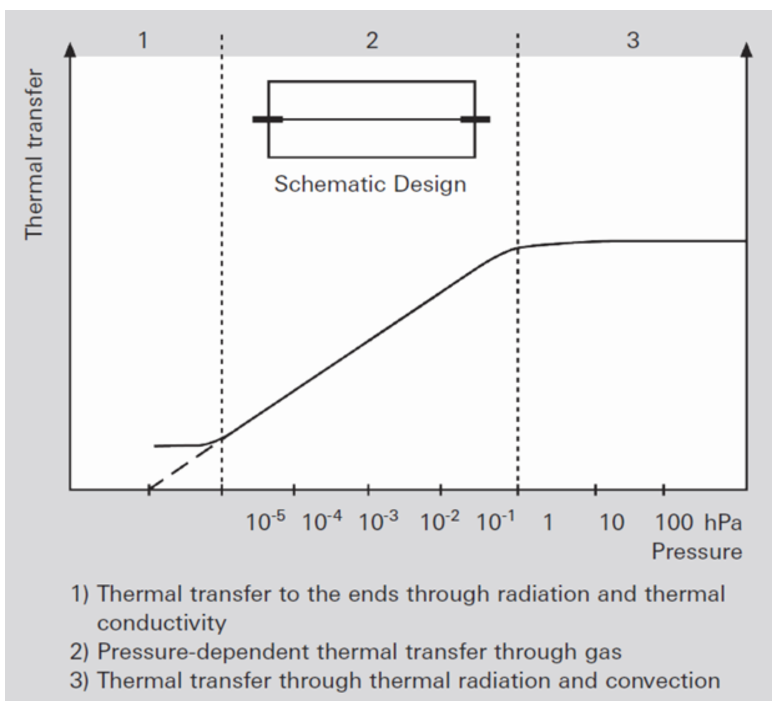
Heat up the wire approximately at a temperature of 110°C to 130°C. The heated wire forms a part of a Wheatstone bridge.

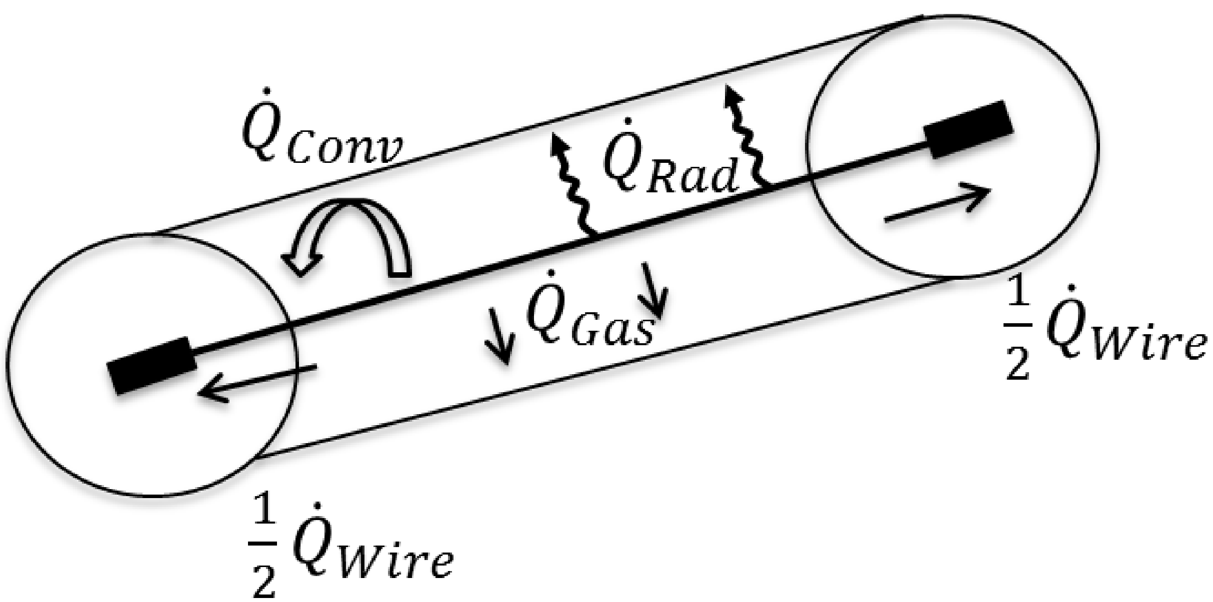


Process engineering tools (sensor technology)

Pressure measurement (vacuum and overpressure)

The Pirani sensor works with radiation which changes depending on the available pressure.





Pressure measurement (vacuum and overpressure)

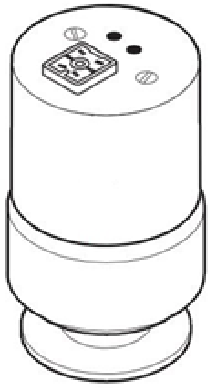
Adjustment of Pirani:

- adjustment of Pirani takes place under real installation conditions
- depending on the age and usage of the Pirani sensor it is necessary to do a zero point calibration (offset)

Pressure measurement (vacuum and overpressure)

When using a Pirani you must think about the following:

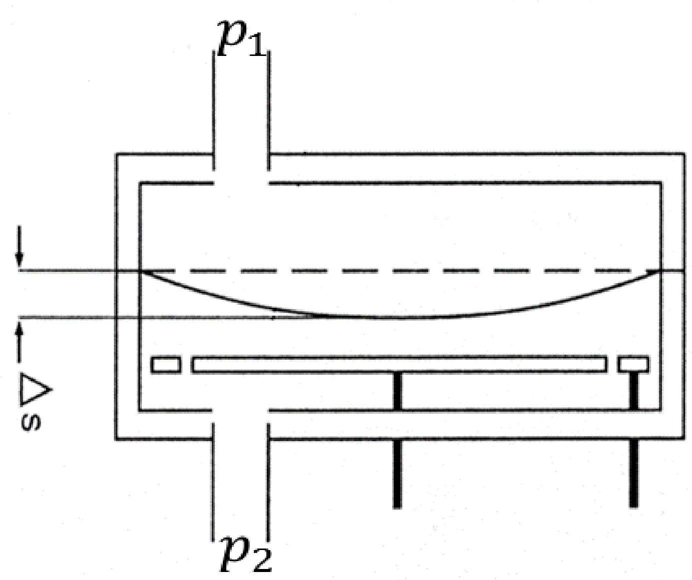
- vertical installation of the Pirani
- Regular Changing of the Pirani depending on Life Time and Process Turnaround
- depending on the age and usage of the Pirani it is necessary to do a zero point adjustment (offset)
- the accuracy of the Pirani sensor depends on the measured gas



Pressure measurement (vacuum and overpressure)

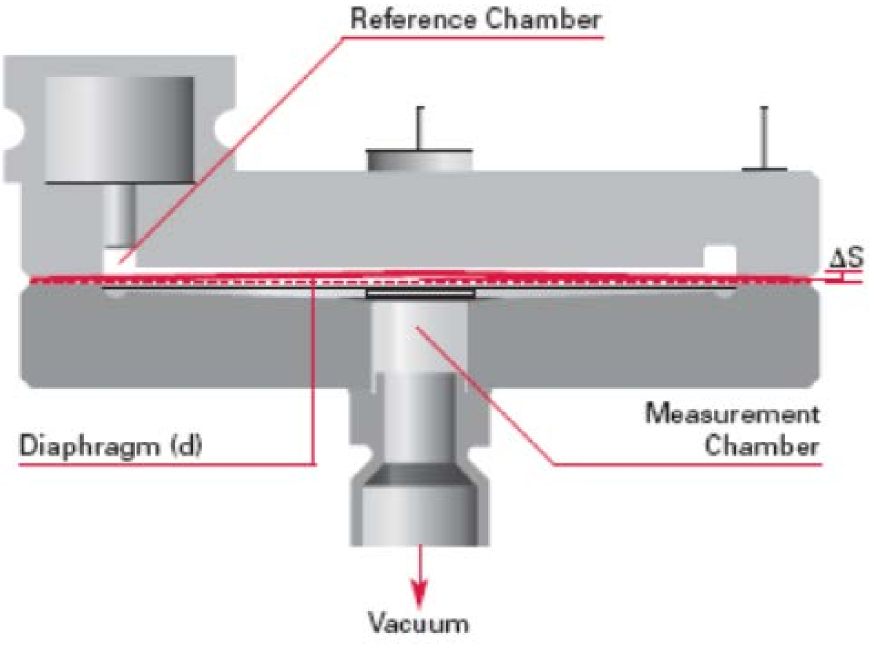
Construction of a capacitive pressure measurement system:

- a capacitive pressure measurement system is independent of the measured gas
- a flexible membrane is mounted inside the Sensor



Pressure measurement (vacuum and overpressure)

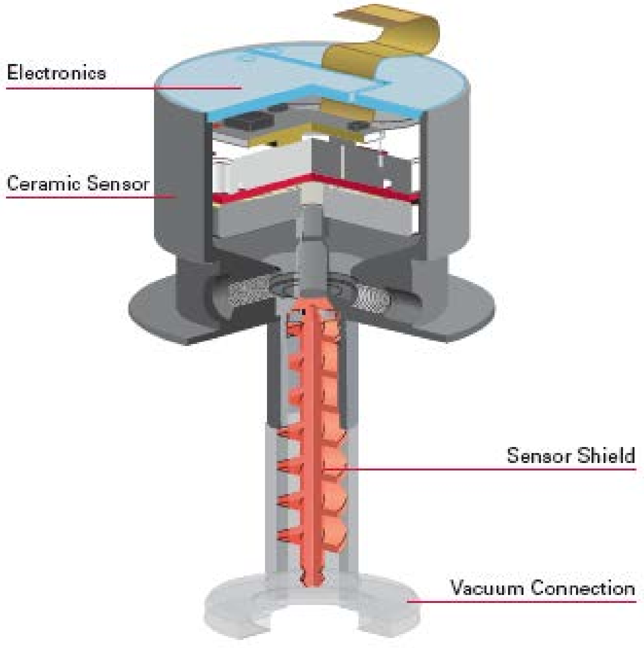
Construction of a capacitive pressure measurement system:



Pressure measurement (vacuum and overpressure)

Construction of a capacitive pressure measurement system:

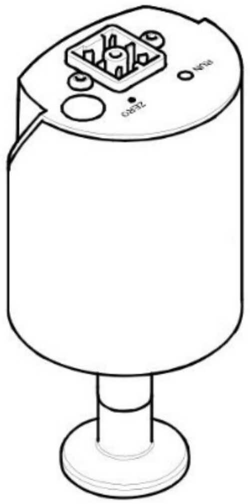
- To avoid a risk of an influence from Temperatures, the capacitive measurement sensors is heated. The temperature of the Sensor is between 45 °C and 200 °C depends on the type of the sensor.
- a freeze dryer which can be sterilized, the capacitive sensors should be heated higher than 150 °C because of the wet sterilisation (Clean Steam).



Pressure measurement (vacuum and overpressure)

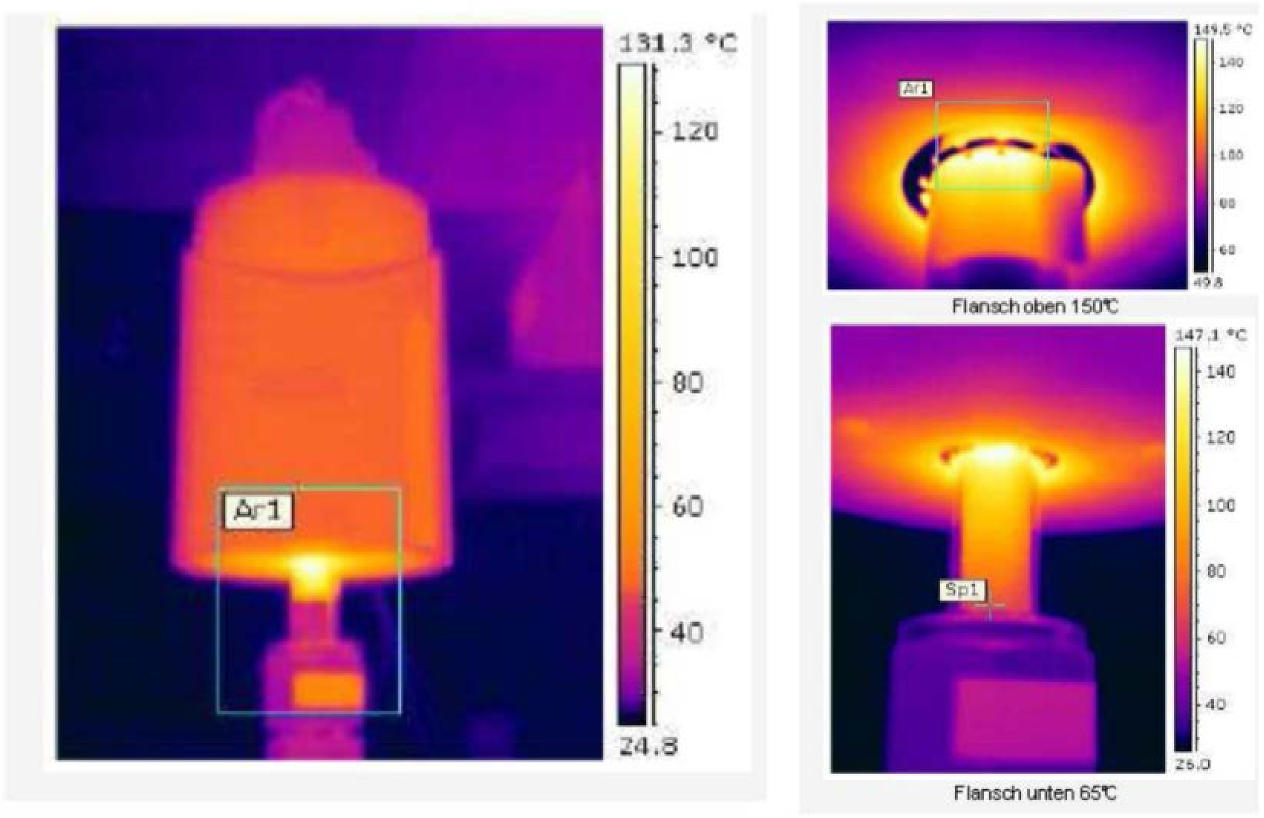
When using a capacitive measurement sensor it should be remembered:

- measurement sensor have a heating up Time (some Sensors around 9h)
- a contaminated membrane have an influence to the accuracy of the Sensor
- Because of the mounted flexible Membrane the installation position is important



Pressure measurement (vacuum and overpressure)

Temperaturverteilung Anschlussrohr der 160°C beheizten CLR 39x



Temperatur in der Nähe der Bodenplatte des Gehäuses: ~ 150°C

Im Inneren der Messröhre sind alle prozessgasführenden Bereiche oberhalb 150°C

Comparative pressure measurement (Pirani / capacitive pressure measurement)

Pressure measurement

Principle:

pressure measurement for determining the end of main drying

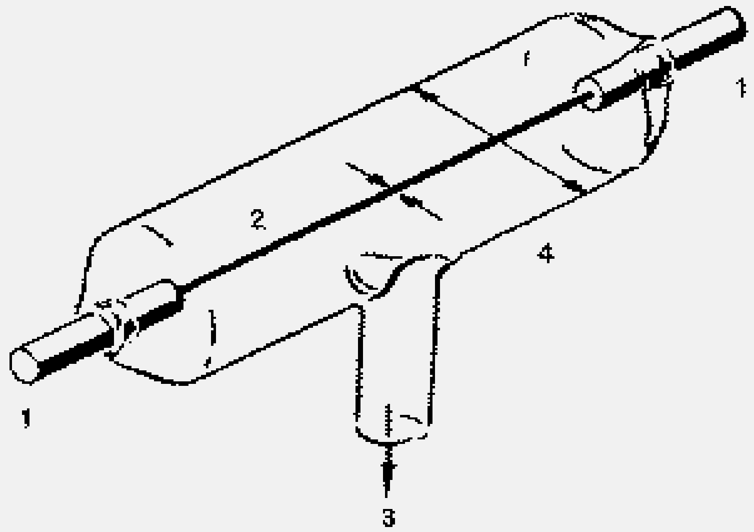
Measurement of camber pressure with

Pirani sensor

based on radiation of heatwire;

depends on the gas inside the Freeze Dryer

Pirani sonde



Comparative pressure measurement
(Pirani / capacitive pressure measurement)

Pressure measurement

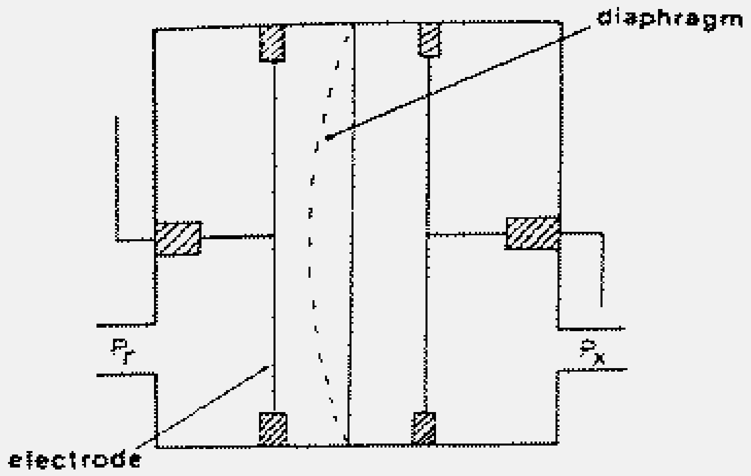
Measurement of camber pressure with

capacitive sensor

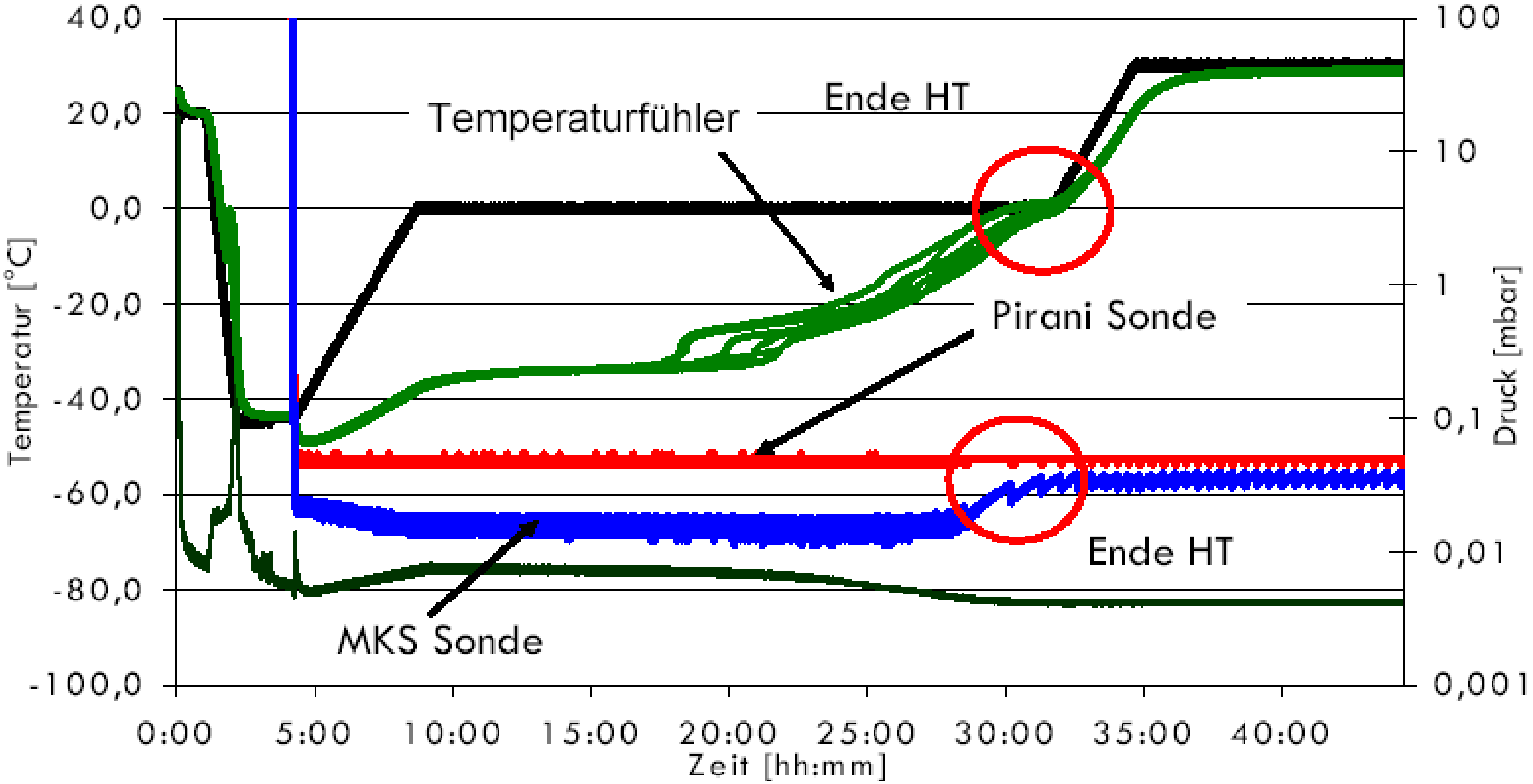
Based on a electrical measurement (Piezo),

independent from gas inside the Freeze Dryer

capacitive manometer



Comparative pressure measurement (Pirani / capacitive pressure measurement)



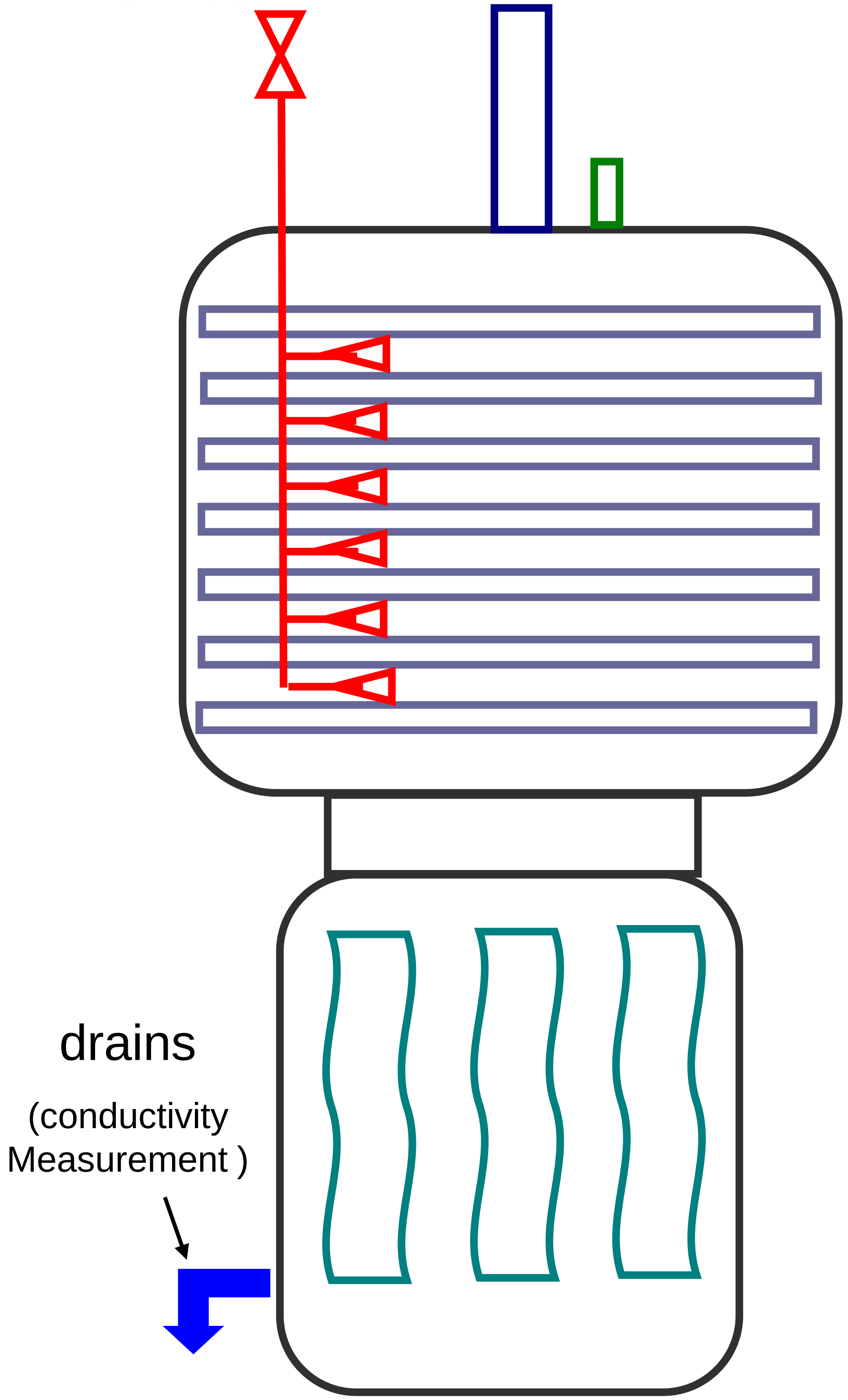
Comparing pressure measurement

- simultaneous measurement of camber pressure with Pirani and capacitive sensor
- in the beginning the Pirani sensor shows a pressure which is higher than the pressure of the capacitive sensor

(high content of water vapor inside the Freeze Dryer)

- at the end of main drying the measured values of the two sensors approach each other this is an indicator for the end of main drying

(less content of water vapor inside the Freeze Dryer)



Conductivity Measurement

to check the efficiency of a CIP Cycle a conductivity sensor is usually used.

the conductivity sensor should be fit to the relevant requirements e.g. WFI.

the Sensor should be designed for the expected temperatures of the measuring point (usually the sensor is located inside of the sterile boundary and will be charge with clean steam).

to mix up a specified dosage of CIP Medium, the Sensor also can be used e.g. acid, base solutions

- the cleaning Media e.g. Concentrate Base or acid are injected with dosing valves into the CIP System. A conductivity sensor is mounted in circulation loops or in the vesele to monitor the dosing of the cleaning Medias.

- after a CIP Cycle with cleaning Medias the cleaning Medias must be completely removed from the Freeze Dryer. These include that the complete system must be rinsed with WFI. The rinsing process is monitored a conductivity sensor at drain.

Condumax

Indumax (both Endress+Hauser)

Wireless temperature measurement

These sensors are used for:

- temperature measurement
- relative humidity
- pressure measurement

Process control tools (sensor technology)

Wireless temperature measurement

Freeze Dryer Logger - 85C to +140C

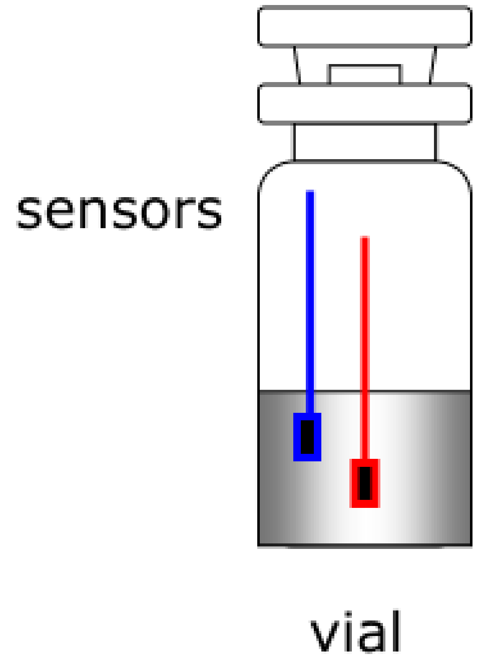
Cryologger

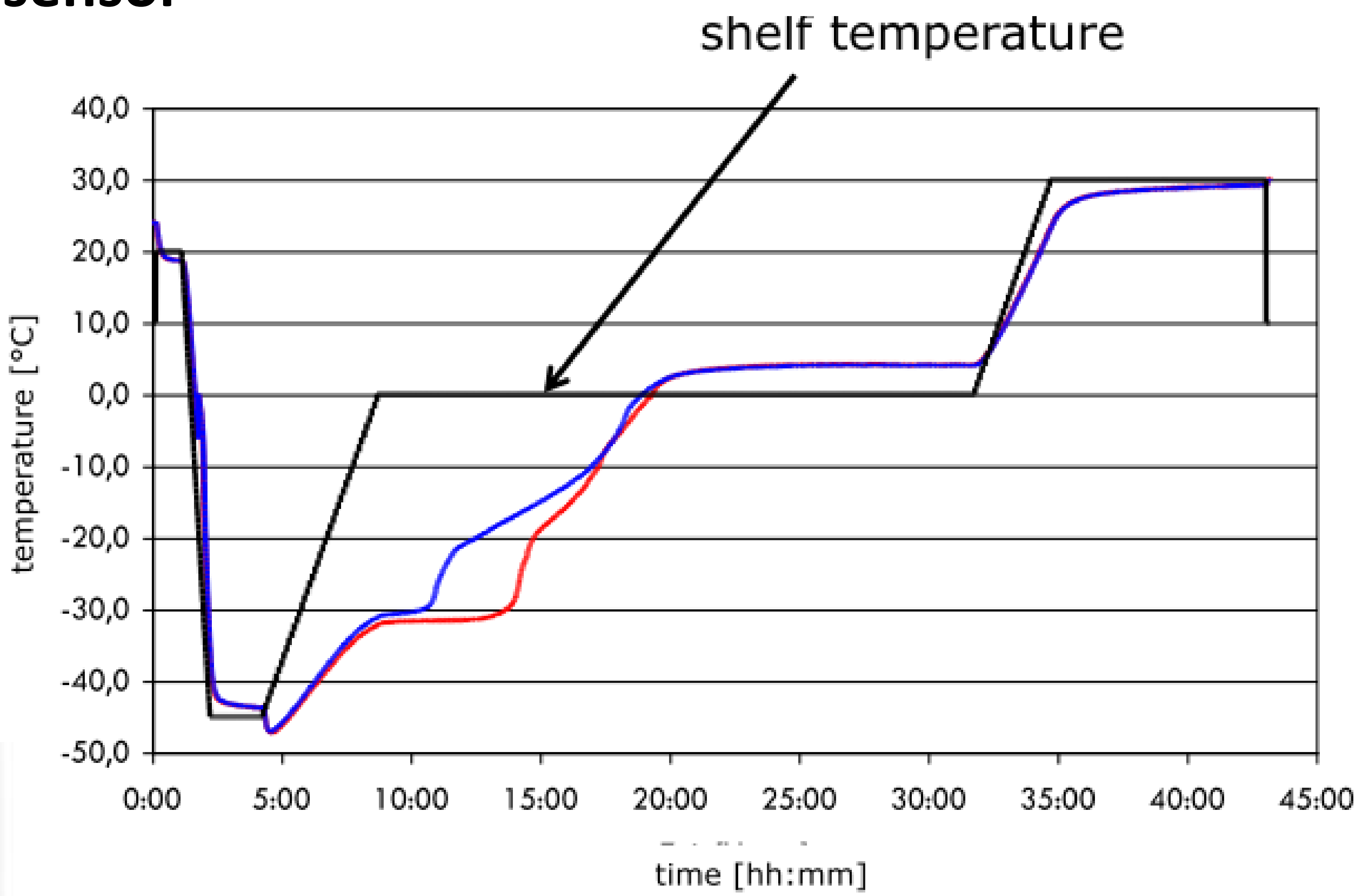
-85C to +140C

Wireless temperature measurement

positioning equipment

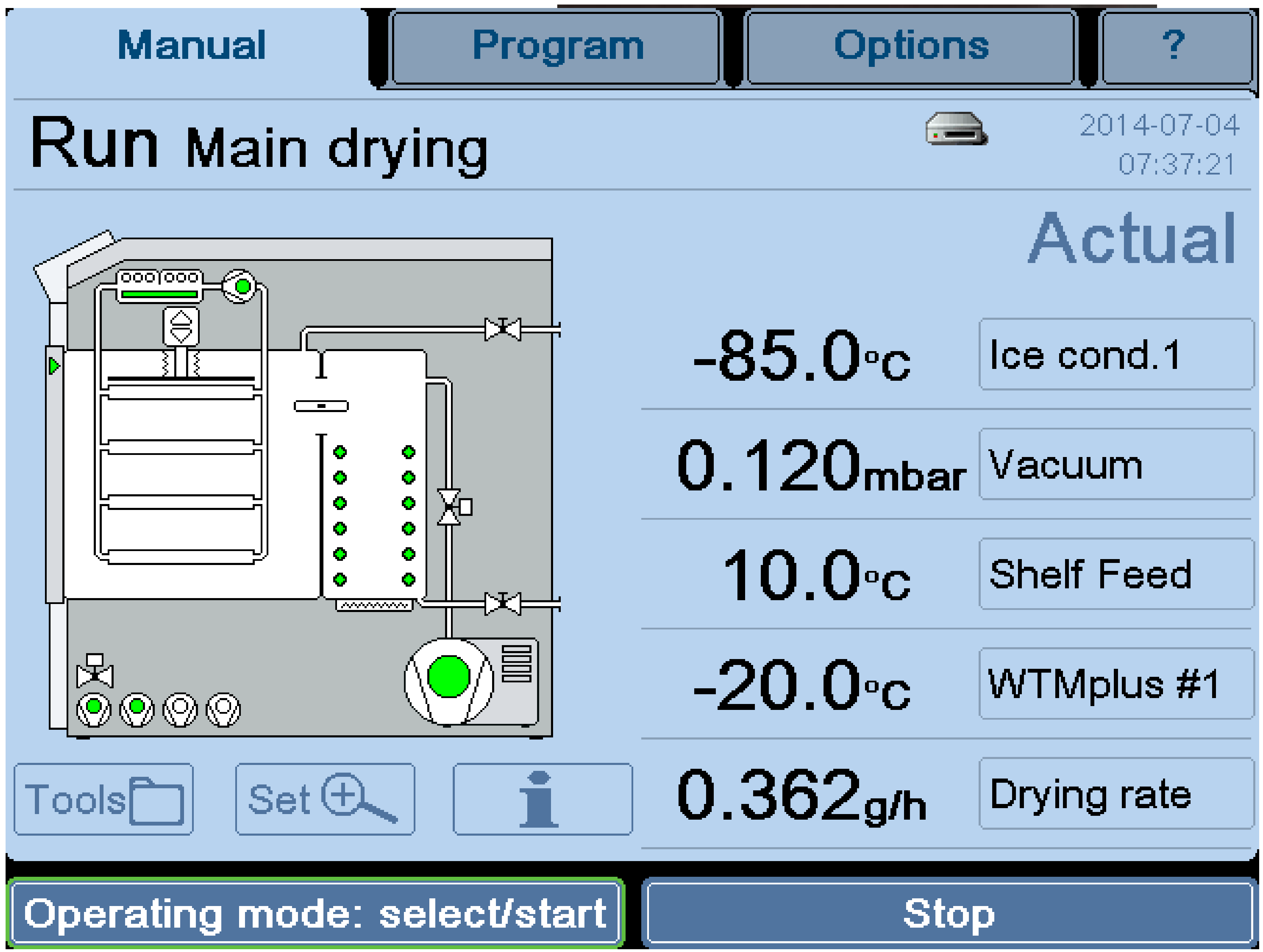
Principle: temperature sensor

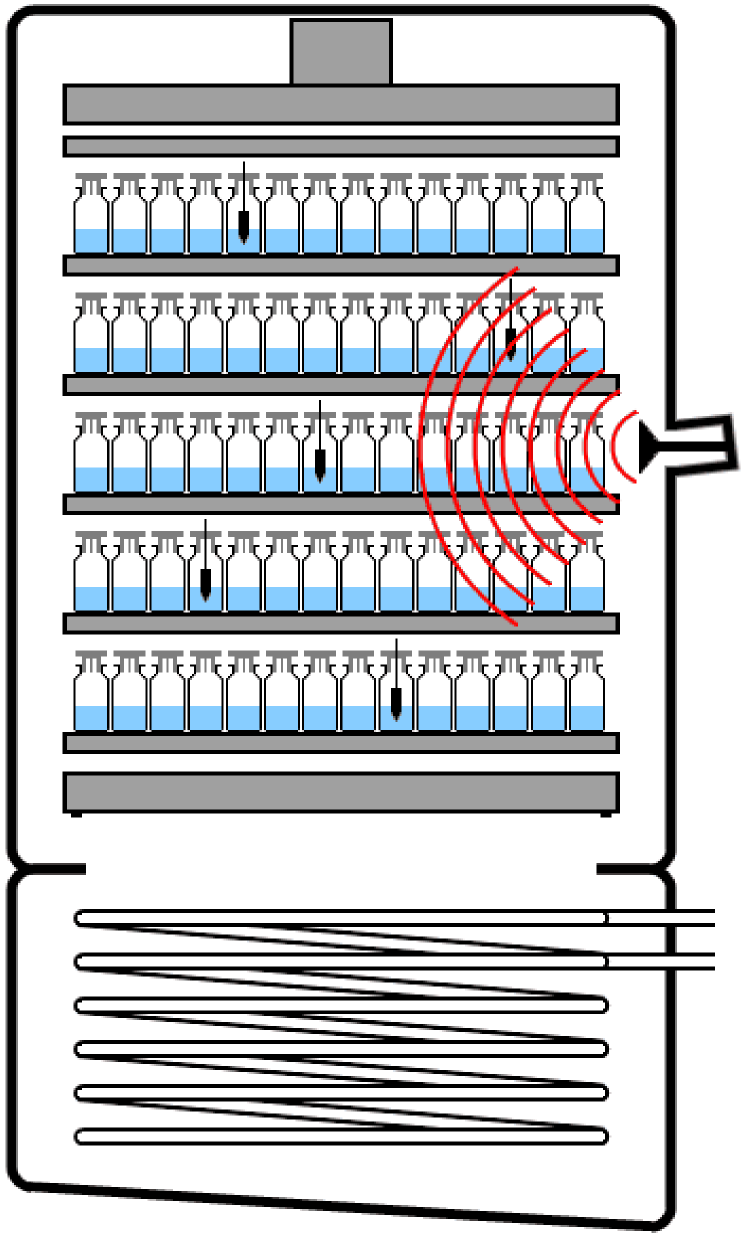




WTMplus „wireless“

Process control tools (sensor technology)





Functional principle WTMplus

- energy supply of the sensors by means of a radio frequency within in the 2.4 GHz range, i.e. no battery or other energy storing device necessary
- intermediate storage of energy by stimulation of a quartz crystal
- high precision temperature-dependent detuning of quartz-oscillation frequency
- transmission of frequency modulation via an antenna to the evaluation electronics for temperature determination

WTMplus

easy sensor positioning

small, robust sensors

Process control tools (sensor technology)

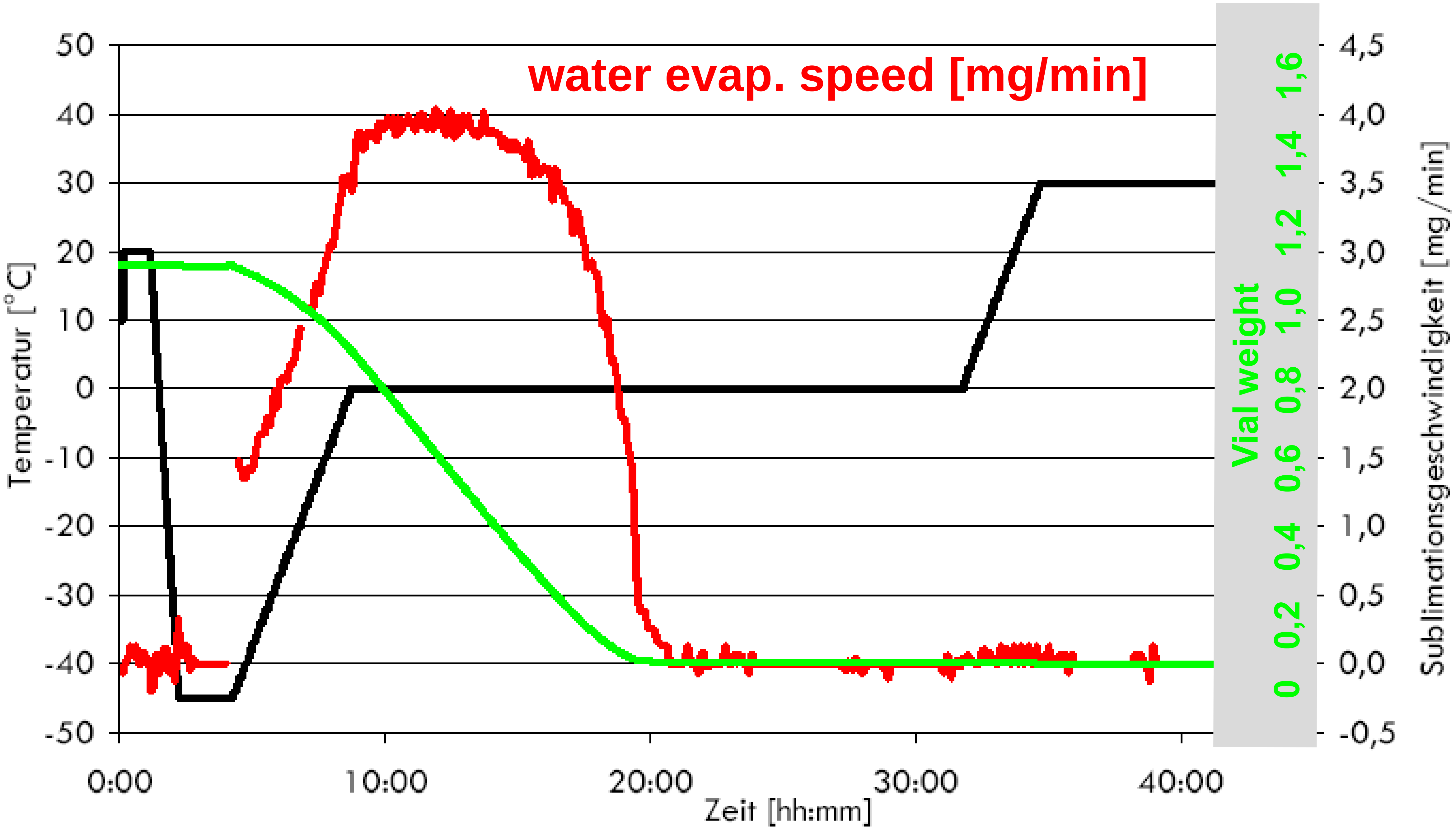
Features
small and robust, also for 2R vials and bulk
no plugs and wires with cleaning and contact problems, GMP-design
small and robust, also for 2R vials and bulk
product temperature in the vial not influenced by energy input of conventional sensors
high accuracy ± 0.5 K , resolution 0.1 K
covers the entire lyophilization cycle (liquid, solid/frozen and dry)
free sensor positioning on shelves or in pre-defined grid square
fully integrated in system controller and process documentation

Measurement of drying rates

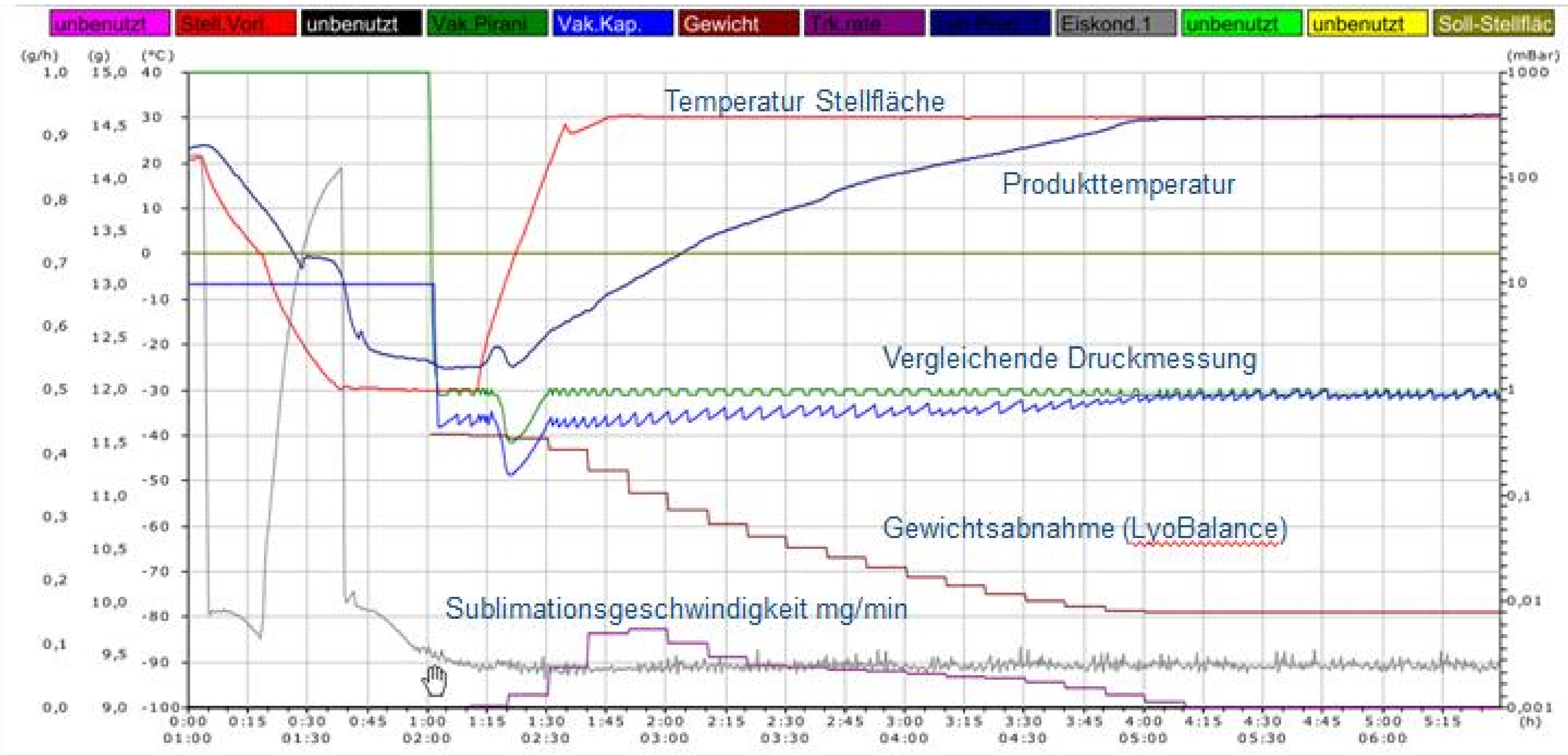
via LyoBalance (can be integrated in LSCplus units)

function principle	electromagnetic force compensation
weight determination	▪ via gripping arm, which can be lifted/unlifted in certain - customer defined - time cycles ▪ the weight of the vial is therefore detected periodically
application range	▪ temperatures of -40°C to +40°C ▪ resolution up to 30g vial weight: 0,001g
advantages	▪ can be placed onto every shelve position in the drying chamber ▪ drying process is not disturbed ▪ automatic documentation of the data ▪ can be used as controlling parameter for the process (main drying - final drying)

Speed of the sublimation from analysis with weight cell



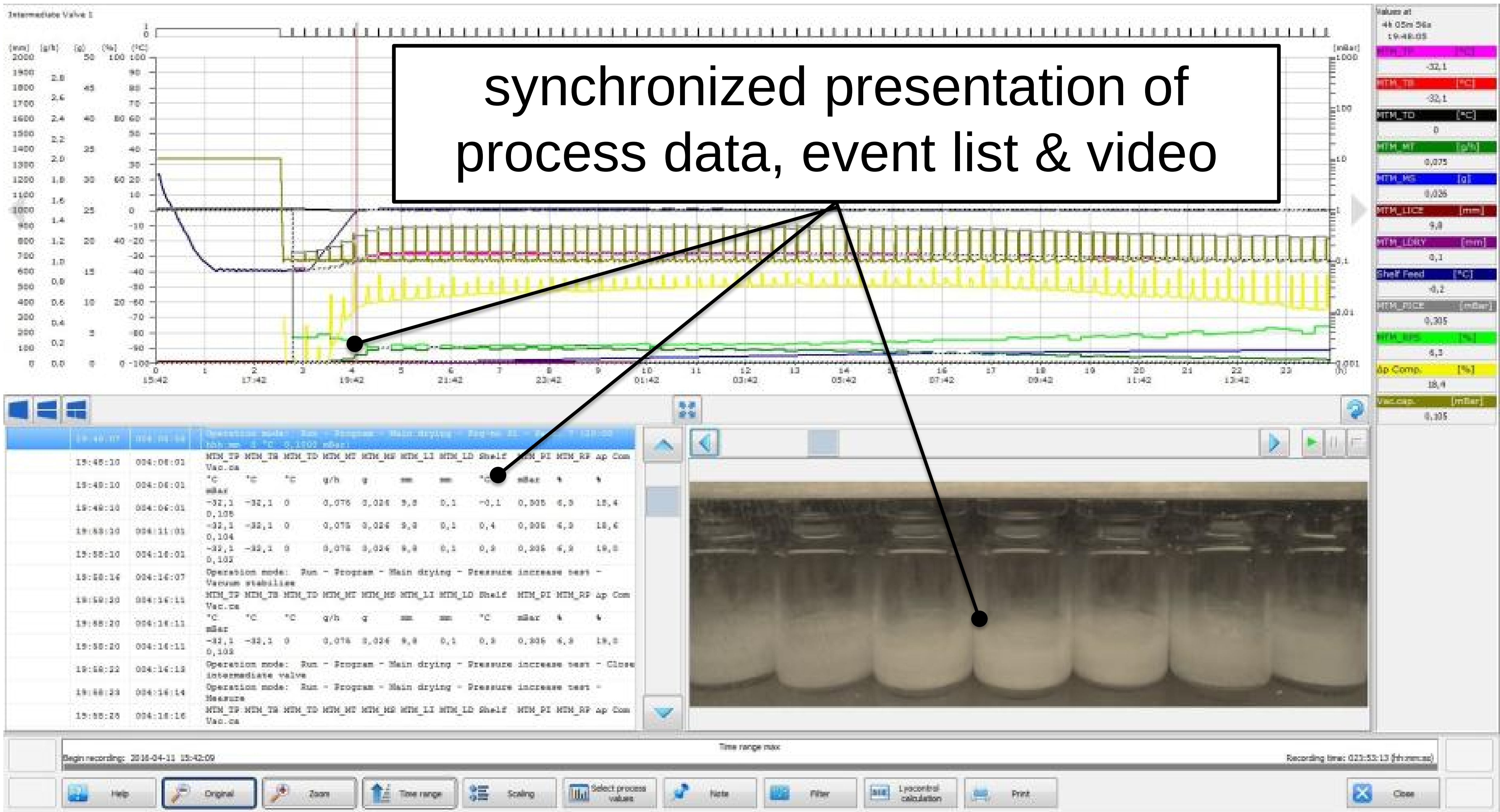
Idealized determination of end drying



Inline camera LyoCam

- monitor and analyze freeze drying processes
- intelligent data storage based on
  - process steps
  - process data (limits, alarms, …)
- fully integrated in process visualization LPCplus
- integrated in process data base (identical time stamp)
- equipped with LED lamps for low energy impact into the product
- up to 4 cameras in LPCplus
- standard sight glasses useable

Inline camera LyoCam



Lyo Engineering

GMP is our passion!