Leading Thermal Analysis.

NETZSCH

Characterization of Pharmaceuticals and Food by Thermal Analysis Instruments coupled with State-of-the-art Gas Analysis Systems

Dr. J. Blumm, S. Eichholz
NETZSCH-Gerätebau GmbH
Wittelsbacherstr. 42
95100 Selb

Overview

- Short Introduction into Thermal Analysis Techniques
- Thermogravimetry (TG) – Principle and Information Output
- Coupling of an Evolved Gas Analyzer to a Thermobalance
  - TG-FTIR Coupling - Impurities in a Pharmaceutical Substance
  - TG-QMS Coupling - Sewage Sludge Contaminations in Soil
  - TG-GC-MS Coupling – Contents of Tobacco Smoke
- Summary

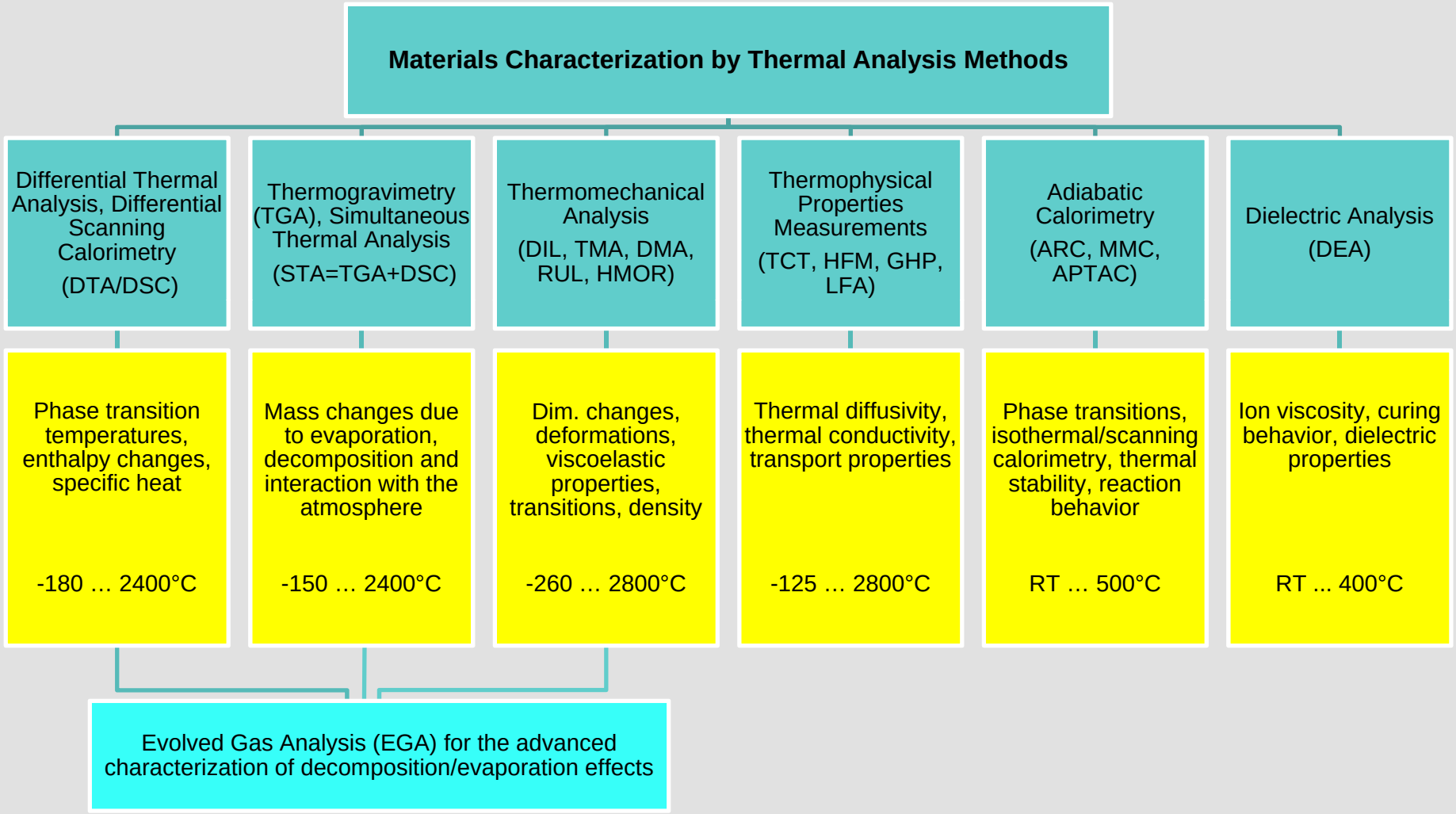
Thermal Analysis - Definition

- **Definition (ICTAC):**

  Thermal analysis (TA) is a group of techniques in which changes of physical or chemical properties of the sample are monitored against time or temperature, while the temperature of the sample is programmed.

  The temperature program may involve heating or cooling at a fixed rate, holding the temperature constant (isothermal), or any sequence of these.

Main Methods of Thermal Analysis (TA)

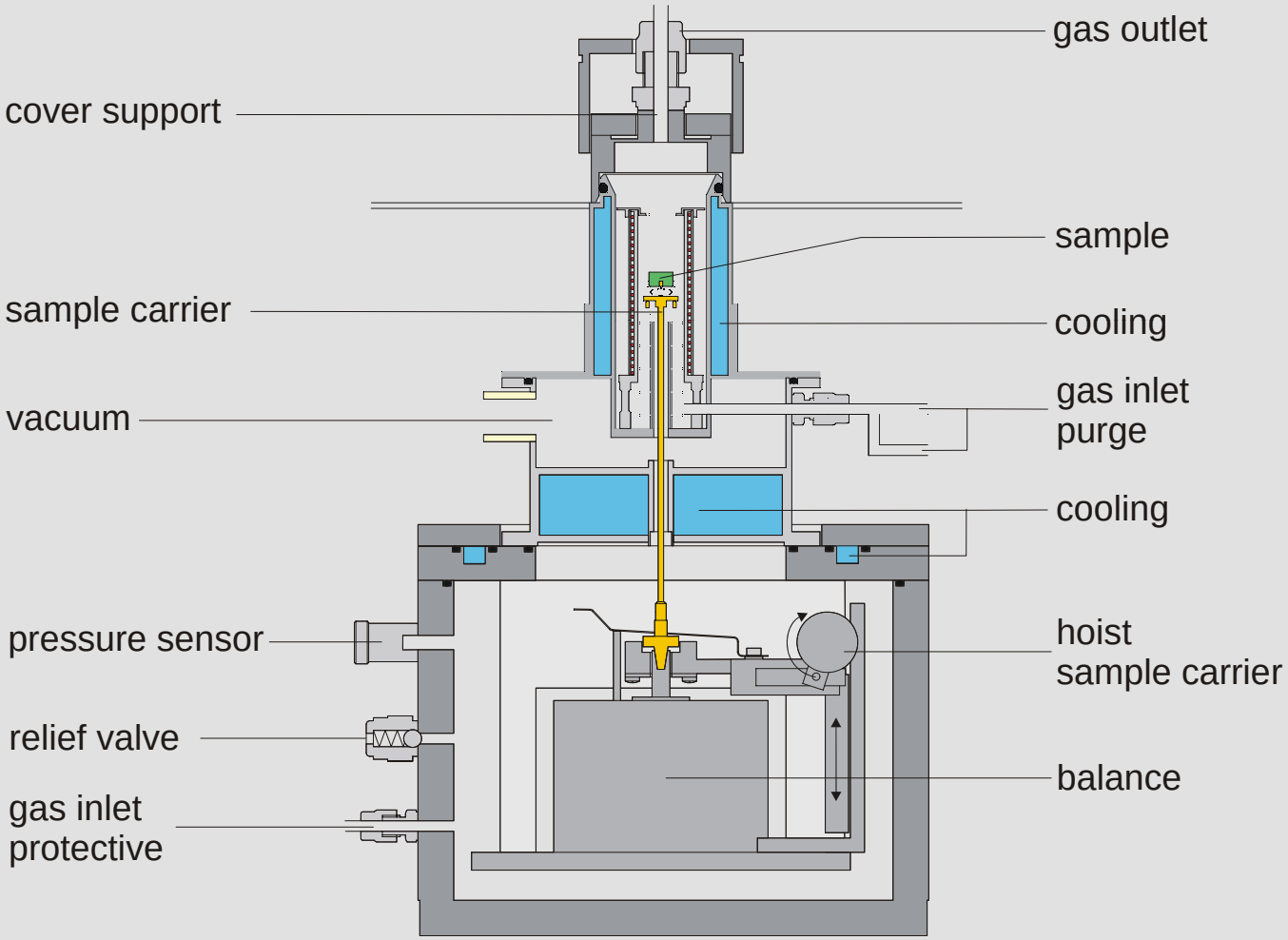


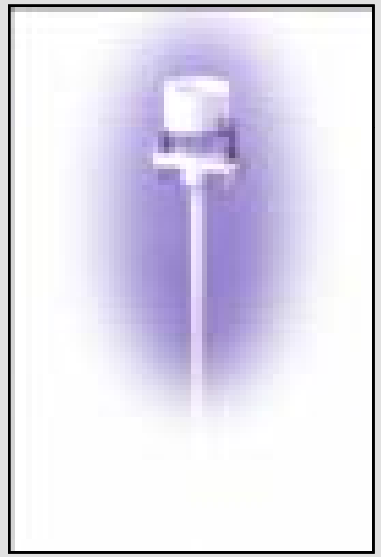
NETZSCH Thermobalances and Simultaneous Thermal Analyzers

STA 449 ***F1*** *Jupiter*®

TG 209 ***F1*** *Libra*® *- ASC*

TG 209 ***F1*** *Iris*® - Technical Design





TGA - Range of Applications

Thermophysical Properties:

Density change

Product Identification and Characterization:

Mass change

Decomposition temperatures

Thermal stability

Compositional analysis

Oxidation behavior

Advanced Material Analysis:

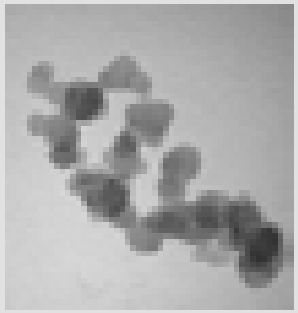
Decomposition kinetics

Rate-controlled mass loss

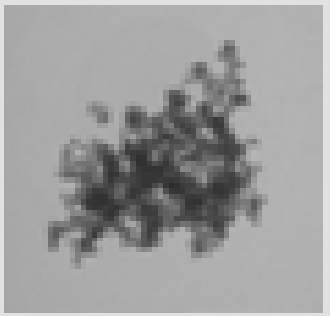
Analysis of different Carbon Modifications

Fine grained carbon modifications are used in many kinds of different industrial applications. Some of them (soot) are known to be carcinogenic.

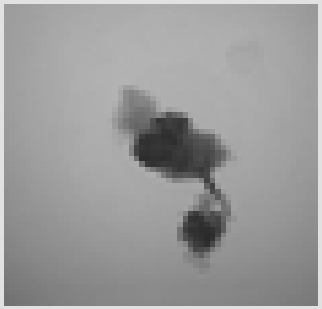
SEM and TEM Measurements on different Carbon Modifications

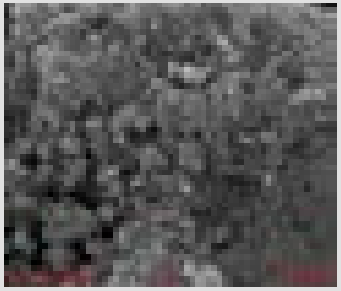
Carbon black

Ethene soot

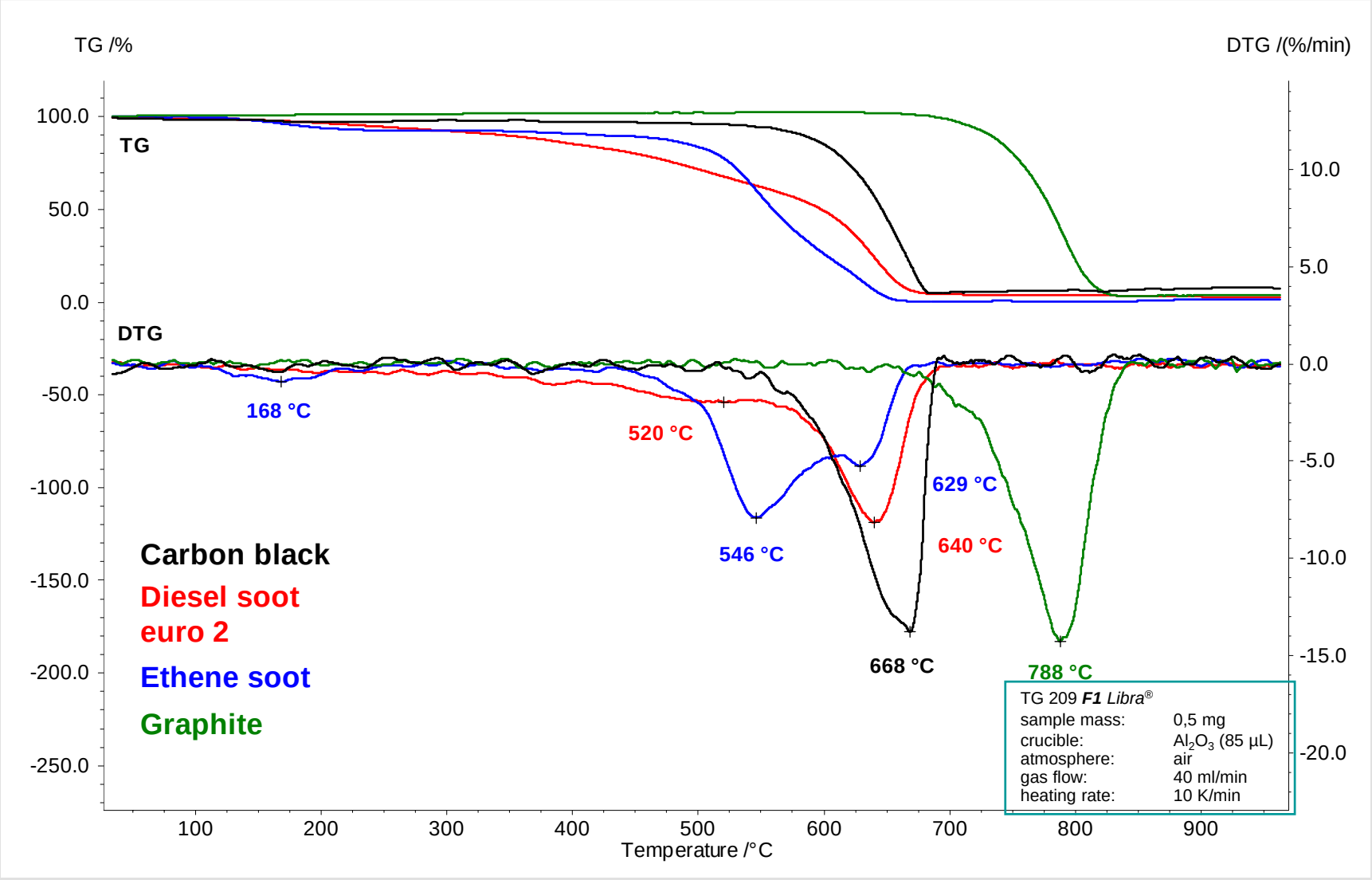



Graphite




Diesel soot

TGA Test Results on on different Carbon Modifications



Evolved Gas Analysis (EGA) in Thermal Analysis

In Thermogravimetry (TG) or Simultaneous Thermal Analysis (STA), the mass change (and transformation energetics) of a sample versus temperature or time is measured.

Evolved Gas Analysis yields additional information regarding the nature (composition) of the gases evolved during a mass-loss step.

In most cases, a **Quadrupole Mass Spectrometer (QMS)**, an **Fourier Transform Infrared Spectrometer (FTIR)** or a **Gas Chromatograph-Mass Spectrometer (GC-MS)** are coupled to a TG/STA system for evolved gas analysis.

Possibilities:

- TG/STA-FTIR Coupling (Transfer Line)
- TG/STA-MS Coupling (Capillary Coupling)
- TG/STA-GC-MS Coupling (Transfer Line)
- STA-MS Coupling (Skimmer)

Evolved Gas Analysis (EGA) in Thermal Analysis

STA/TG-FTIR Coupling: Yields information on the composition (absorption bands) of the evolved gases (bonding conditions).

⇒ Easy interpretation (spectra data bases) of organic vapors without fragmentation

⇒ Symmetrical molecules cannot be detected

STA/TG-MS Coupling: Yields information on the composition (mass numbers of elements and molecules) of the evolved gases.

⇒ High sensitivity

⇒ Fast and easy interpretation of atomic/inorganic vapors and standard gases (H_2, H_2O, CO_2, ...)

⇒ Fragmentation, interpretation of organic molecules sometimes difficult

STA/TG-GC-MS Coupling: Yields information on the composition (mass numbers of elements and molecules) of the evolved gases.

⇒ Very high sensitivity

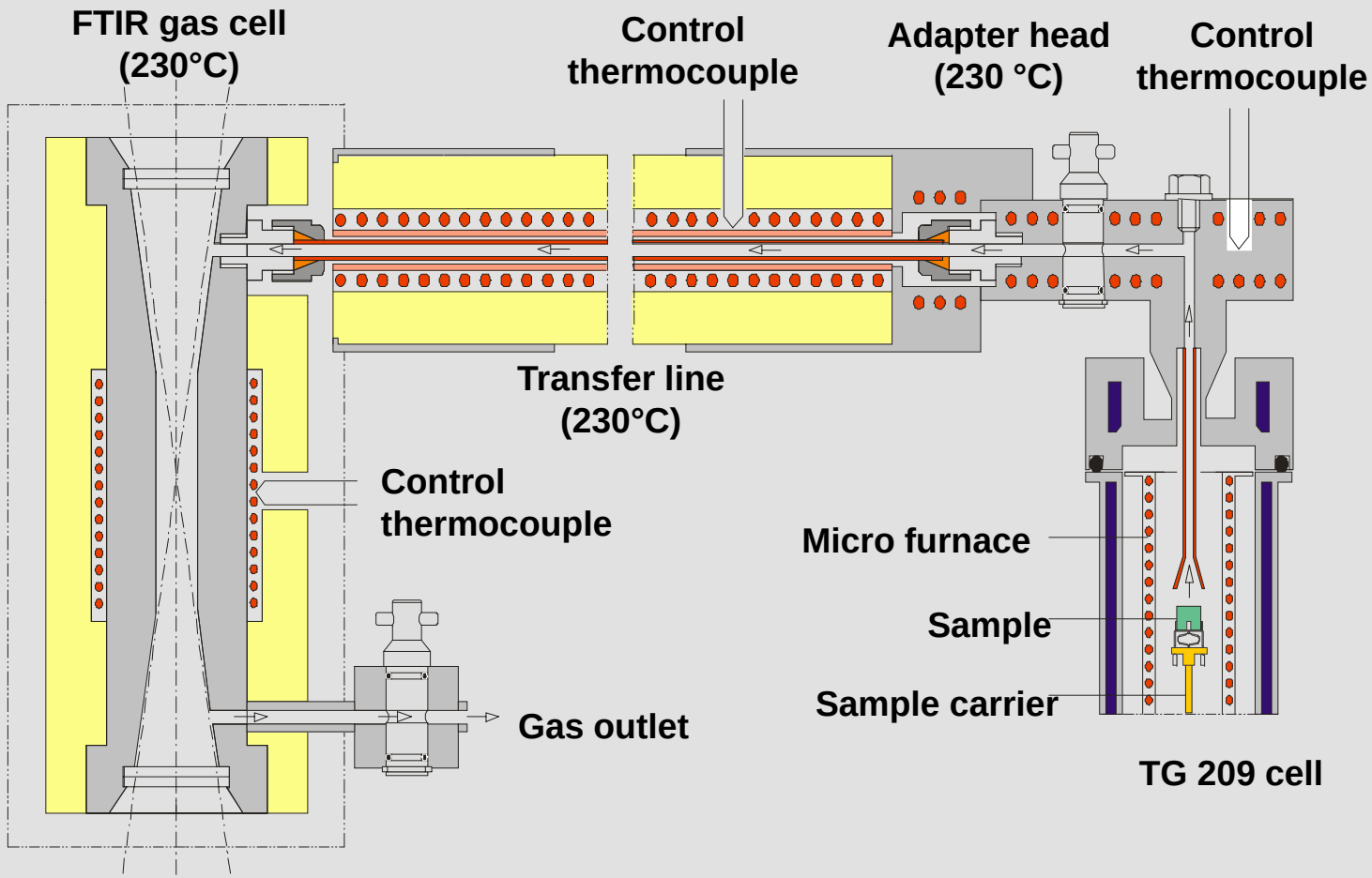
⇒ Separation of the volatiles using the GC column

⇒ Interpretation of organic vapors significantly improved

⇒ Sometimes slow, special measurement processes need to be used or fast GC systems have to be employed

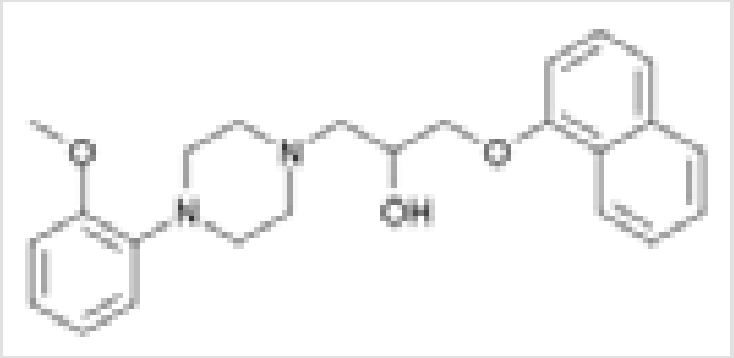
TG-FTIR Coupling - Realization

TG-FTIR Coupling - Realization



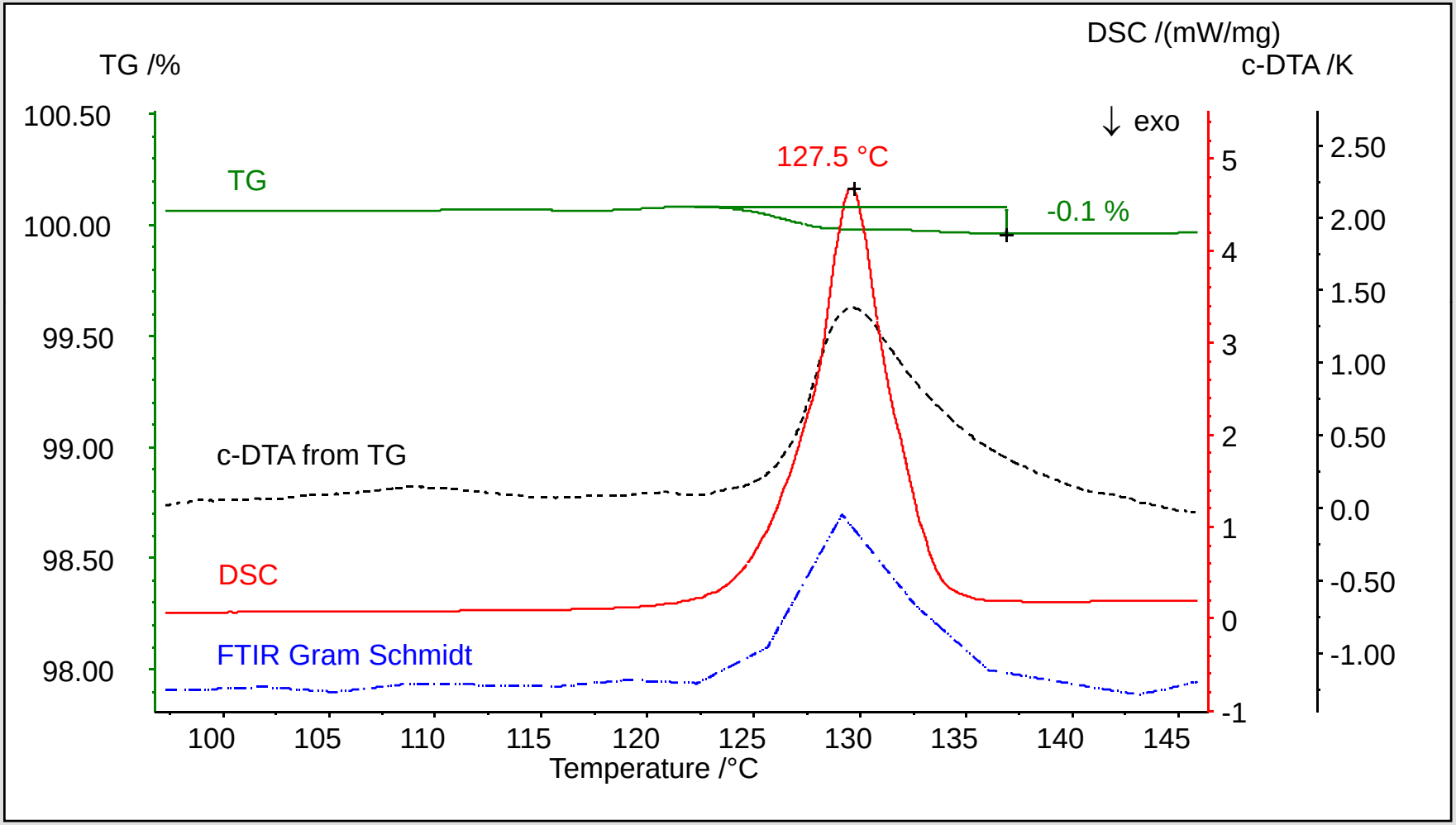
Application: Naftopidil

Naftopidil is used to treat benign prostatic hypertrophy (BPH) which causes urinary problems by prostate gland enlargement. It acts to smooth muscles of the prostate and thus increase urinary flow rate.

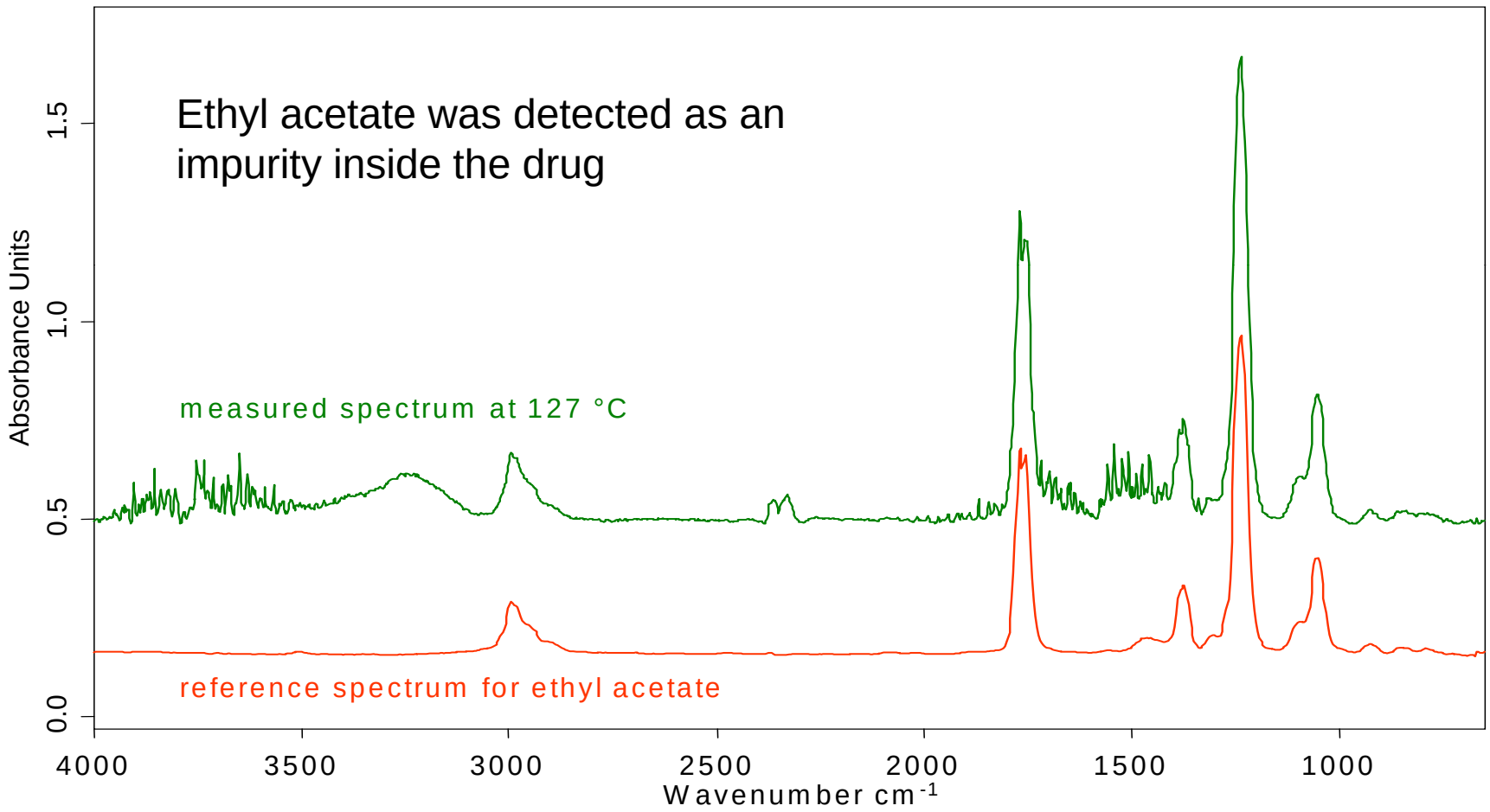


Sample:	crystalline powder
Experimental conditions:	
Analytical Instruments:	DSC 204, TG 209-FTIR
Sample mass:	0.5 to 16 mg
Crucible:	Al crucible
Temperature program	up 20 °C...160 °C
Heating rate:	10 K min^{-1}
Atmosphere:	N_2

Application: Naftopidil



Application: Naftopidil



Evolved Gas Analysis (EGA) in Thermal Analysis

STA/TG-FTIR Coupling: Yields information on the composition (absorption bands) of the evolved gases (bonding conditions).

⇒ Easy interpretation (spectra data bases) of organic vapors without fragmentation

⇒ Symmetrical molecules cannot be detected

STA/TG-MS Coupling: Yields information on the composition (mass numbers of elements and molecules) of the evolved gases.

⇒ High sensitivity

⇒ Fast and easy interpretation of atomic/inorganic vapors and standard gases (H_2, H_2O, CO_2, ...)

⇒ Fragmentation, interpretation of organic molecules sometimes difficult

STA/TG-GC-MS Coupling: Yields information on the composition (mass numbers of elements and molecules) of the evolved gases.

⇒ Very high sensitivity

⇒ Separation of the volatiles using the GC column

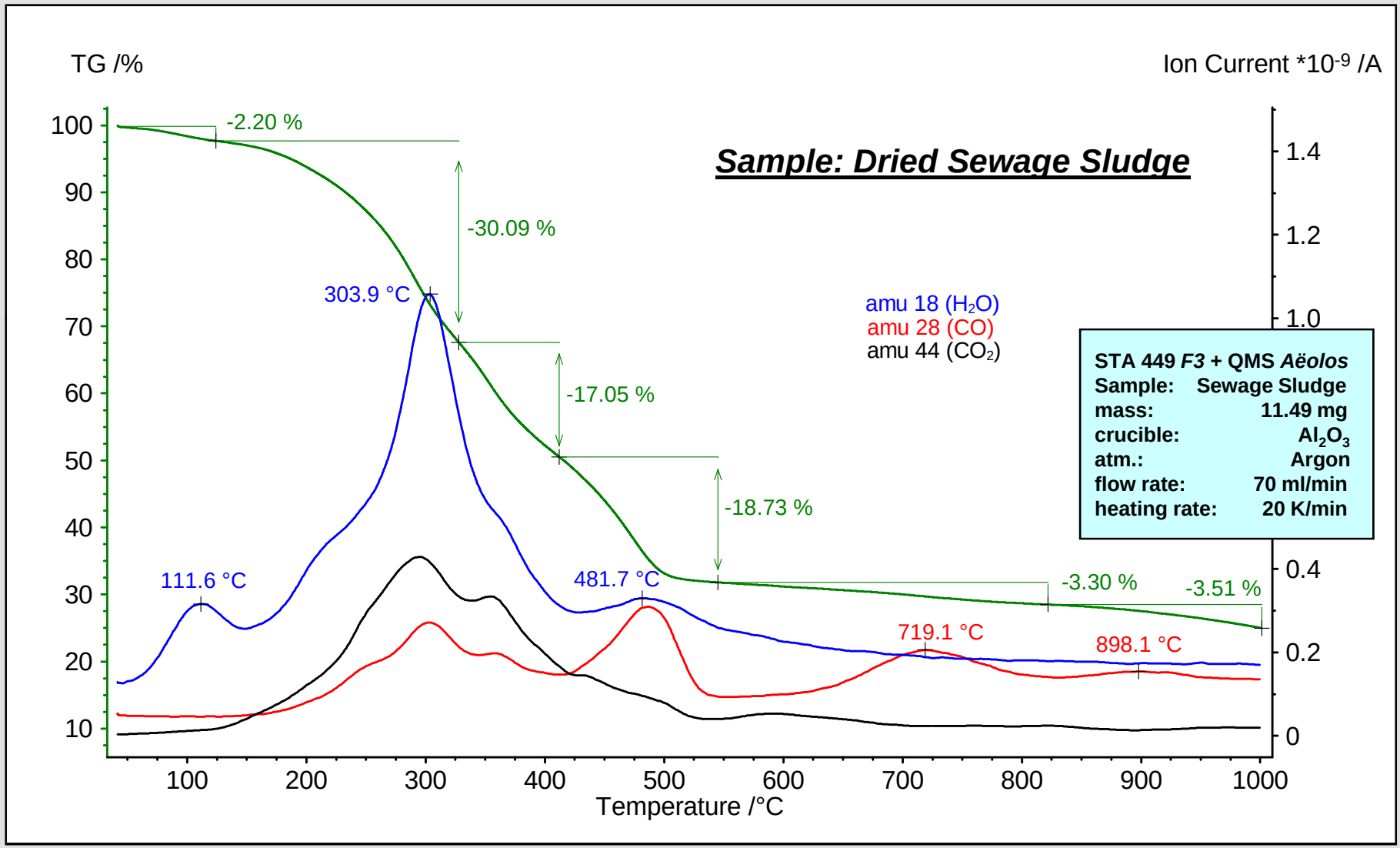
⇒ Interpretation of organic vapors significantly improved

⇒ Sometimes slow, special measurement processes need to be used or fast GC systems have to be employed

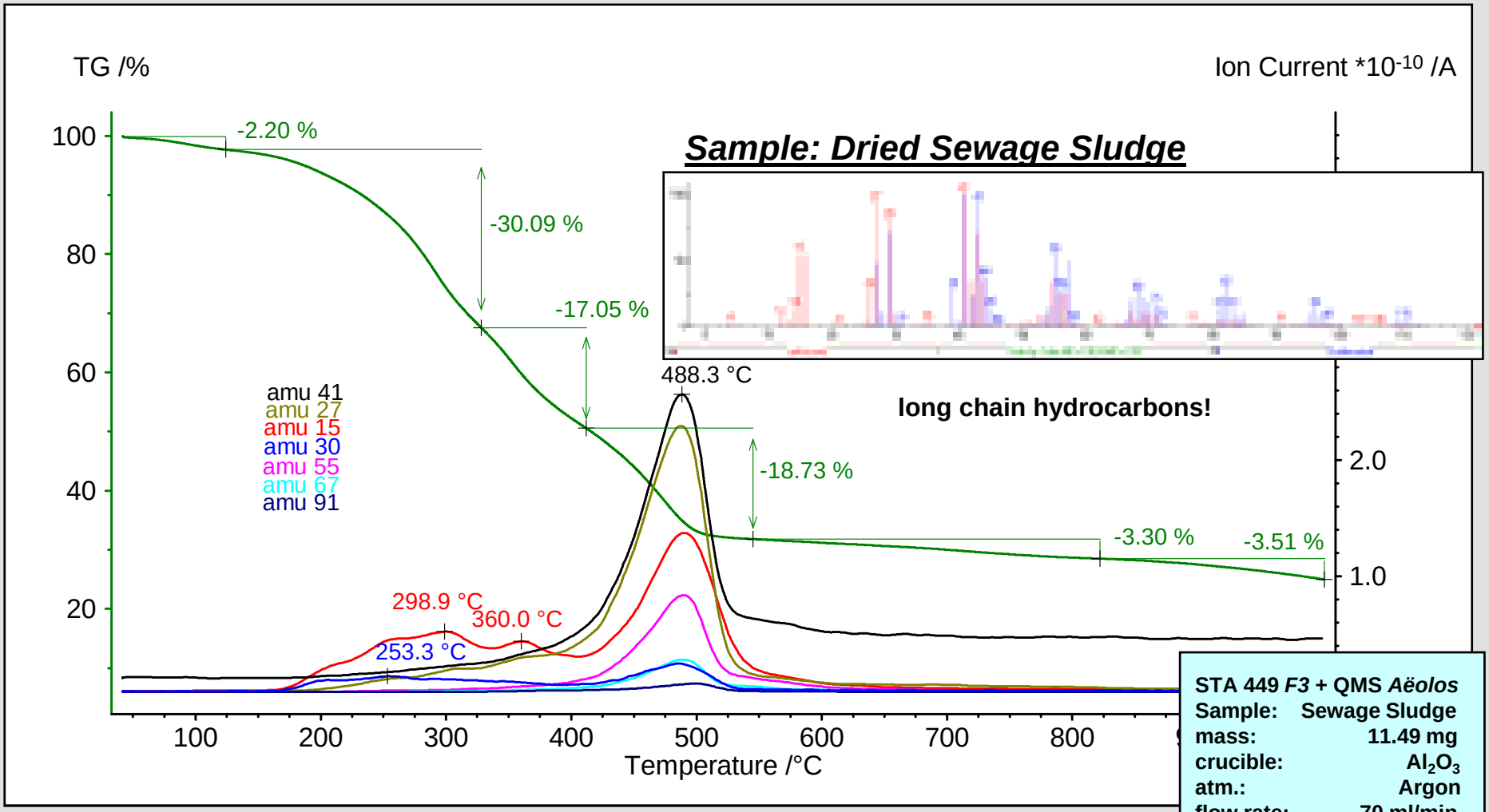
STA 449 ***F1*** *Jupiter*® - QMS 403
Aeolos® Capillary Coupling

Application: Sewage Sludge Contamination in Soil

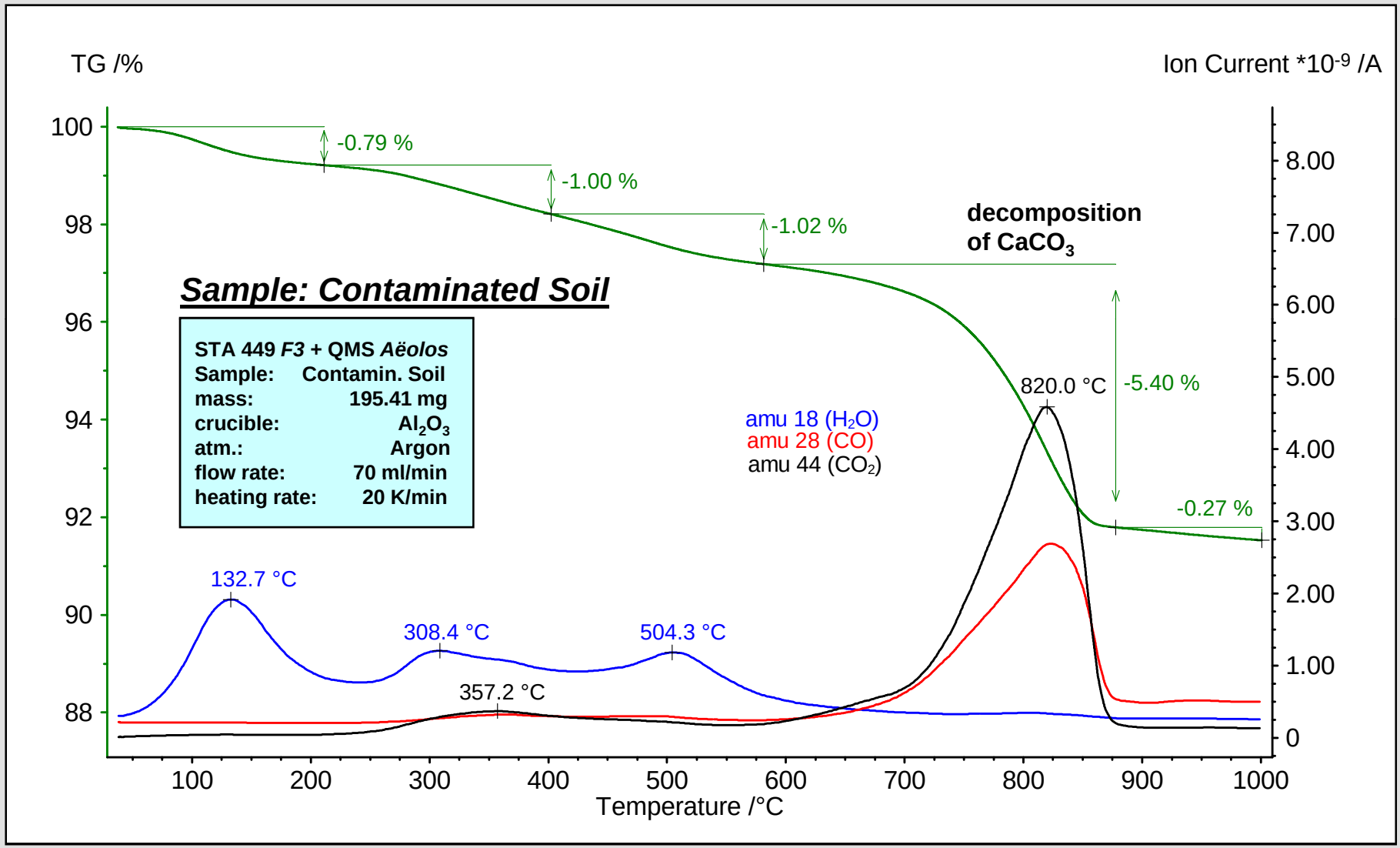
TG-MS on Dried Sewage Sludge (I)



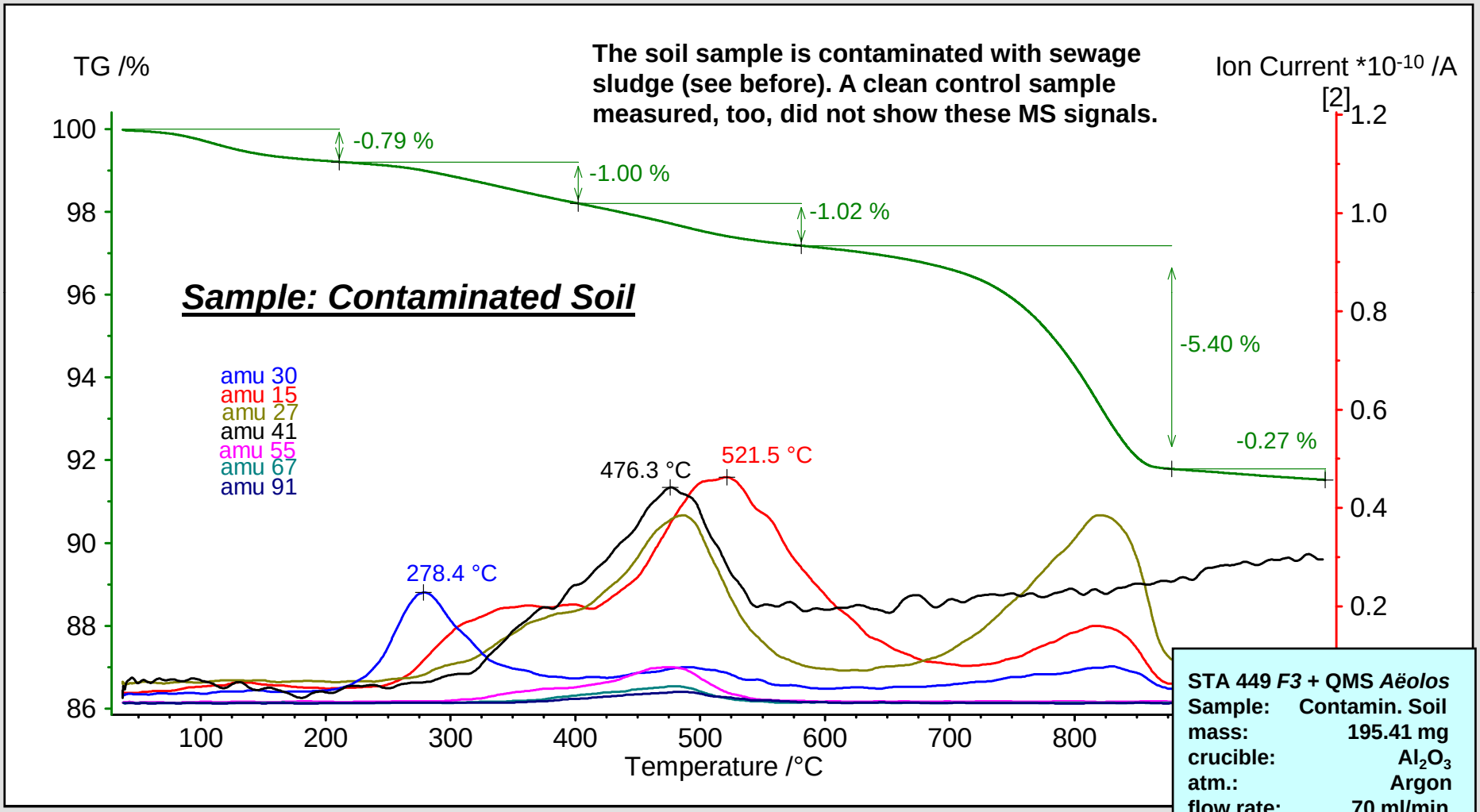
TG-MS on Dried Sewage Sludge (II)



TG-MS on Contaminated Soil (I)



TG-MS on Contaminated Soil (II)



Evolved Gas Analysis (EGA) in Thermal Analysis

STA/TG-FTIR Coupling: Yields information on the composition (absorption bands) of the evolved gases (bonding conditions).

⇒ Easy interpretation (spectra data bases) of organic vapors without fragmentation

⇒ Symmetrical molecules cannot be detected

STA/TG-MS Coupling: Yields information on the composition (mass numbers of elements and molecules) of the evolved gases.

⇒ High sensitivity

⇒ Fast and easy interpretation of atomic/inorganic vapors and standard gases (H_2, H_2O, CO_2, ...)

⇒ Fragmentation, interpretation of organic molecules sometimes difficult

STA/TG-GC-MS Coupling: Yields information on the composition (mass numbers of elements and molecules) of the evolved gases.

⇒ Very high sensitivity

⇒ Separation of the volatiles using the GC column

⇒ Interpretation of organic vapors significantly improved

⇒ Sometimes slow, special measurement processes need to be used or fast GC systems have to be employed

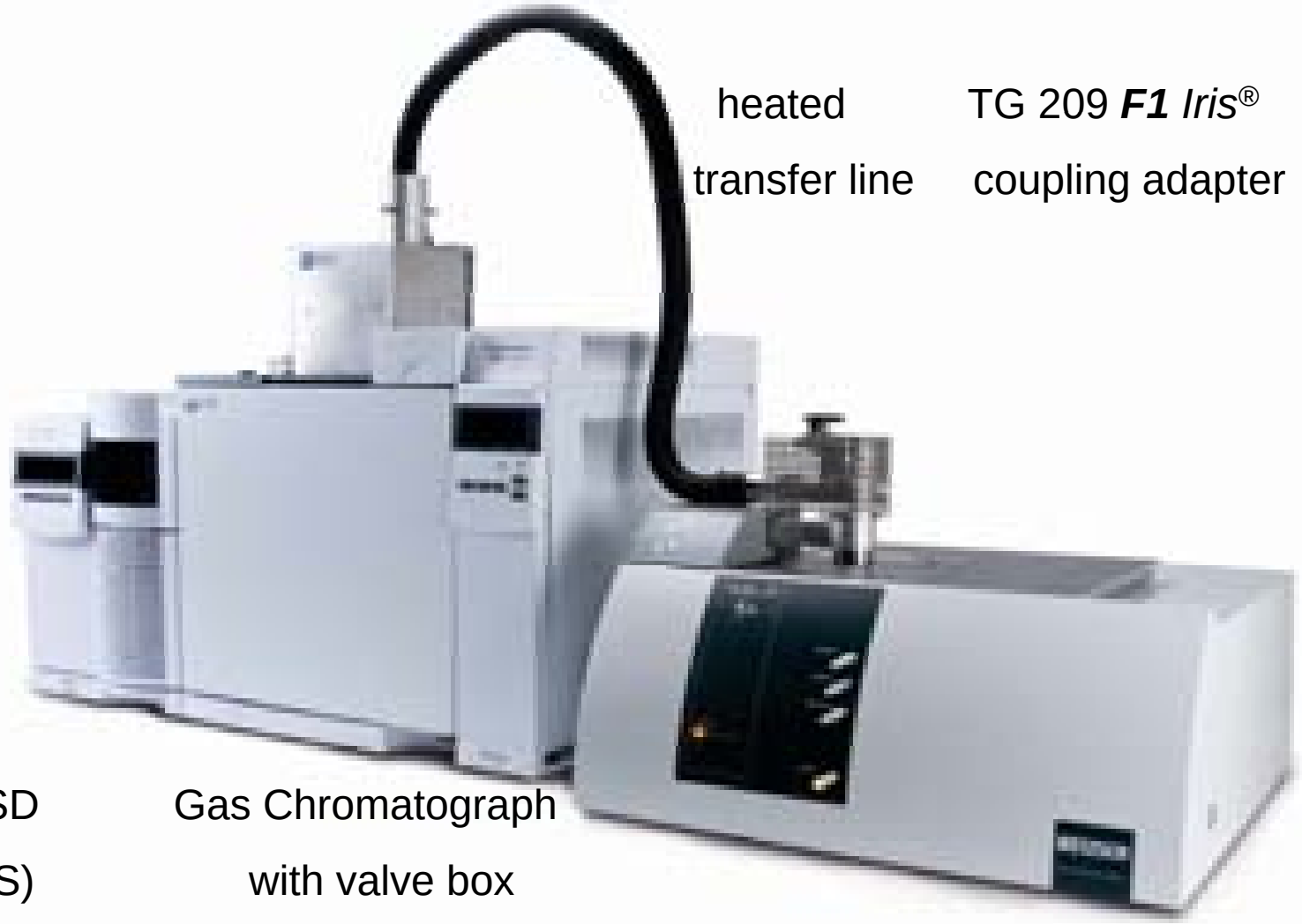
TG-GC-MS Coupling in Thermal Analysis

NETZSCH

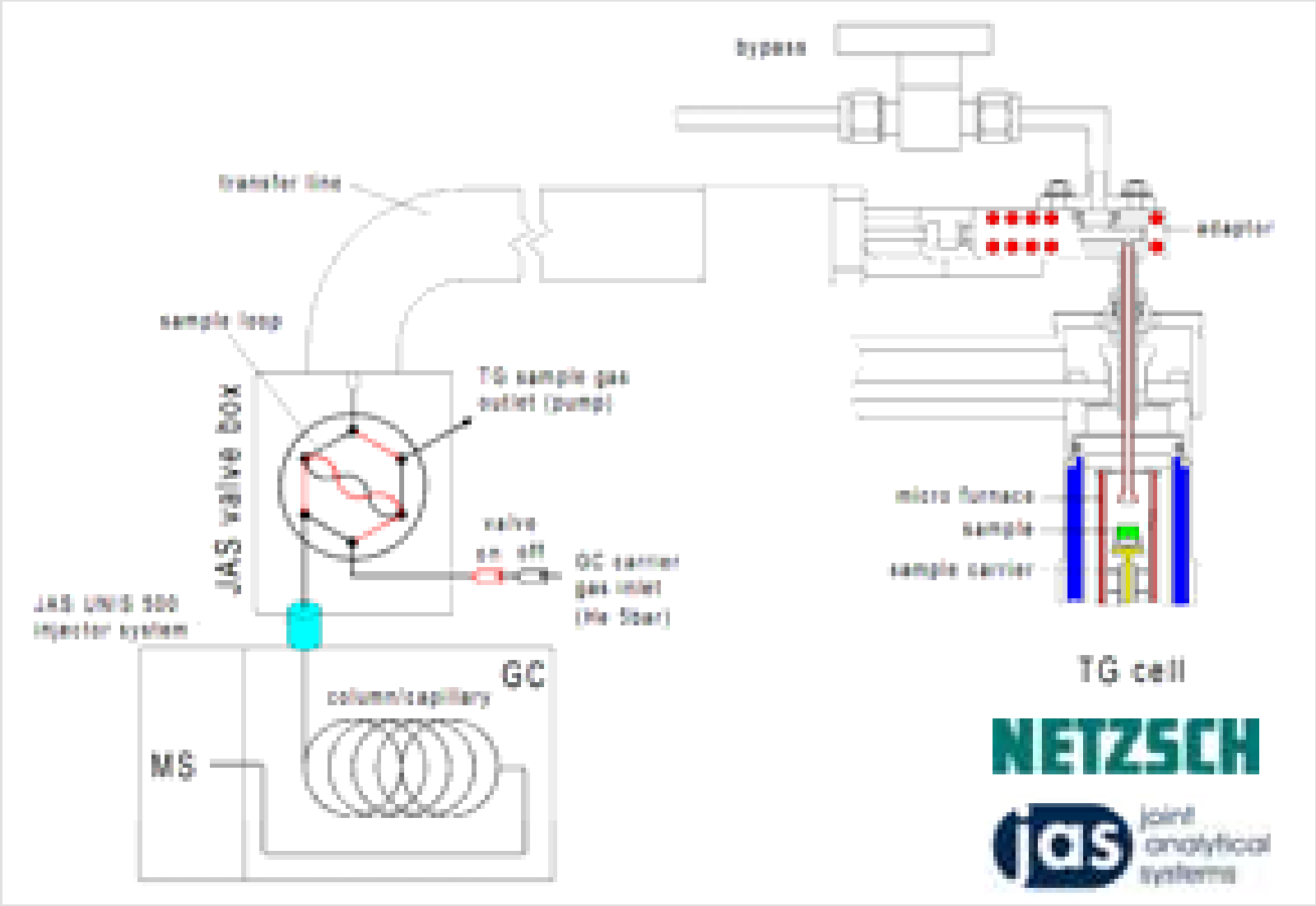
Yields information on the composition (mass numbers of elements and molecules) of the evolved gases.
⇒ Very high sensitivity
⇒ Separation of the volatiles using the GC column
⇒ Interpretation of organic vapors can be improved

Anyway GC-MS tests generally require minutes to be carried out. This means that a real time analysis which generates a relationship between time/temperature of the TGA run with the GC-MS is often difficult. Solutions:
⇒ Continuous GC-MS with limited separation possibilities
⇒ Event controlled GC-MS triggering (high sensitivity and relation between mass loss step and GC-MS result)

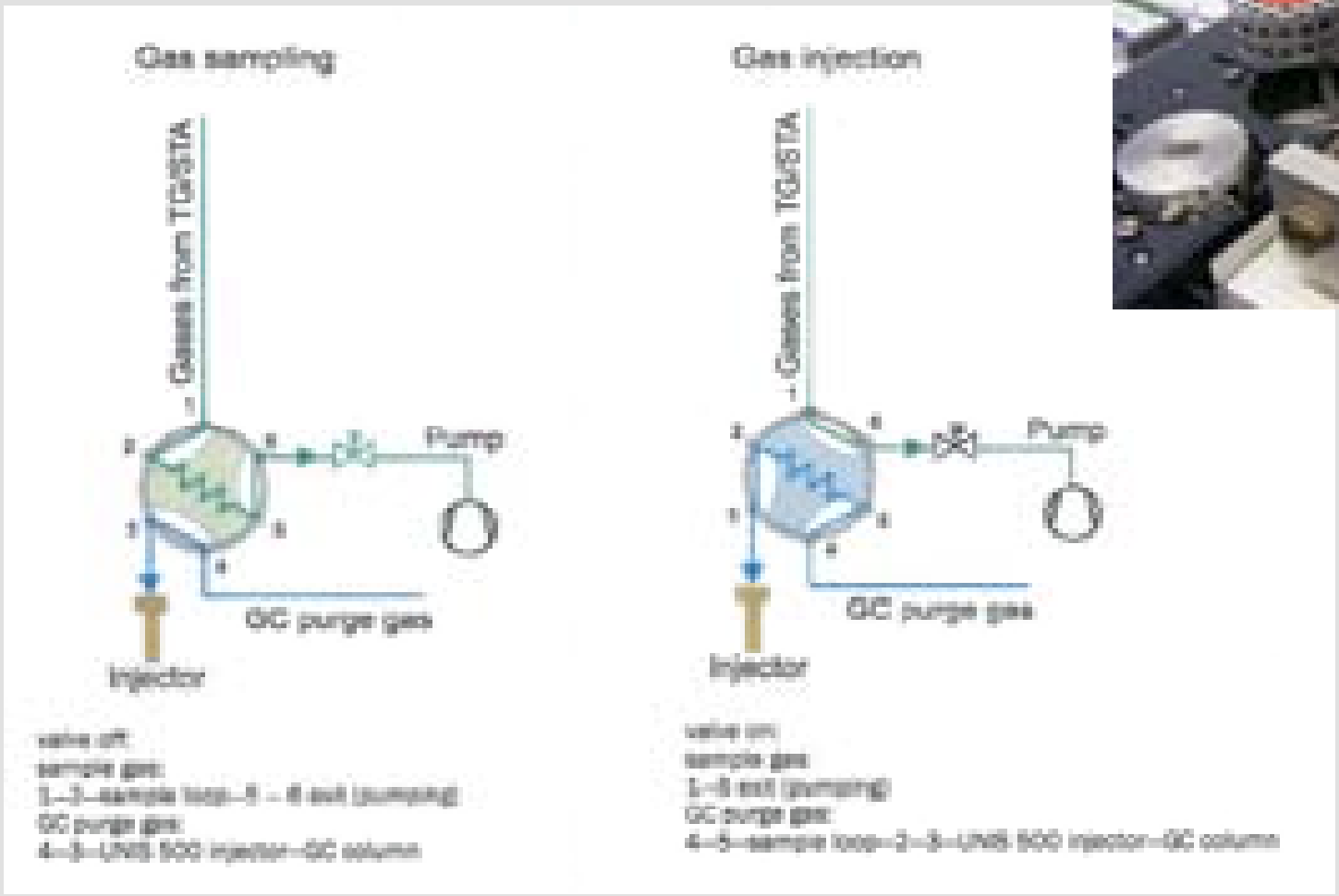
Fully Integrated TG/STA-GC-MS System



Coupling with chromatographic pre-separation



Valve box

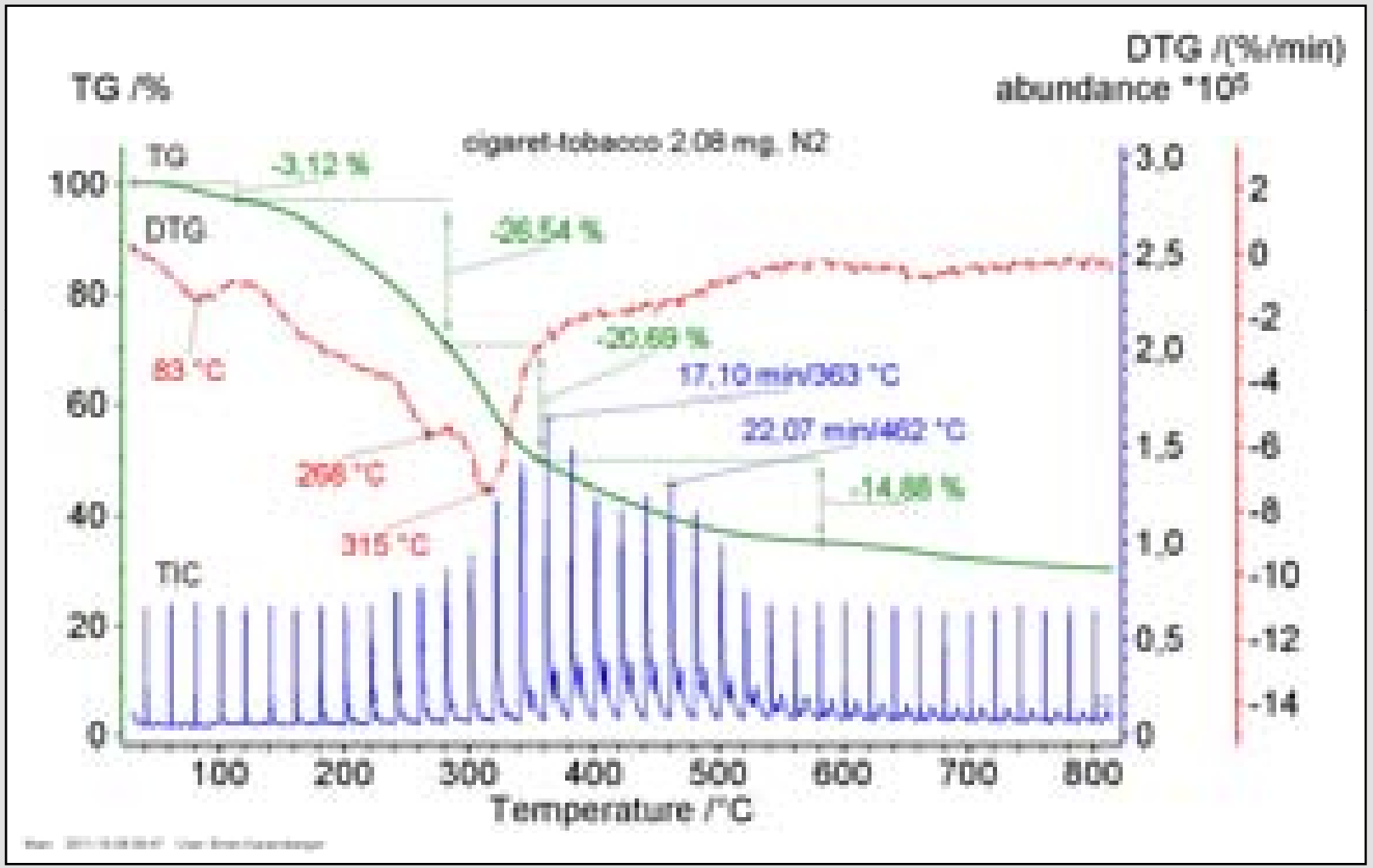

Gas sampling
Gases from TG/STA
Pump
GC purge gas
Injector
Gas injection
Gases from TG/STA
Pump
GC purge gas
Injector

Tobacco – Analysis with TG-GC-MS

Introduction

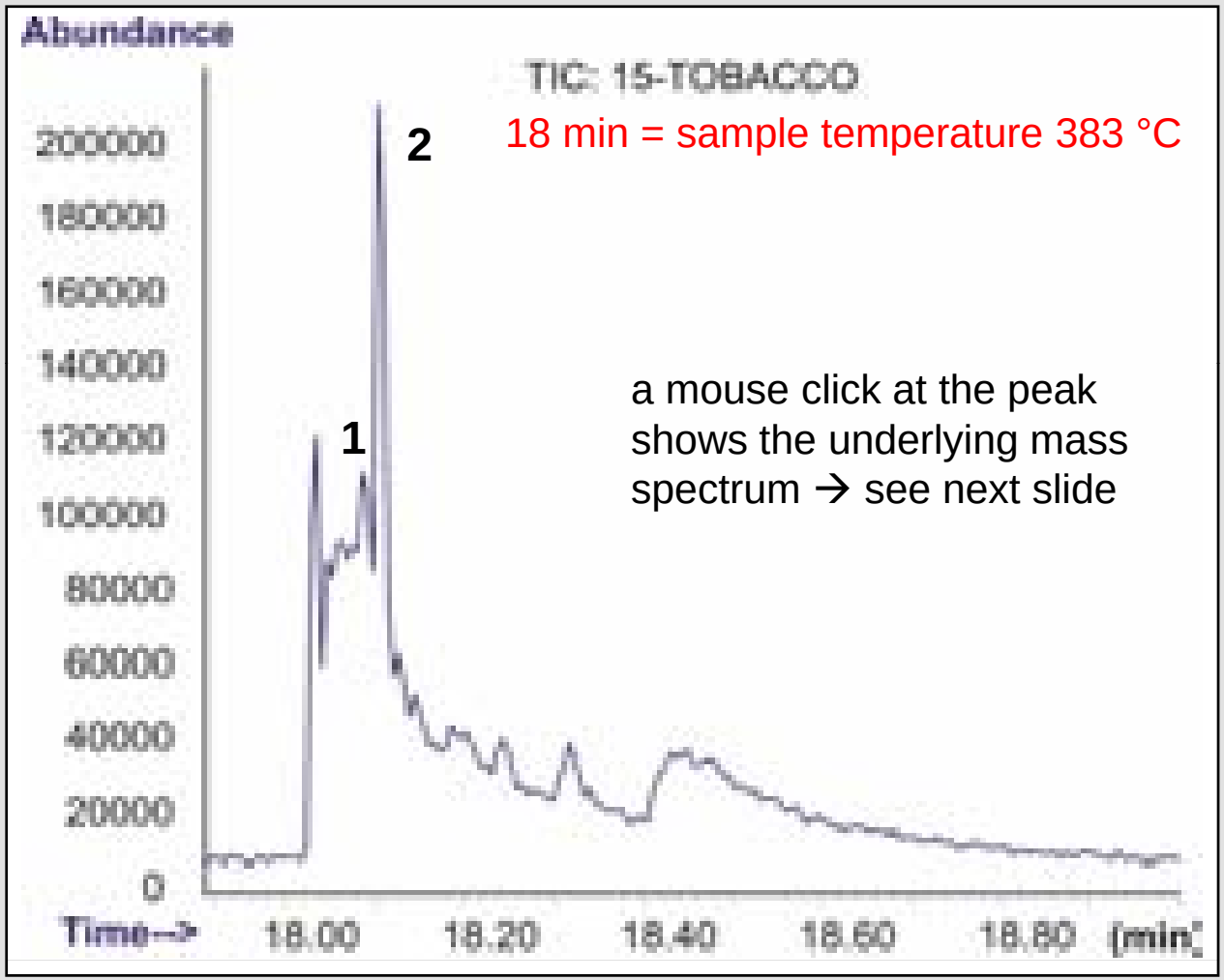
- In a coupled TG-GC-MS all atmosphere conditions can be realized and the influence on the evolved gases can be clearly demonstrated
- Small amounts of ground cigarette-tobaccos were analyzed in the TG 209 **F1** *Libra*® coupled to the Agilent GC-MS via a heated transfer line, the heated JAS valve box and injector system
- Nitrogen atmosphere was used for the pyrolysis experiments, and Nitrogen with 10.7 % oxygen for the combustion experiments (to provide smooth oxidative conditions); heating rate was always 20 K/min for fast results
- The GC-MS was started by the Proteus software simultaneously with the TG 209 F1 for the continuous experiments, and as well started at the selected DTG threshold values for the event-controlled experiments.

Cigaret-tobacco: continuous mode TG-DTG-TIC



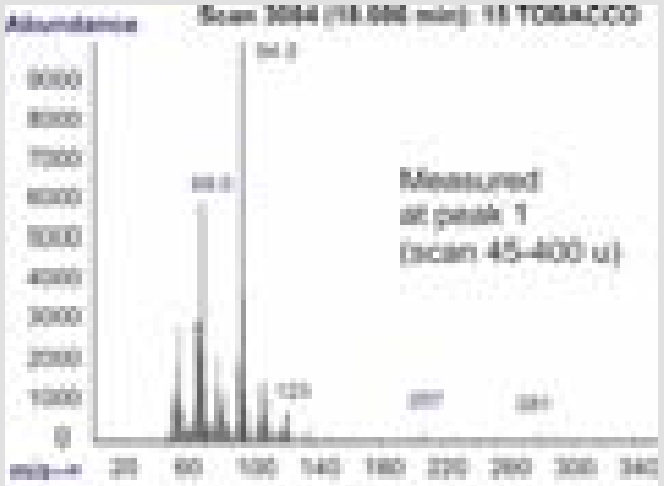
there is always a precise time-temperature correlation for all results

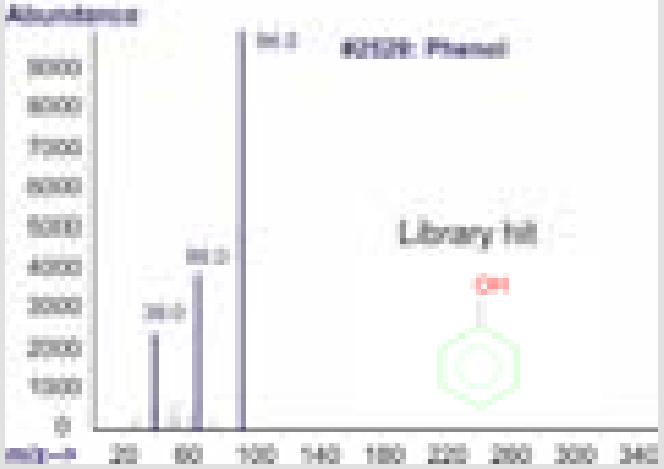
Chromatogram evaluation of a continuous run

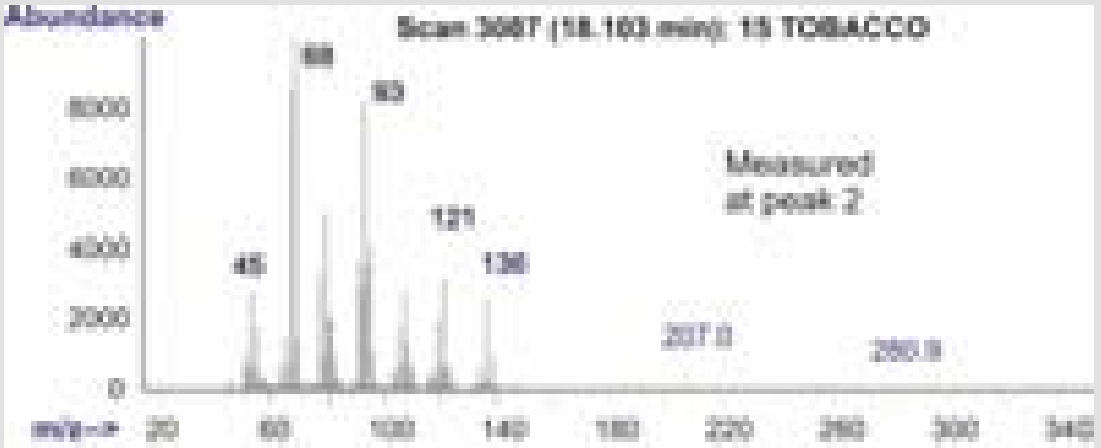


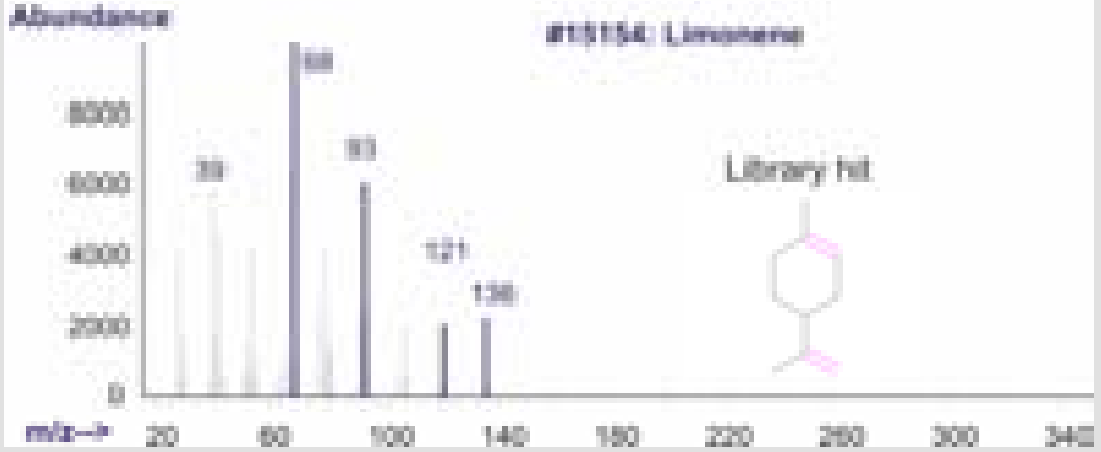
TIC of injection at 18 min (column temperature 250 °C); the gas separation (retention peaks) is mostly sufficient for the identification of the main fragments and molecules

Chromatogram evaluation of a continuous run

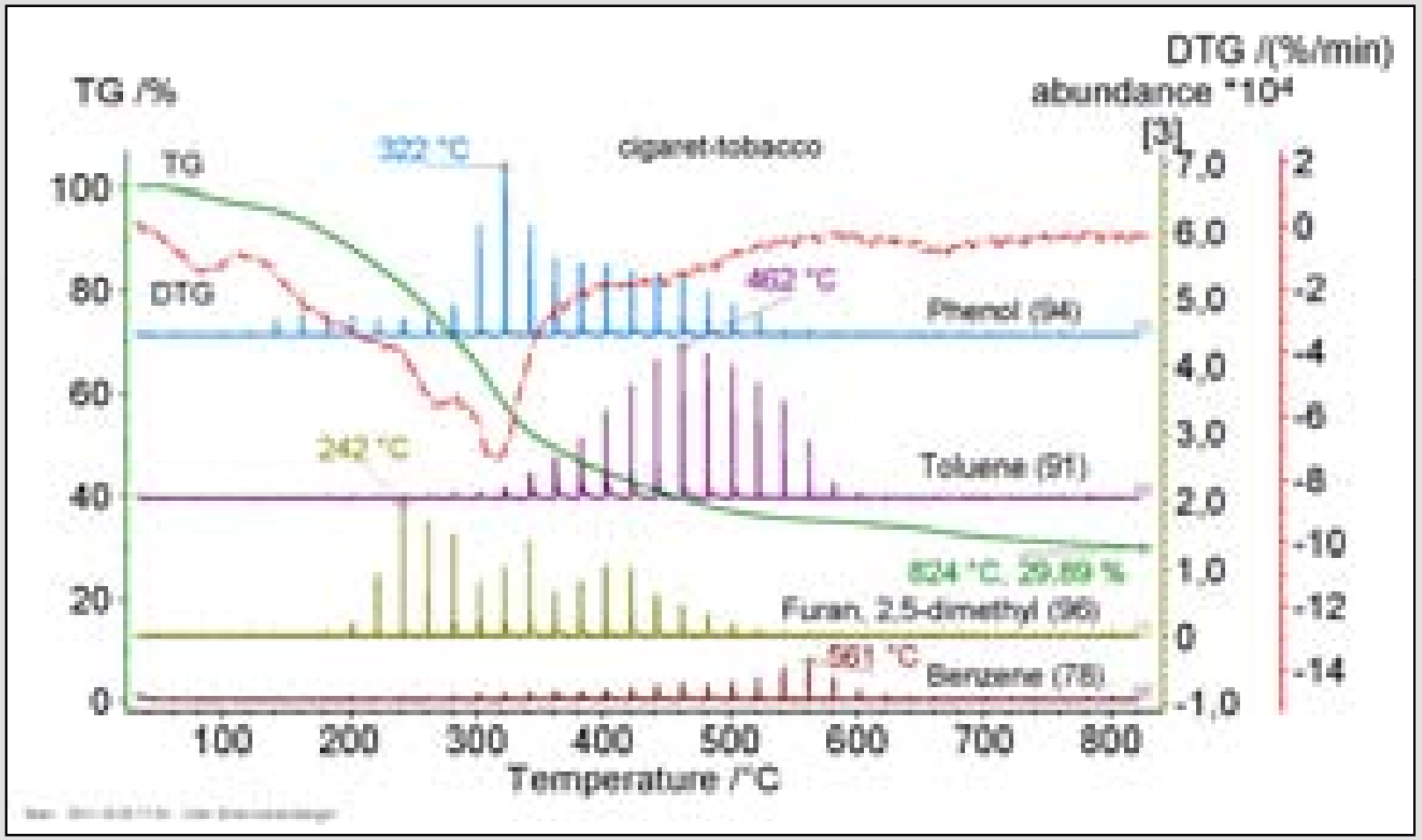




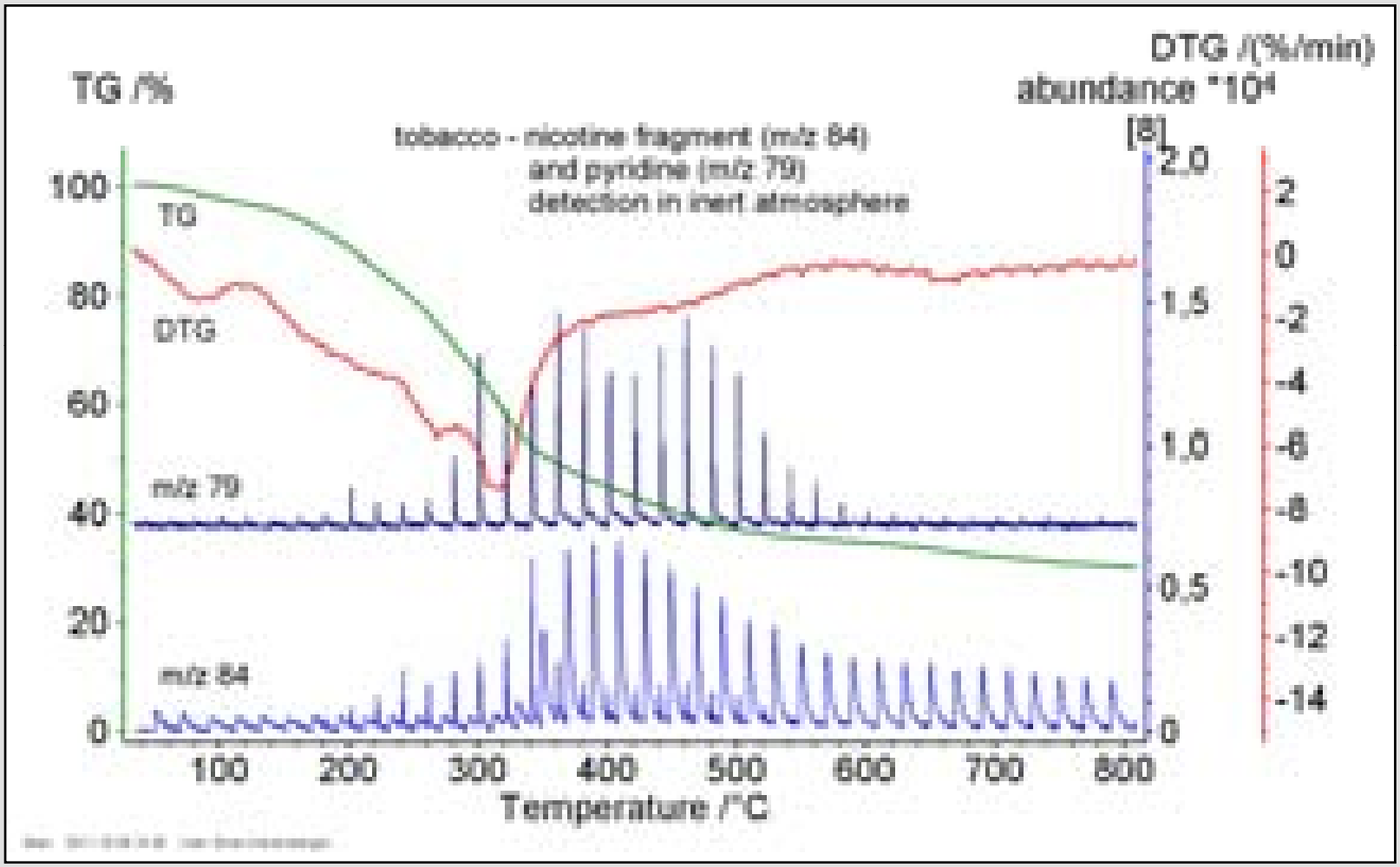




Single ion monitoring on time/temperature scale

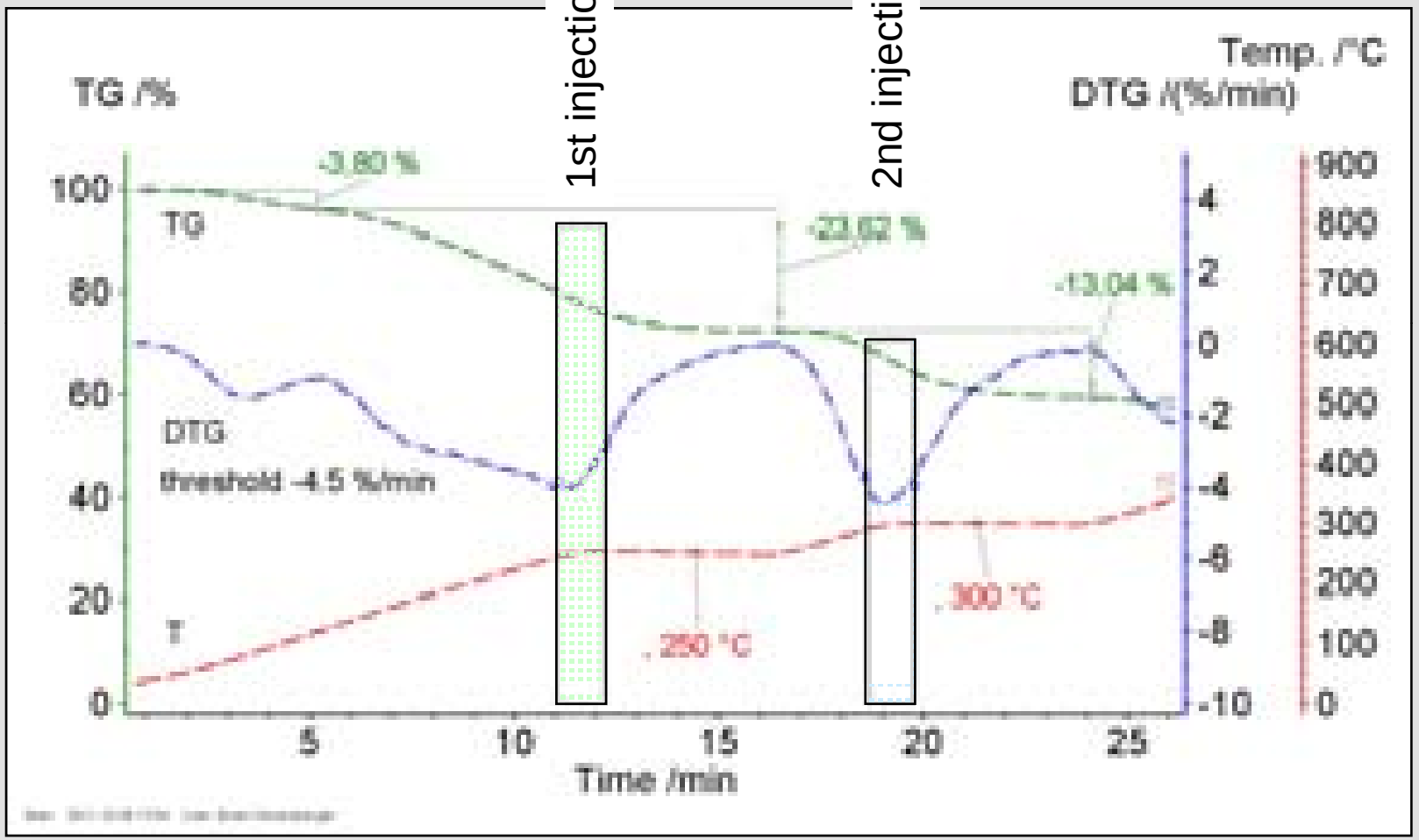


Detection of nicotine in tobacco (> 200 °C)



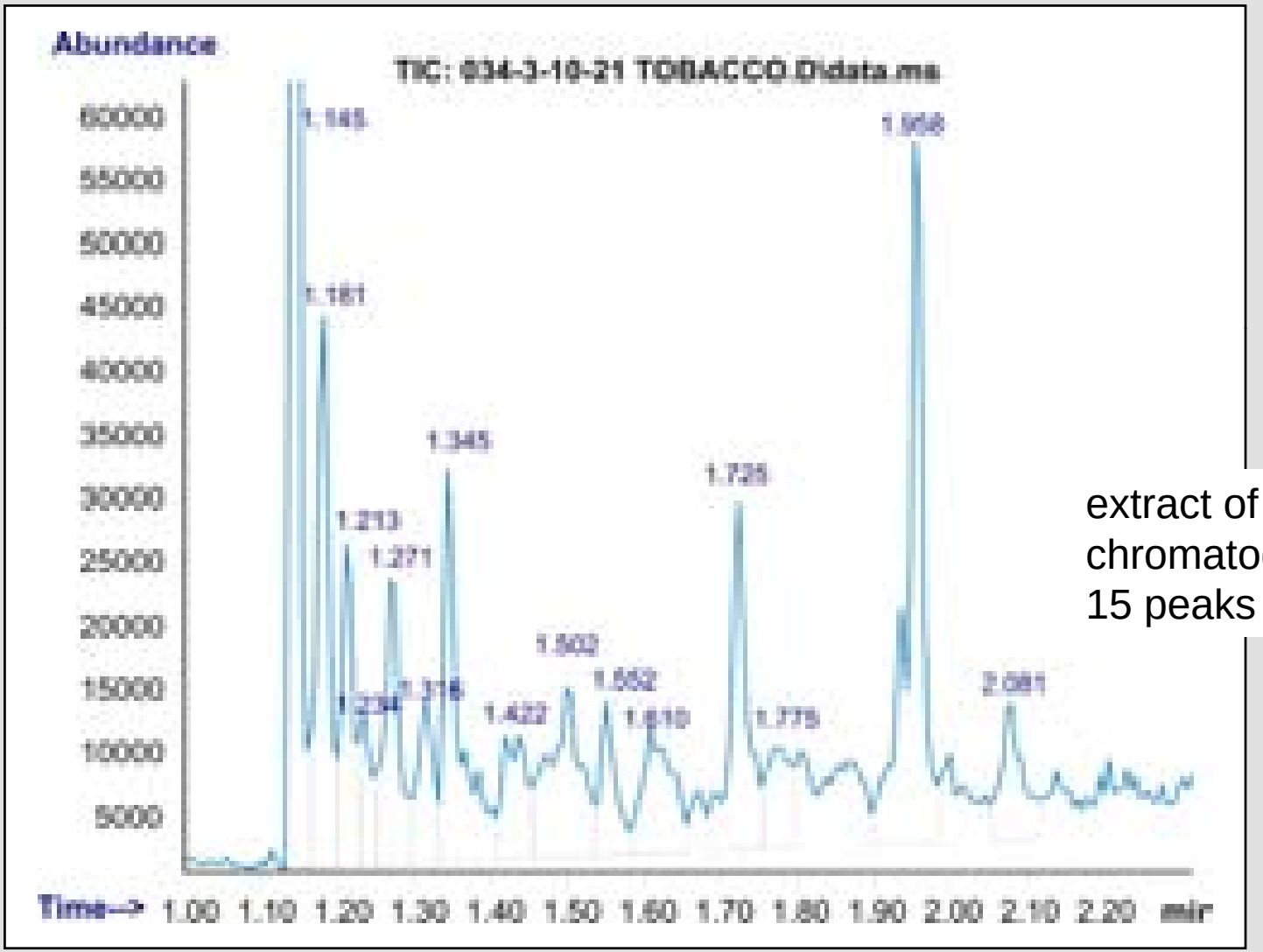
m/z 79 →Pyridine;
m/z 84 →Pyridine, 2-(1-methyl-2-pyrrolidinyl)- [84=main peak of nicotine]

Event-control: tobacco, 1.48 mg, N2, 20 K/min



reaching the DTG threshold, the injection of the gas onto the column is started and the TG temperature program goes on hold until the GC-oven program is completed; then the TG heating starts again up to the next threshold

Event-controlled run: Chromatogram at 300 °C



extract of full chromatogram, 15 peaks identified

Automatic evaluation of Chromatogram at 300 °C

NETZSCH Library Search Report

Data File : 034-3-10-21 TOBACCO.D Sample : **TOBACCO 1.48 mg**

Search Libraries: C:\Database\NIST05.L

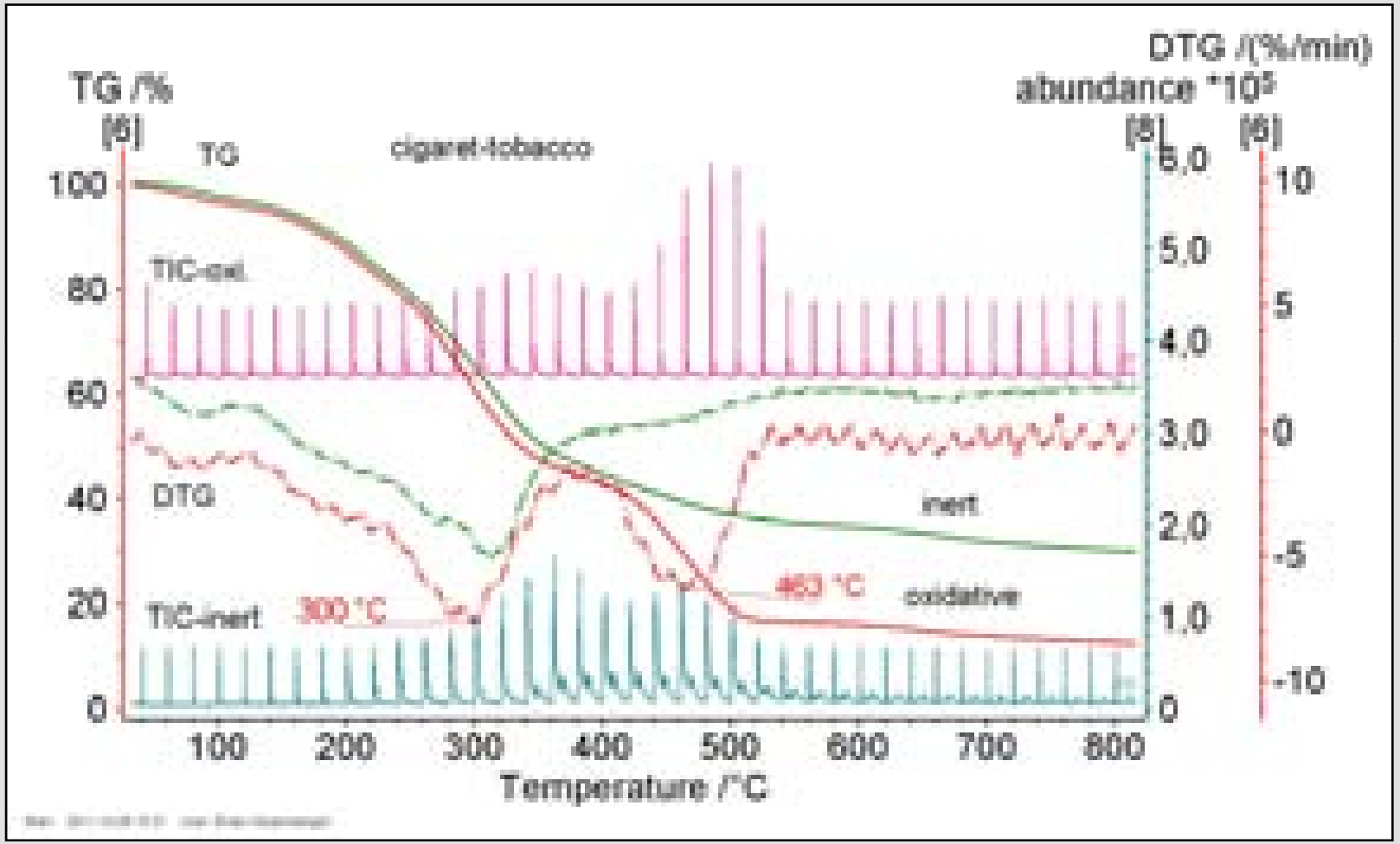
Peak #	RT(min)	Area%	Identity	Ref #	CAS #	Hit-Qual
1	1.145	19.86	Heptane, 1-(methylthio)- *[background]*	21310	020291-61-6	20
2	1.180	6.96	1,3-Pentadiene, (E)-	440	002004-70-8	72
3	1.215	3.93	Furan, 3-methyl-	1145	000930-27-8	72
4	1.232	1.80	3-Vinyl-1-cyclobutene	1066	006555-52-8	49
5	1.272	4.57	Furan, 2,5-dimethyl-	2739	000625-86-5	91
6	1.313	2.63	1,5-Cyclooctadiene, 3,8-dimethyl-	15250	1000155-84-1	64
7	1.347	6.62	1,5-Hexadien-3-yne, 2-methyl-	2421	000820-54-2	74
8	1.423	3.01	alpha.-Bourbonene	59835	1000293-01-9	78
9	1.503	5.63	p-Xylene	4946	000106-42-3	76
10	1.550	2.43	Bicyclo[4.2.0]octa-1,3,5-triene	4758	000694-87-1	81
11	1.613	3.87	2,4-Hexadiene, 3,4-dimethyl-	5877	002417-88-1	38
12	1.723	5.99	Phenol	2533	000108-95-2	90
13	1.775	2.46	Butanoic acid, 3-methyl-, 3,7-dimethyl-2,6-octadienyl ester	83868	1000131-82-9	47
14	1.960	11.44	D-Limonene	15162	005989-27-5	94
15	2.081	3.09	Phenol, 3-methyl-	5233	000108-39-4	94

Influence of atmosphere

All former test were done in inert atmosphere (nitrogen 50 ml/min); Further tests were done under oxidative atmosphere (nitrogen with 10.7 % oxygen, total 56 ml/min) for demonstration of differences in evolved gases.

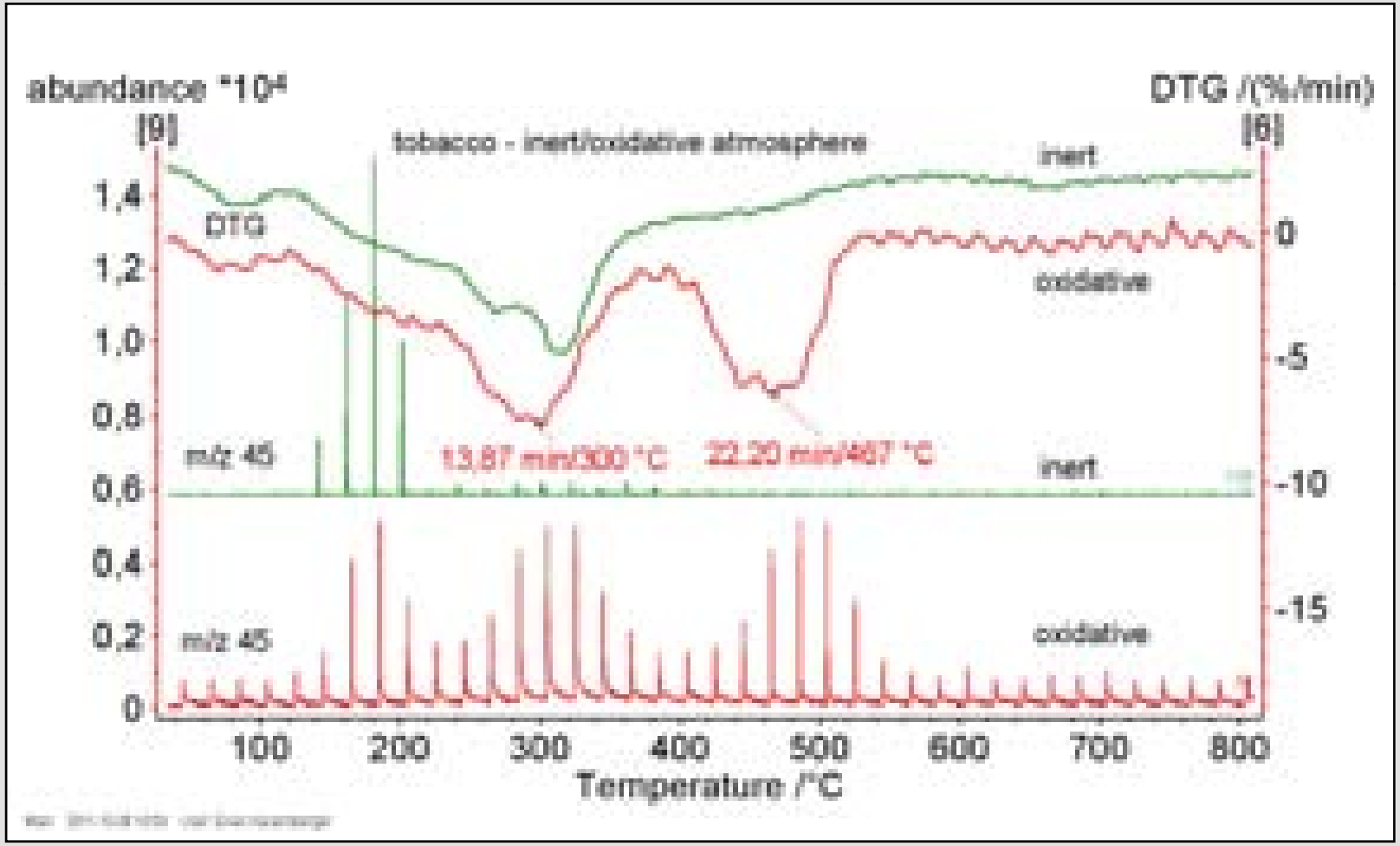
Cigarette in 100% Oxygen

Atmosphere influence – pyrolysis/combustion

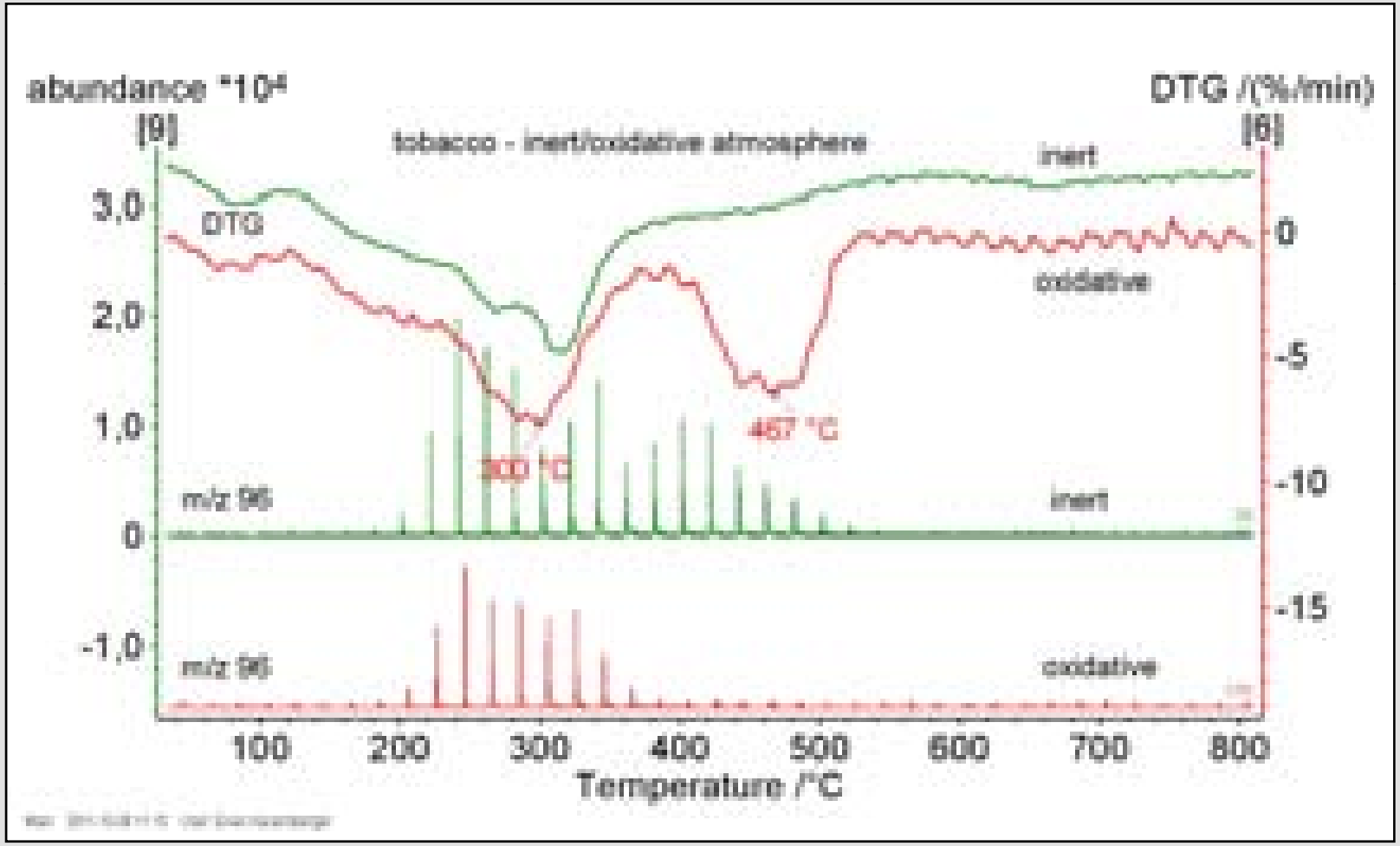


The TG and DTG show quite strong changes due to the oxygen influence

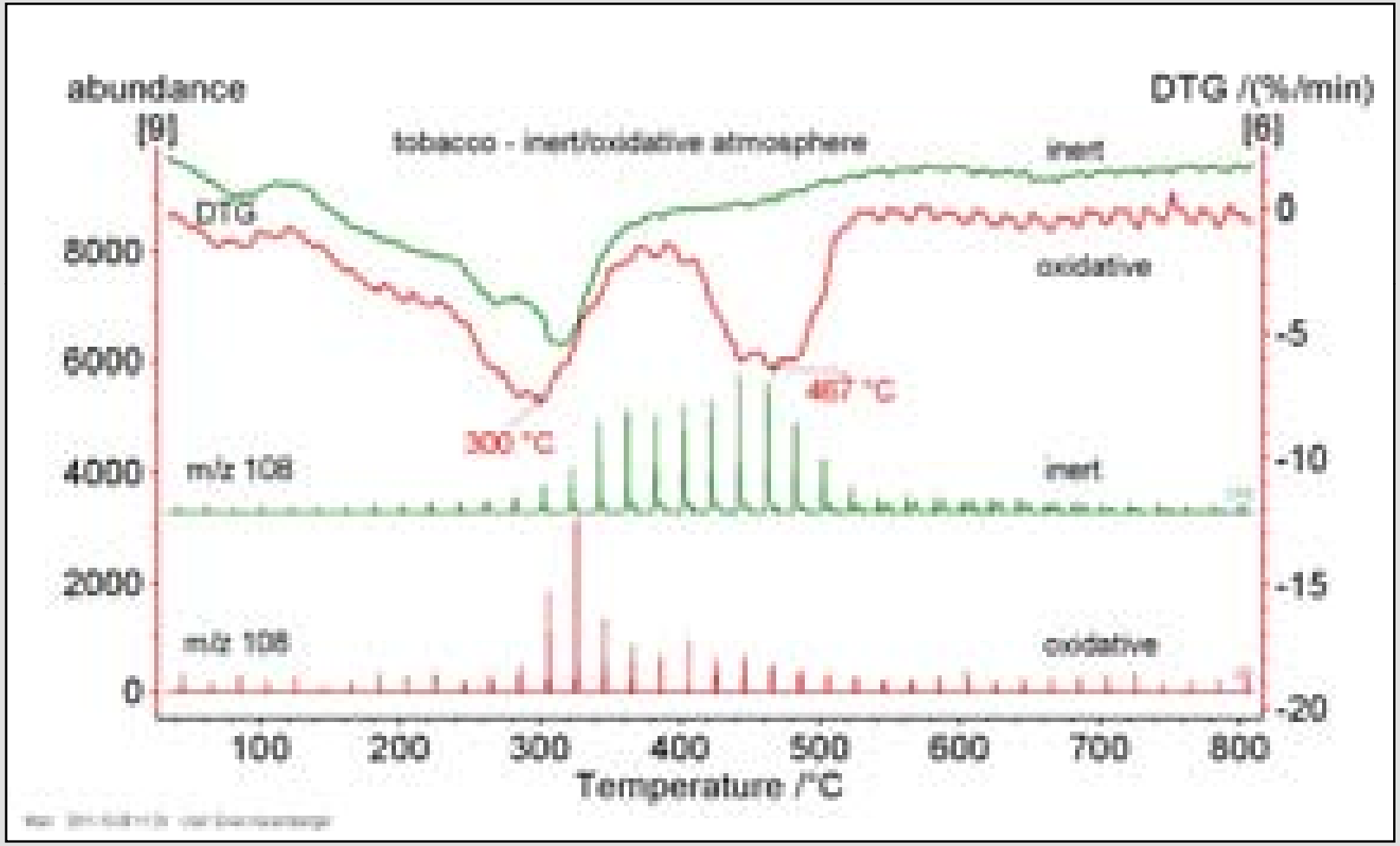
Atmosphere influence – m/z 45 (propylene glycol)



Atmosphere influence – m/z 96 (2,5-methyl-Furan)



Atmosphere influence – m/z 108 (4-methyl-Phenol)



Summary

- Thermal Analysis Instruments are standard in research and development, e.g. in the organic chemistry.
- Coupling to MS, FTIR or GC-MS yields additional information on the material's behavior at high temperatures and the nature of the evolved gases.
- The integrated TG-GC-MS coupling offers the advantage of separating the evolved gases for easier and more accurate interpretation of organic vapors.
- The different examples clearly demonstrated the benefit of using advanced thermal analysis instruments for the characterization of pharmaceuticals, food and related products.