

Near-Infrared Spectroscopy: Analytical Applications, Research and Process Control



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Outline of the Presentation

- **Introduction**
- **Some qualitative aspects of NIR spectroscopy**
- **Selected research and quality/process control applications by NIR spectroscopy**
- **Miniaturization**
- **Conclusions**

Today NIR Spectroscopy is Ubiquitous

- Agriculture
- Food
- Chemistry
- Polymers
- Petrochemistry
- Pharmaceuticals
- Medicine
- Environment
- Geology

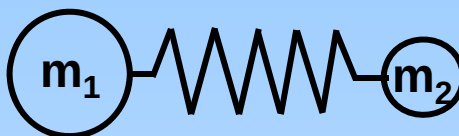
This is also reflected in the number of globally sold units (2011):

near-IR: ~ 8500 (~ \$ Mil 225)

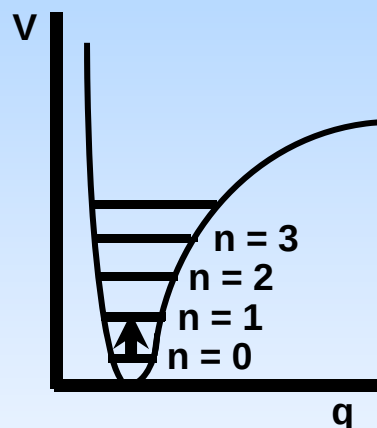
mid-IR: ~ 10000 (~ \$ Mil 450)

Notwithstanding these facts there is still a lot of persuading to do.

The Principles of MIR $\Leftrightarrow$ NIR



MID-INFRARED



FUNDAMENTALS

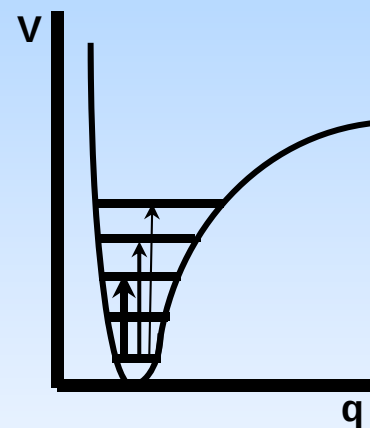
4000 – 400 cm^{-1}

2.5 – 25 μm

$$\frac{\partial \mu}{\partial q} \neq 0$$

**ALL POLAR
FUNCTIONALITIES**

NEAR-INFRARED



OVERTONES/COMBINATIONS

12500 – 4000 cm^{-1}

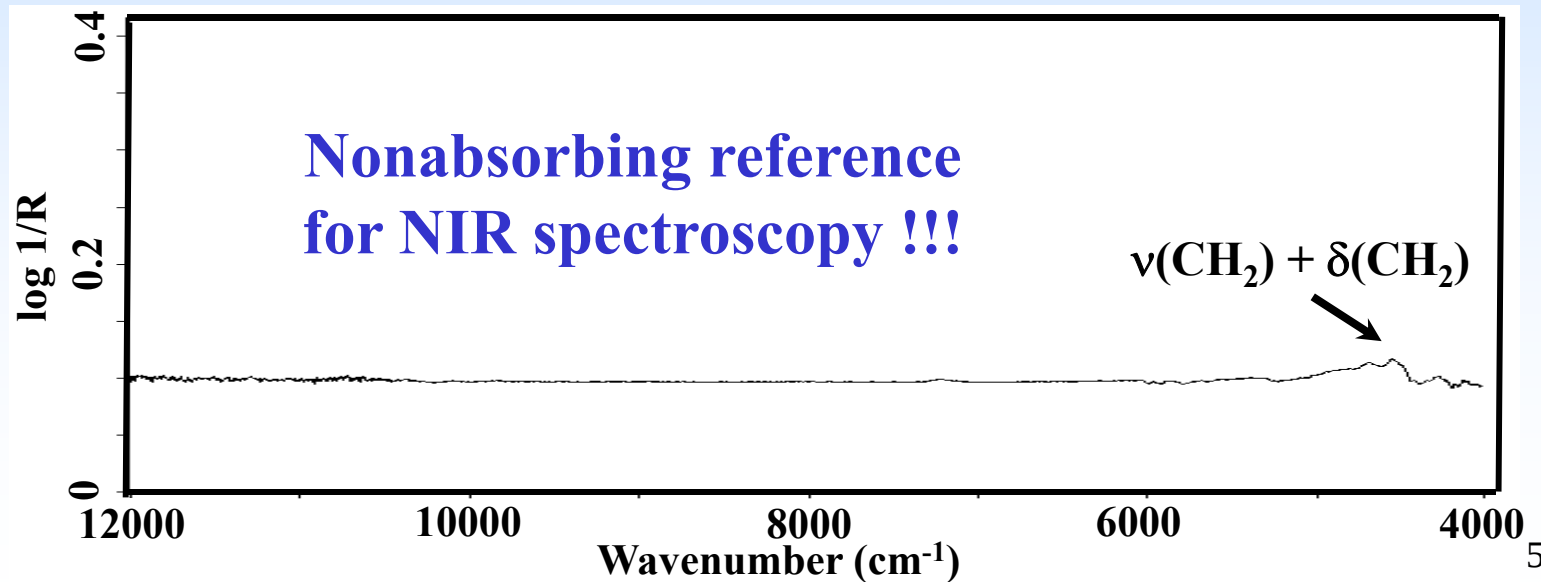
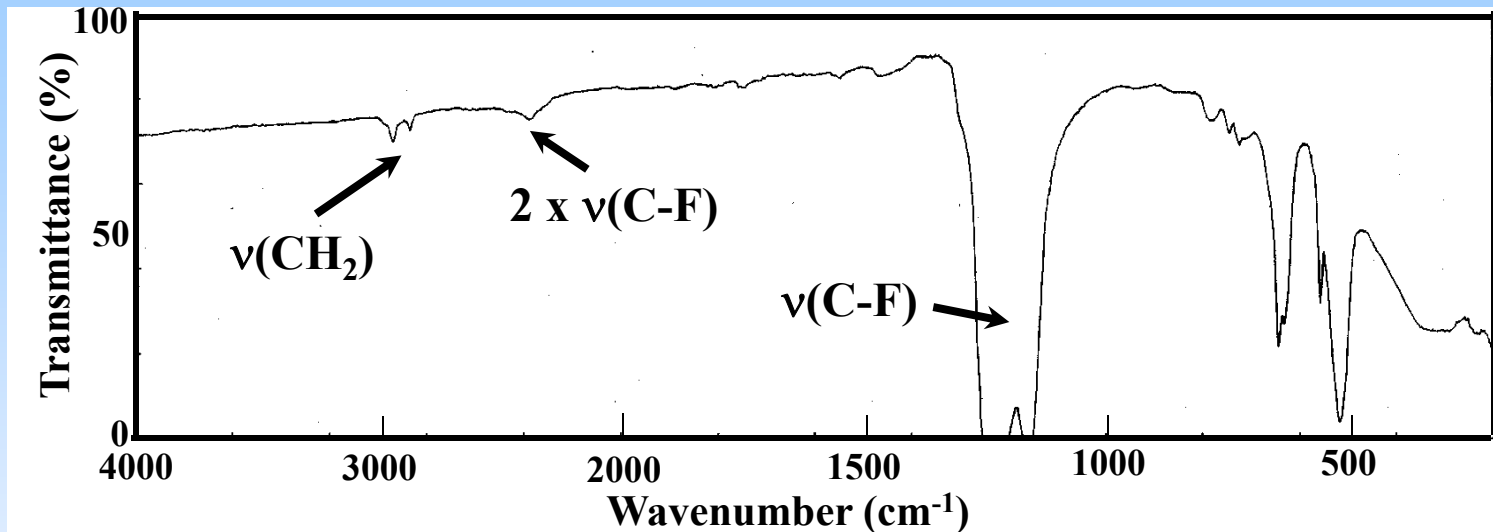
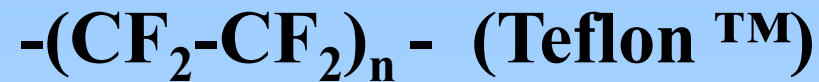
0.8 – 2.5 μm

$$\frac{\partial \mu}{\partial q} \neq 0 \quad / \quad \text{ANHARMONICITY}$$

$m_2 \ll m_1$

**CH / OH / NH
FUNCTIONALITIES**

The Most Striking Case: MIR $\Leftrightarrow$ NIR

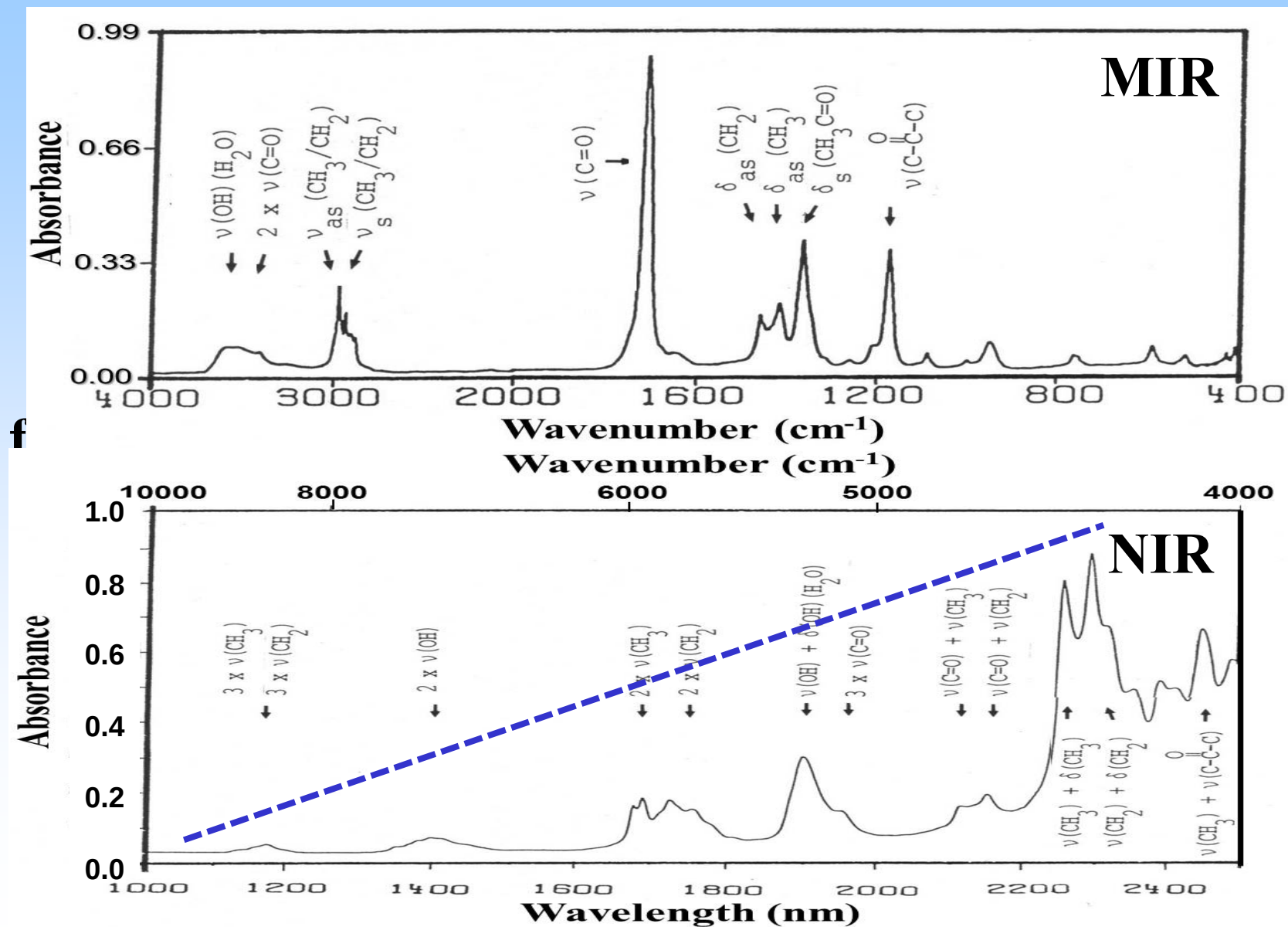


Outline of the Presentation

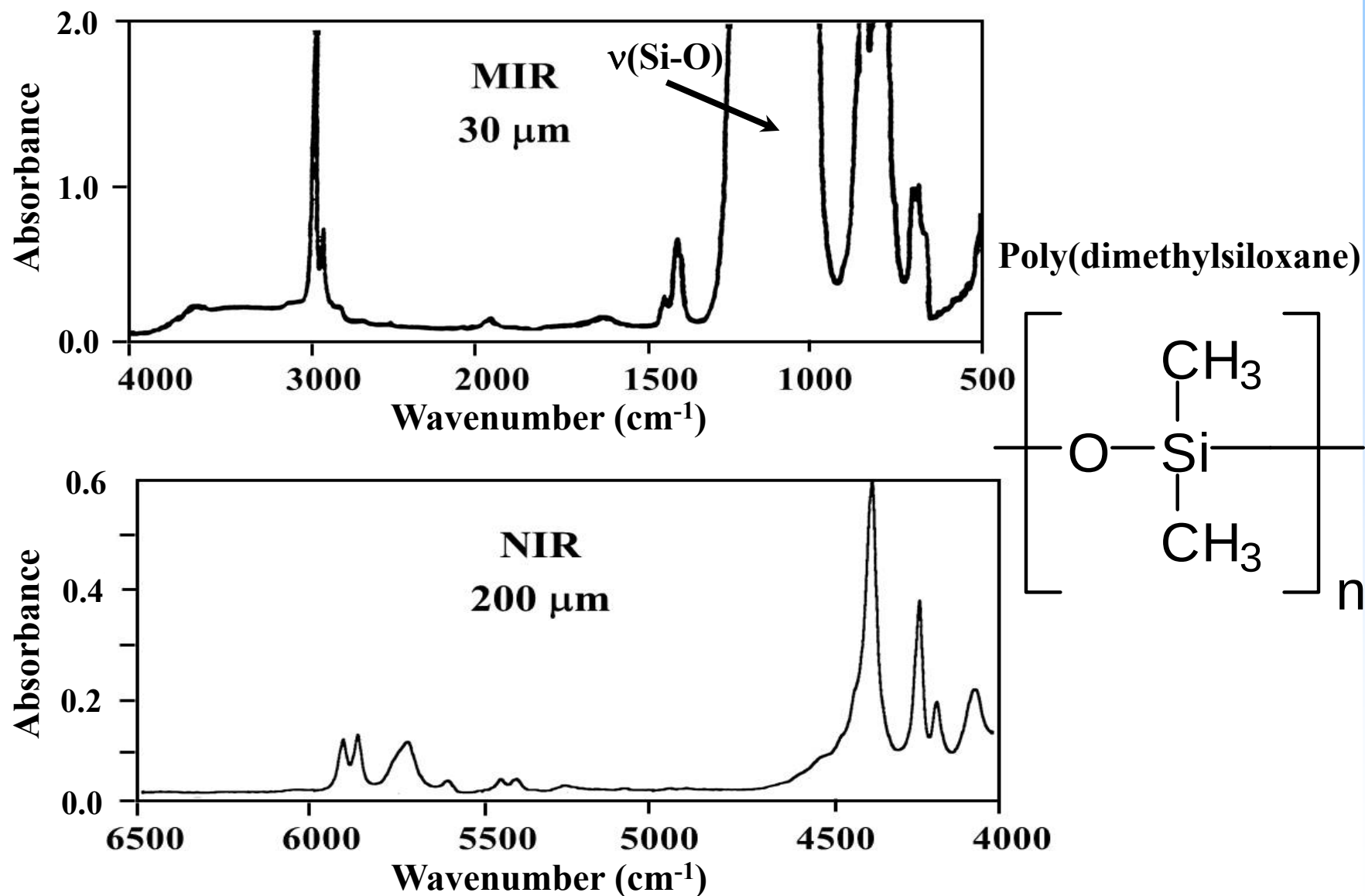
- **Introduction**
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Interpretation of MIR/NIR Spectra

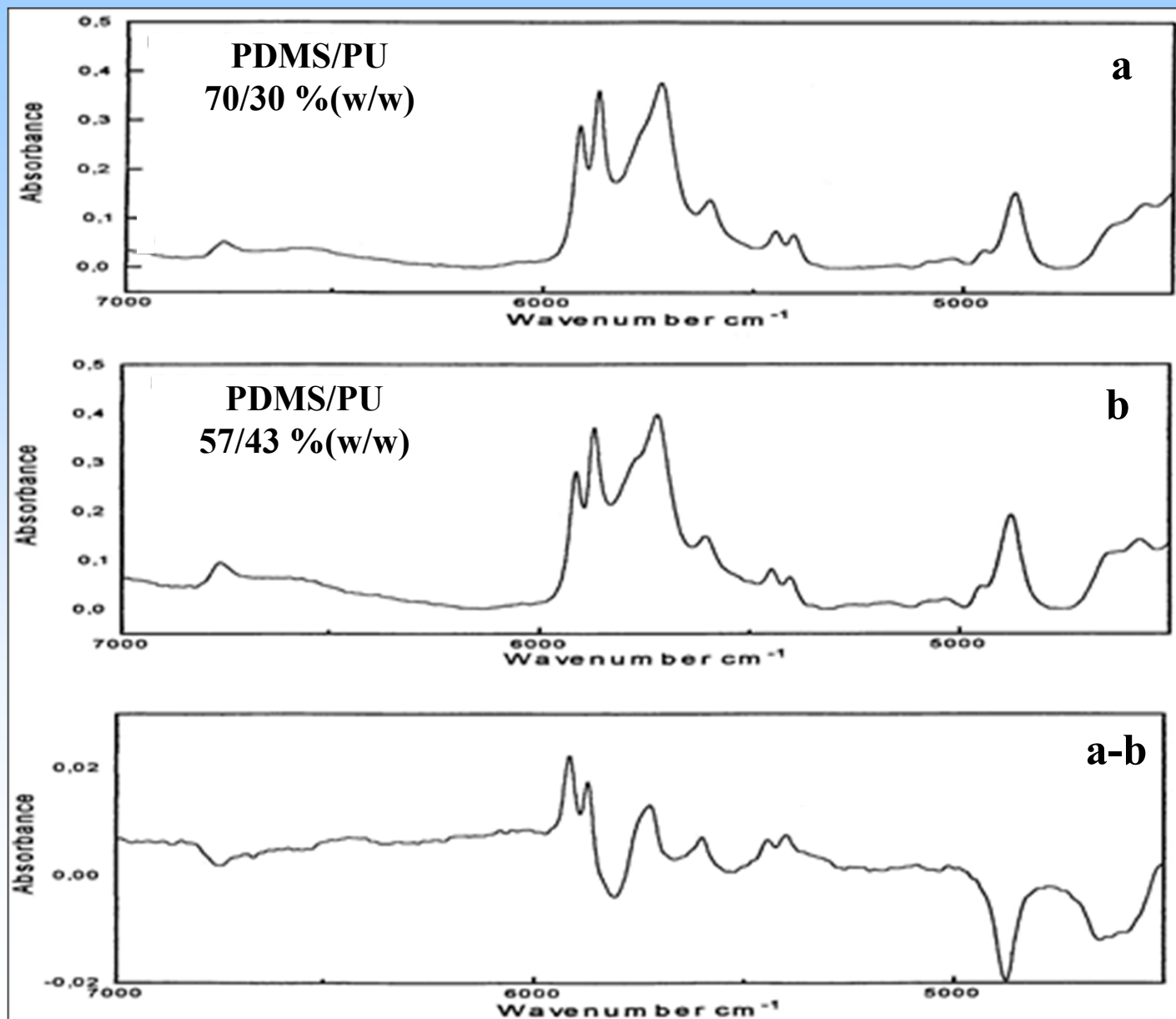
(CH₃CH₂COCH₃ + 5% H₂O)



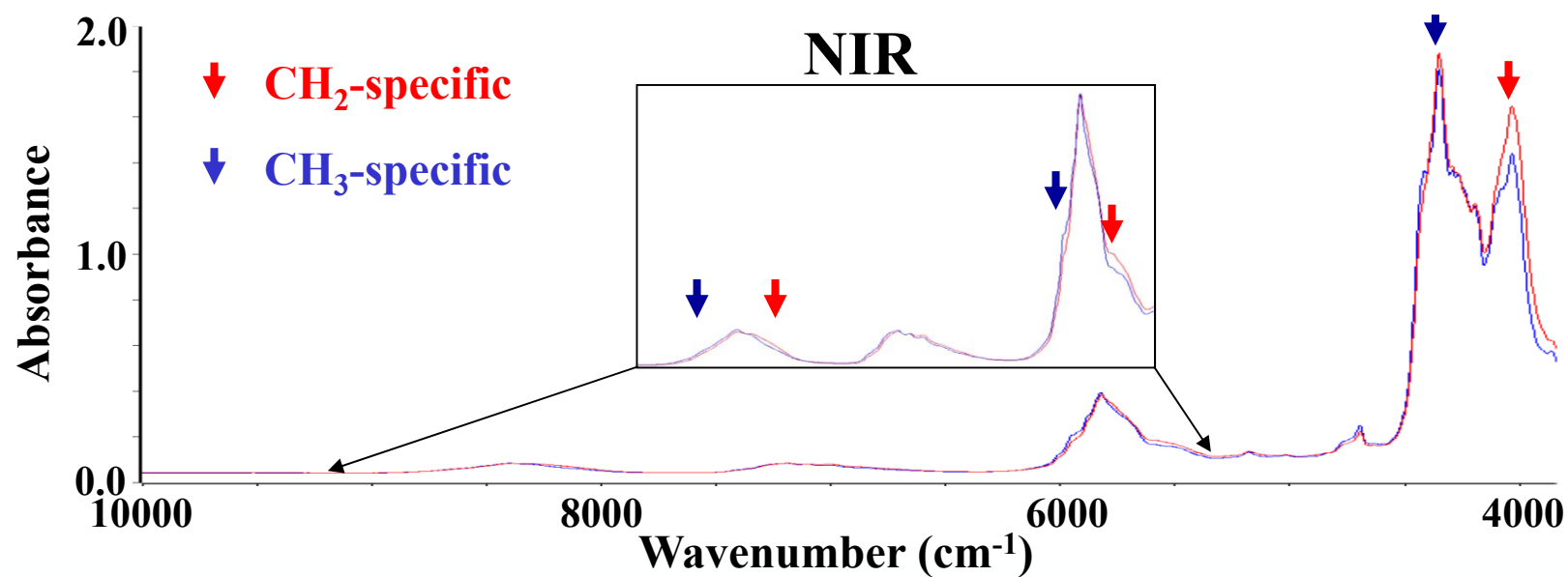
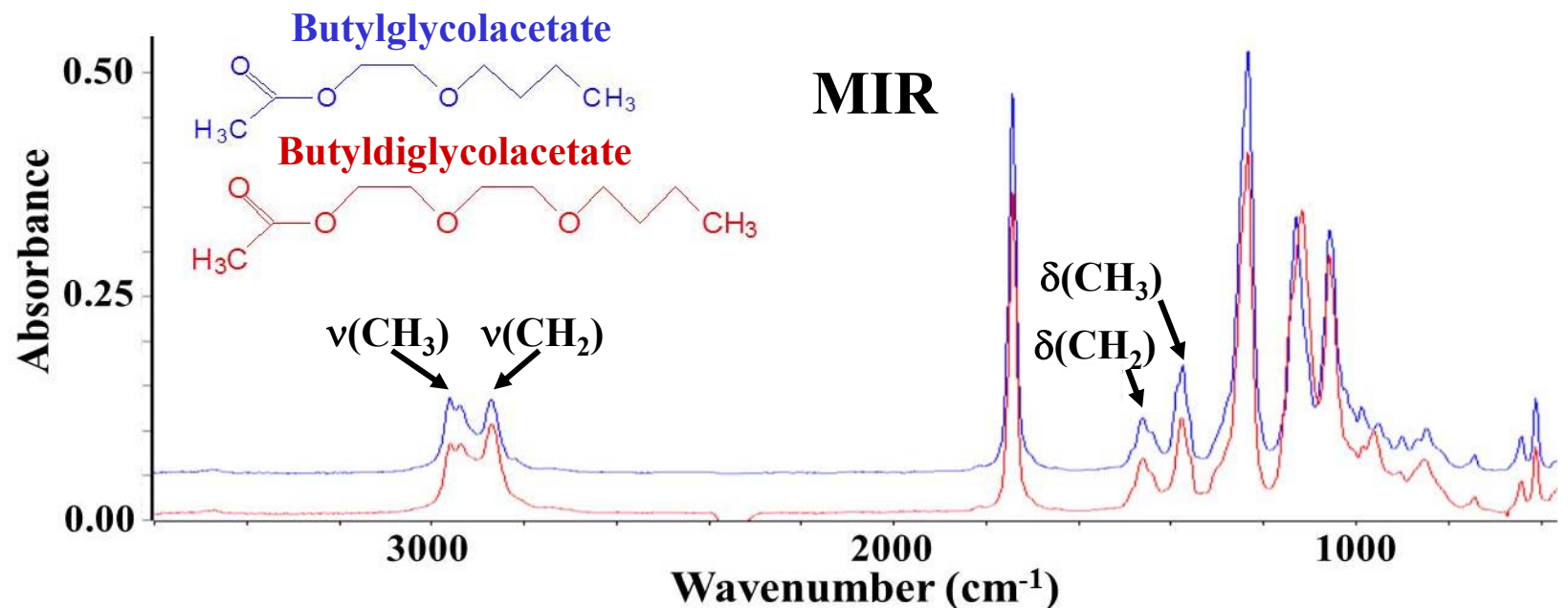
“NIR spectra have only broad absorption bands”



Interpretive Aspects of NIR Spectra



Interpretive Aspects of MIR/NIR Spectra



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Driving Forces for the Implementation of NIR

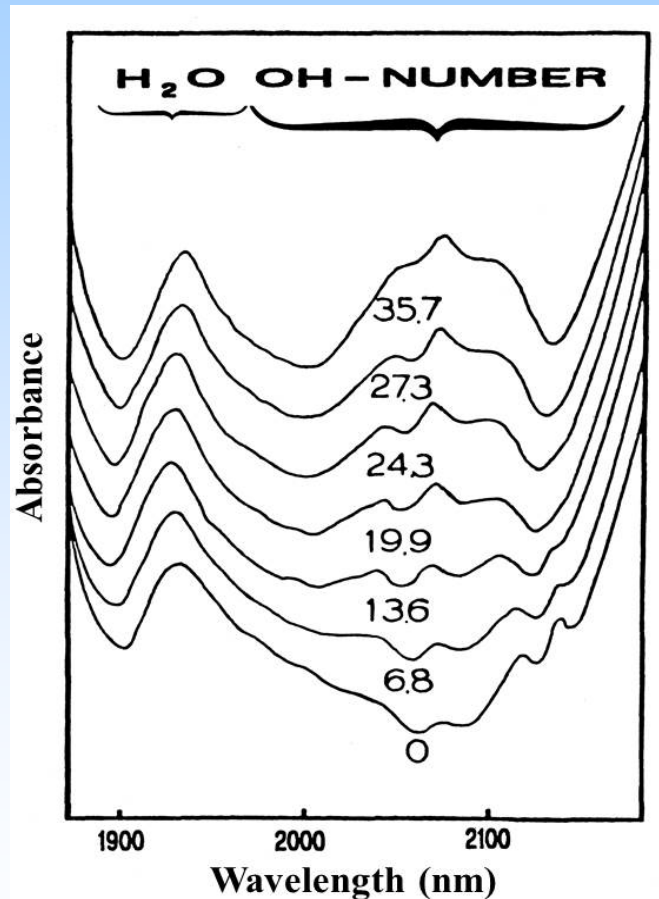
The acceptance of NIR-spectroscopy for research and quality/process control has steadily increased because of:

- occasionally higher selectivity than MIR
- time savings in comparison to other analytical techniques
- simplified or no sample handling of toxic samples
- measurement flexibility in hostile environments
- speed of data acquisition

The following exemplary applications will demonstrate the versatility of NIR spectroscopy for these applications.

Organic OH-Functionality $\Leftrightarrow$ H₂O

Contrary to MIR spectroscopy in the NIR spectra the bands of organic OH-groups are separated from the water bands.



NIR spectra of a polyether with different OH-number

This is of importance for polymer quality control applications:

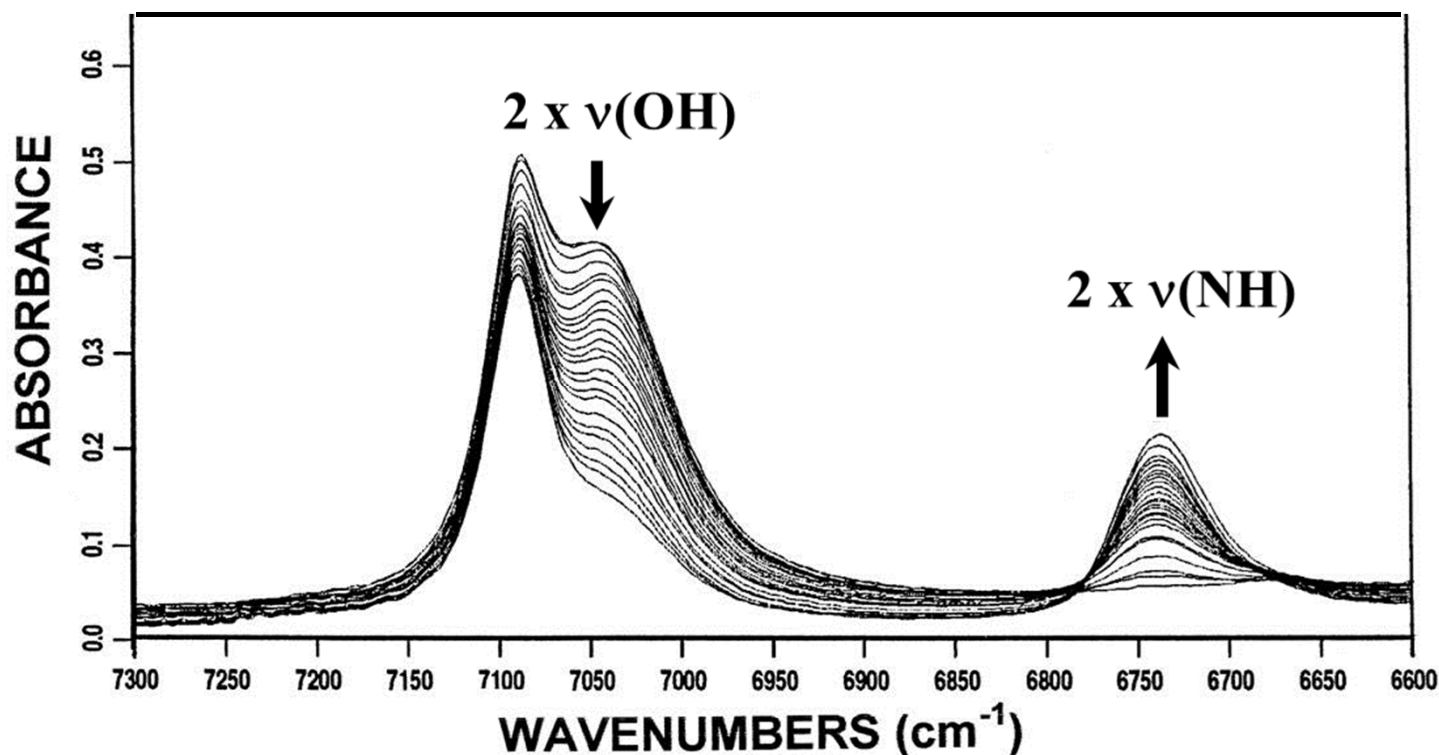
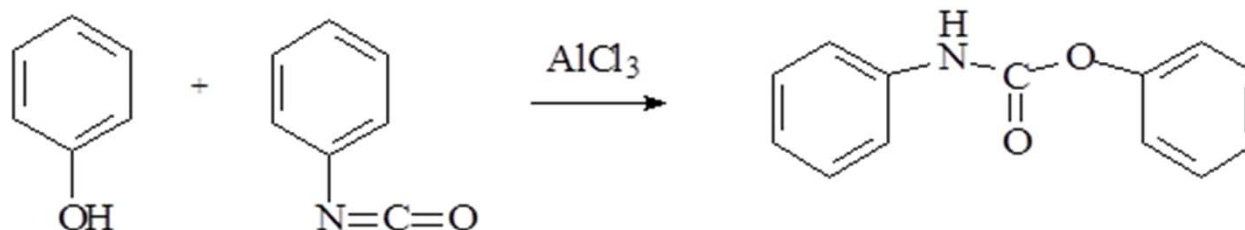
Simultaneous determination of OH-number and water content.

How can you discriminate:

Upon peracetylation the band of the organic OH-group disappears.

OH/NH-Functionalities

Contrary to MIR spectroscopy in the NIR spectra the bands of organic OH- and NH-groups are separated.



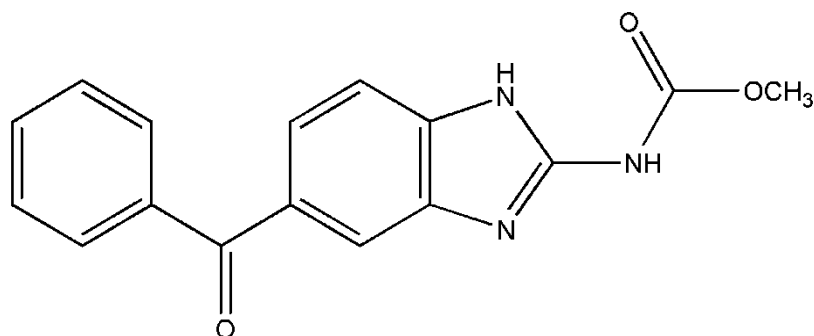
Polymorphism $\Leftrightarrow$ Pharmaceutical Industry

- Polymorphism is the ability of a substance to exist in two or more crystalline forms.
- More than half of the drug substances described in monographs crystallize in more than one solid form.
- Solid state properties of active ingredients have a direct impact on: bioavailability/quality/efficacy safety/patent situation
- What analytical techniques are available for the rapid discrimination of different polymorphs ?

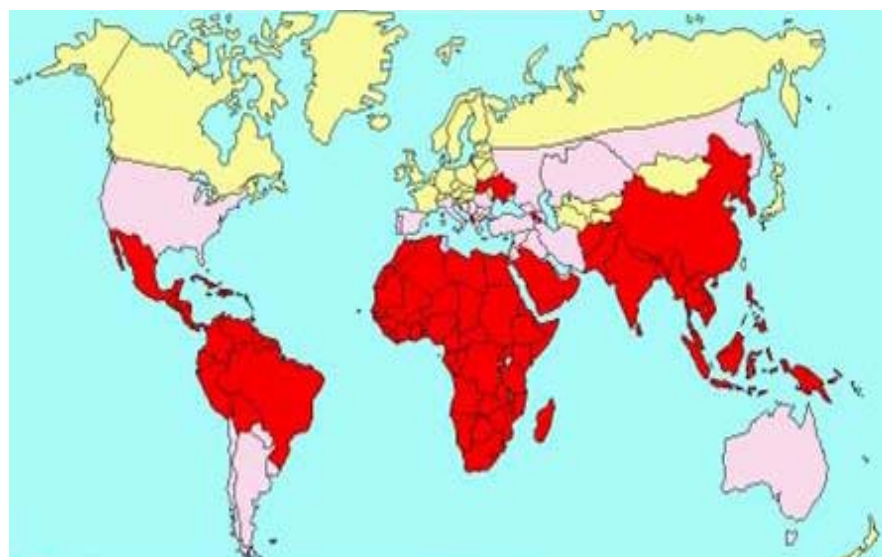
A Case Study of Polymorphism in a Pharmaceutical Active

(cooperation with A. P. Ayala, Fortaleza, Brazil)

Mebendazole



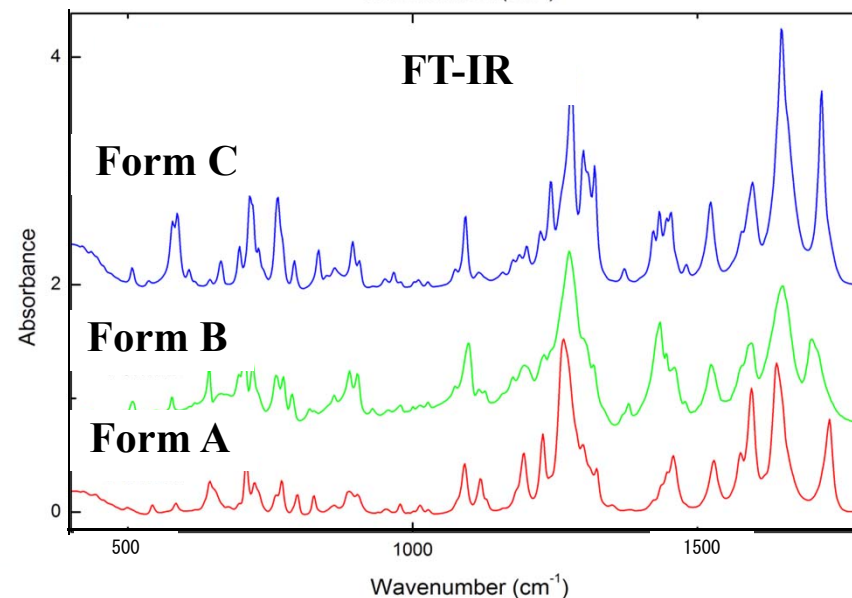
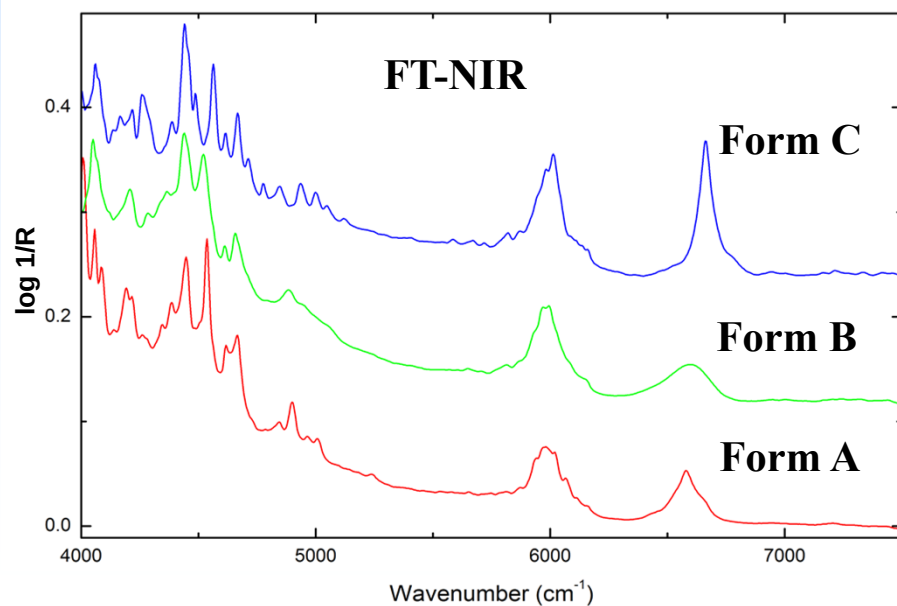
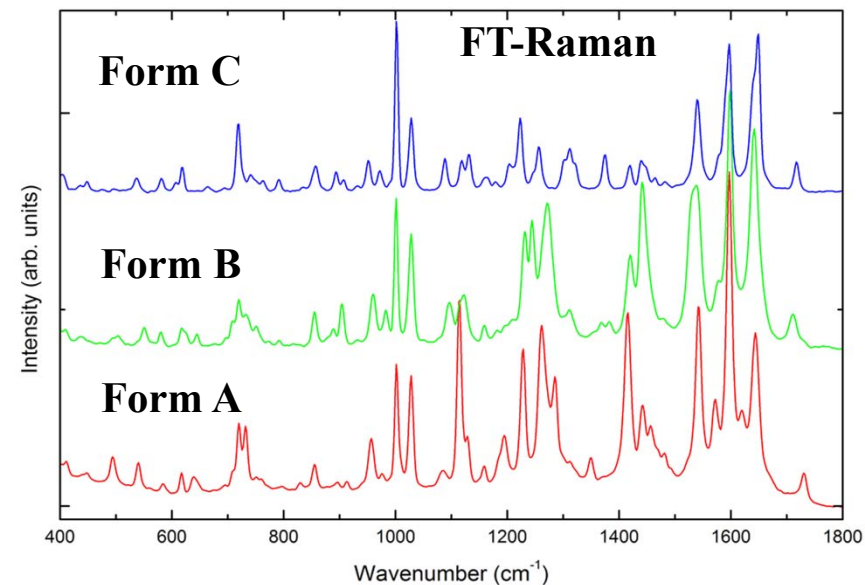
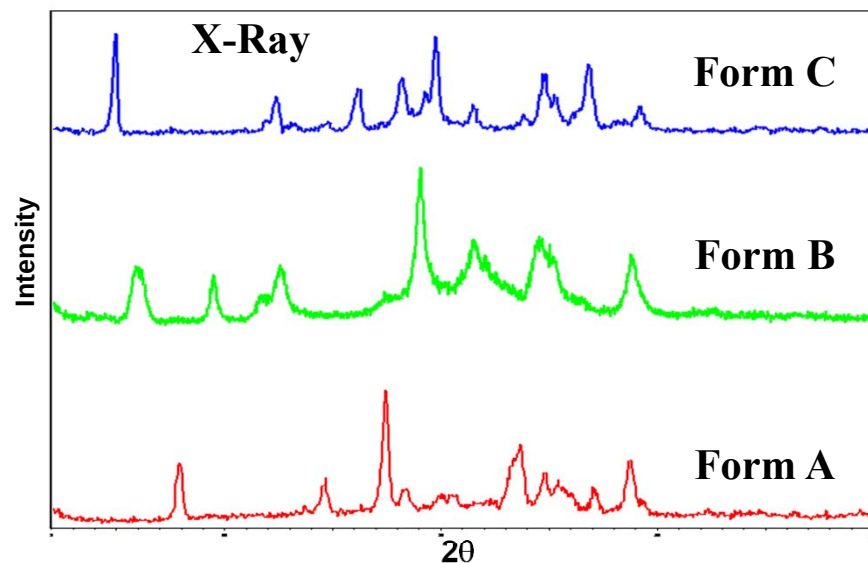
- Broad-spectrum anthelmintic against worms
- Three polymorphs (A, B, C): solubility **B > C > A**
- Therapeutic trials: **A is inactive**
Publications: **B is toxic**
- **polymorph C is pharmaceutically preferred**
- **USP test is not able to distinguish between forms A and C.**



WHO estimates that **one quarter of the world's population is infected** with one or more of the parasites.

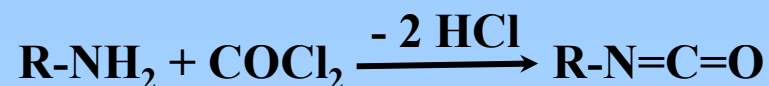
Detection of Polymorphism in Mebendazole:

X-Ray Diffraction, Raman, NIR and MIR Spectroscopy



Analysis of Phosgene in o-Dichlorobenzene Solutions

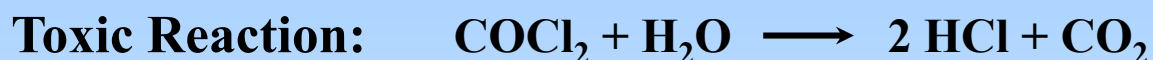
Phosgene (COCl_2) is used extensively in the production of isocyanates:



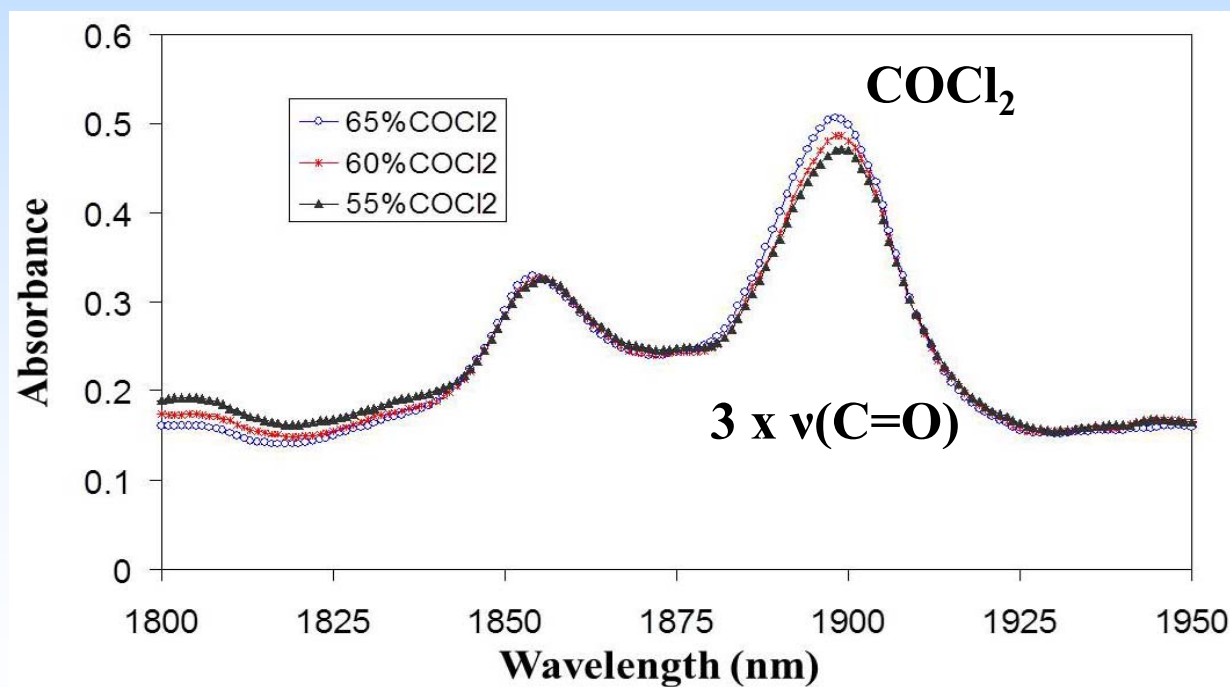
Synthesis:



Toxic Reaction:



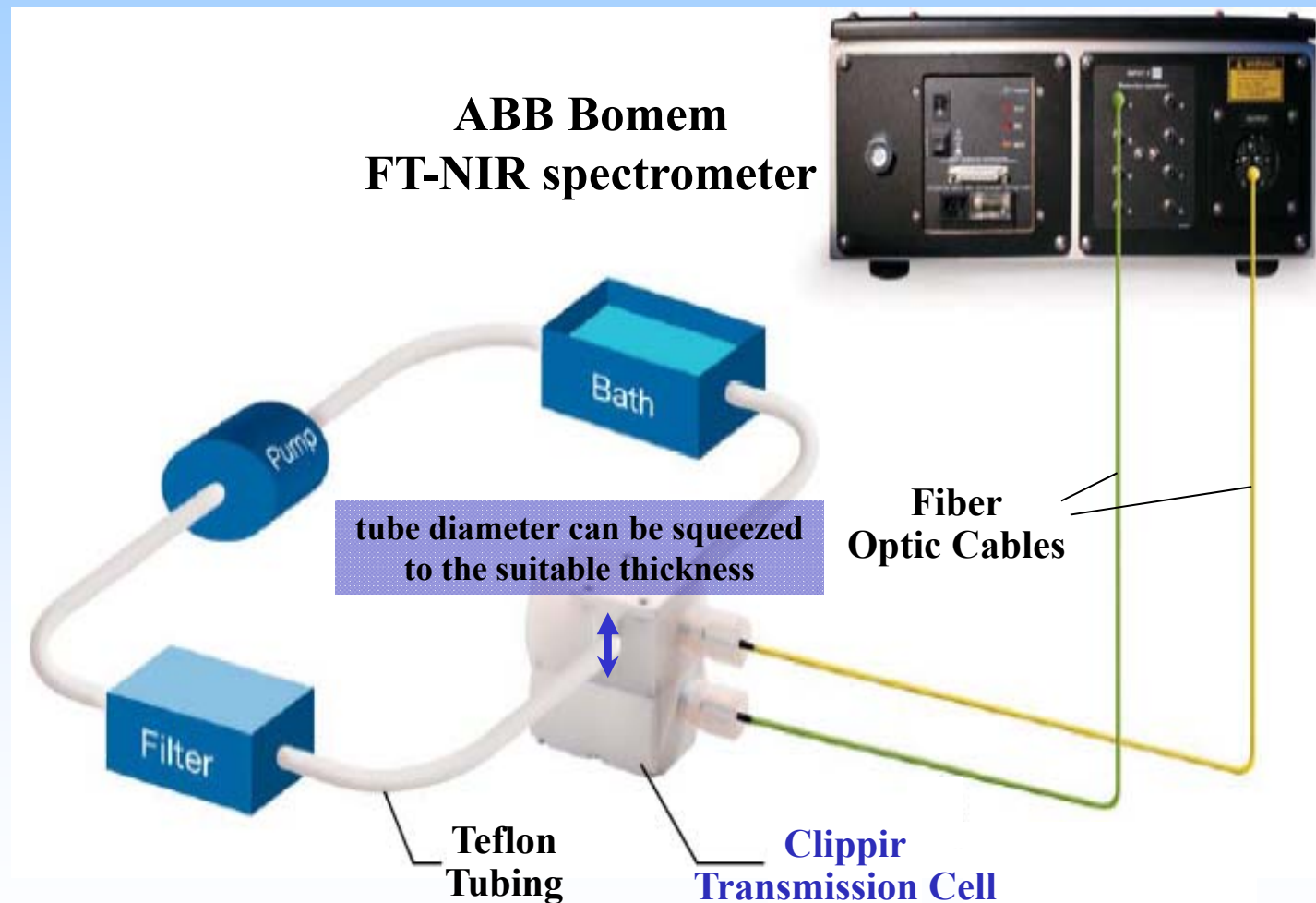
Because it is a highly toxic gas, it had to be analyzed off-line under extreme precaution measures (gas mask etc.)



NIR in-line control has alleviated the situation significantly. 18

NIR-Spectroscopic On/In-Line Determination of **HF and HNO₃** in **Si Wafer Etching Solutions** of the Semiconductor Industry

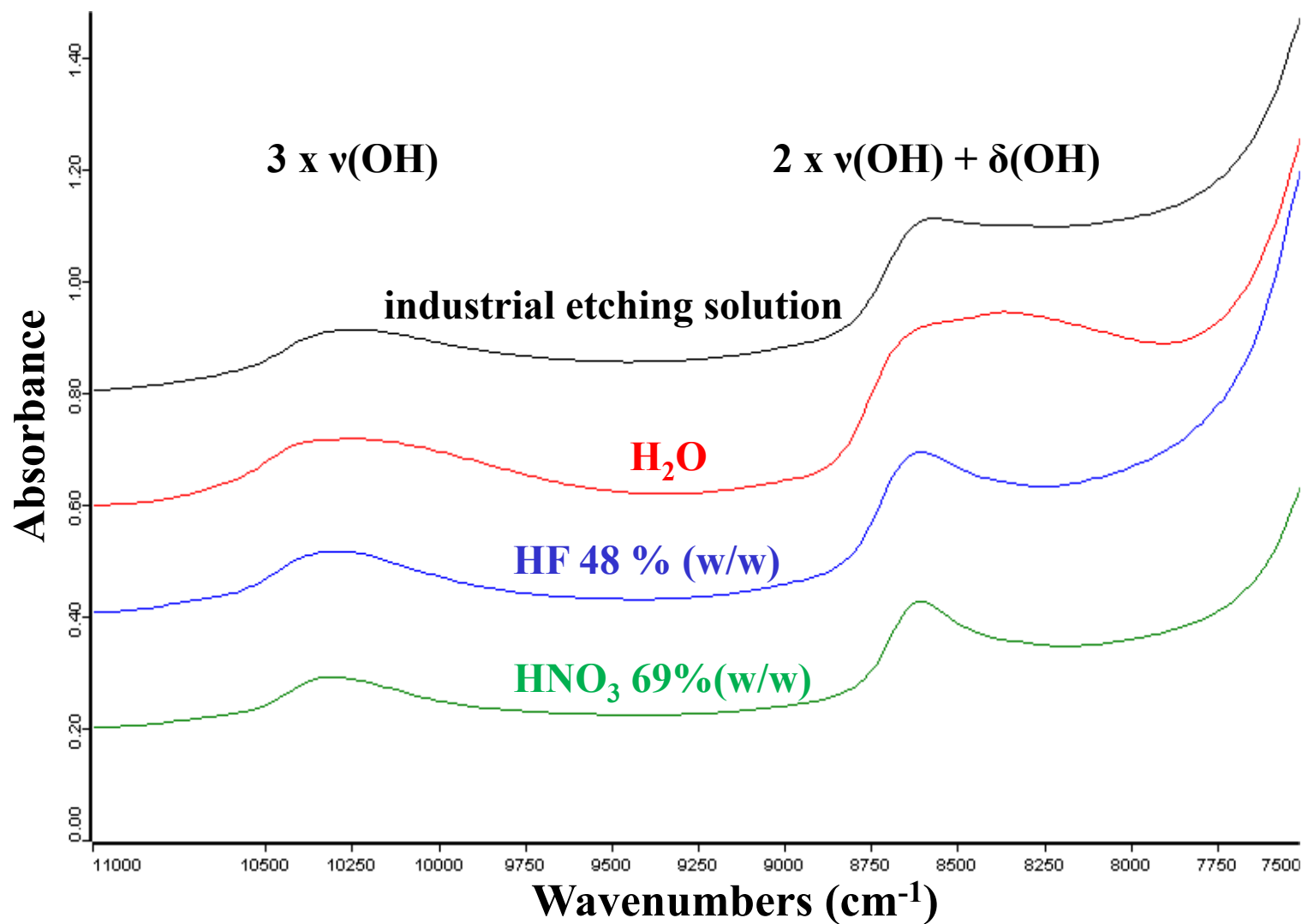
The etching solution is circulated in an all-Teflon™ closed loop.



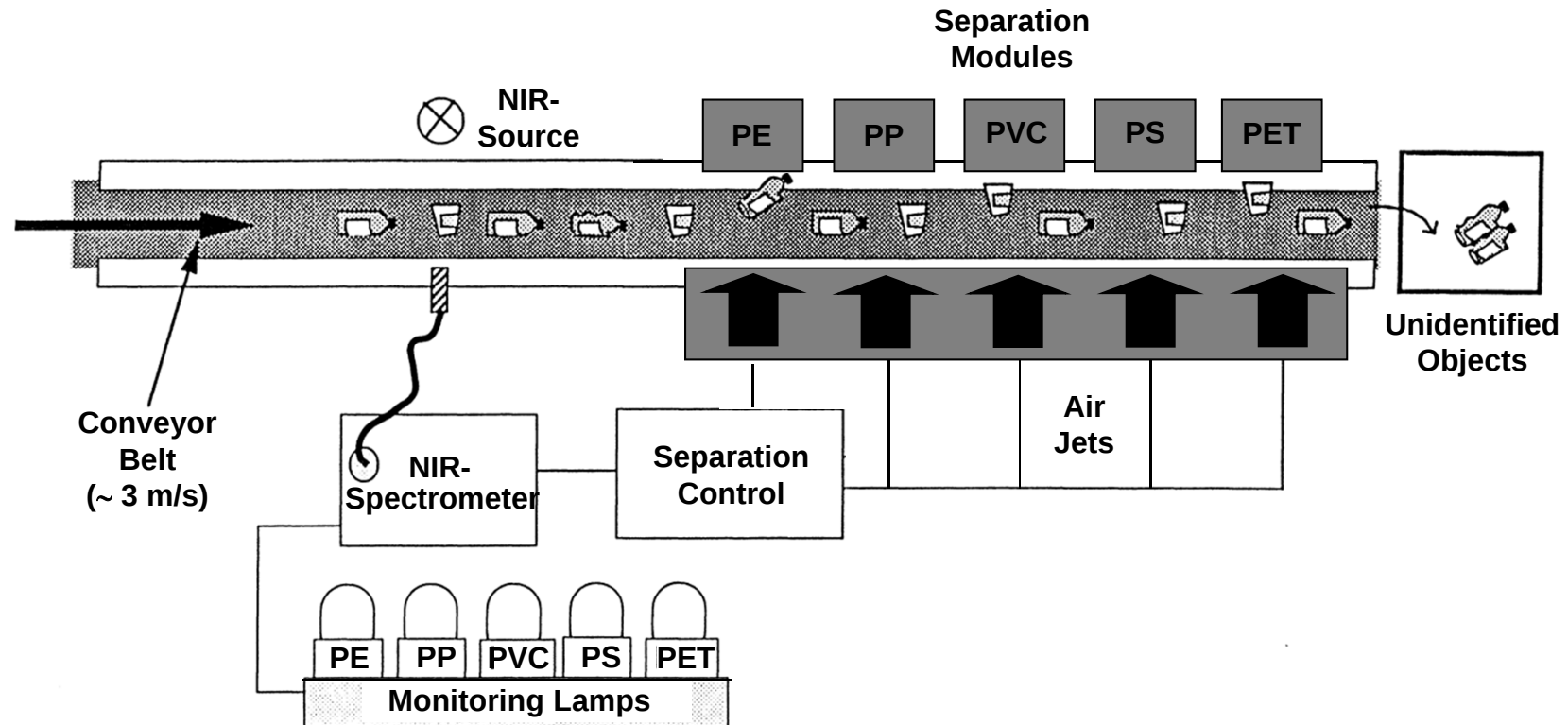
Teflon is **transparent** in the NIR.

The Spectral Calibration Range

Aquaphotomics !!!



Polymer Recycling by NIR Spectroscopy



Approximately 95% of the polymer waste is correctly identified.

No other technique could cope with this task.

On-Line Control of Pharmaceutical Processes by NIR Spectroscopy

- **In a Continuous Mixer (Blend Uniformity)**
- **On the Tablet Press (Content Uniformity)**

- **256 Diode Array**
- **Wavelength Range: 1100 – 2100 nm**
- **Integration time: typical: 3 -10 ms**
- **Background: Spectralon**

VisioNIR **visiote****c**

Technical Information: Continuous Mixer

- **Continuous Mixer: KM5**
Lödige GmbH, Paderborn, Germany
- **Flow Rate: 10 - 300 kg/h**
- **Dwell Time: 10-30 s**

Side View



Front View



light fiber optics behind
sapphire window

Technical Information: Tablet Press

- **Tablet Press: Fette 102i**
Fette Compacting, Schwarzenbek, Germany
- **Tableting Velocity: 18.000 – 216.000 Tab/h (-120 Rot./min)**
Standard: 150.000 Tab/h (80 Rot./min)
- **Time between Tablets: app. 18 - 50 ms (20 - 55 Hz)**

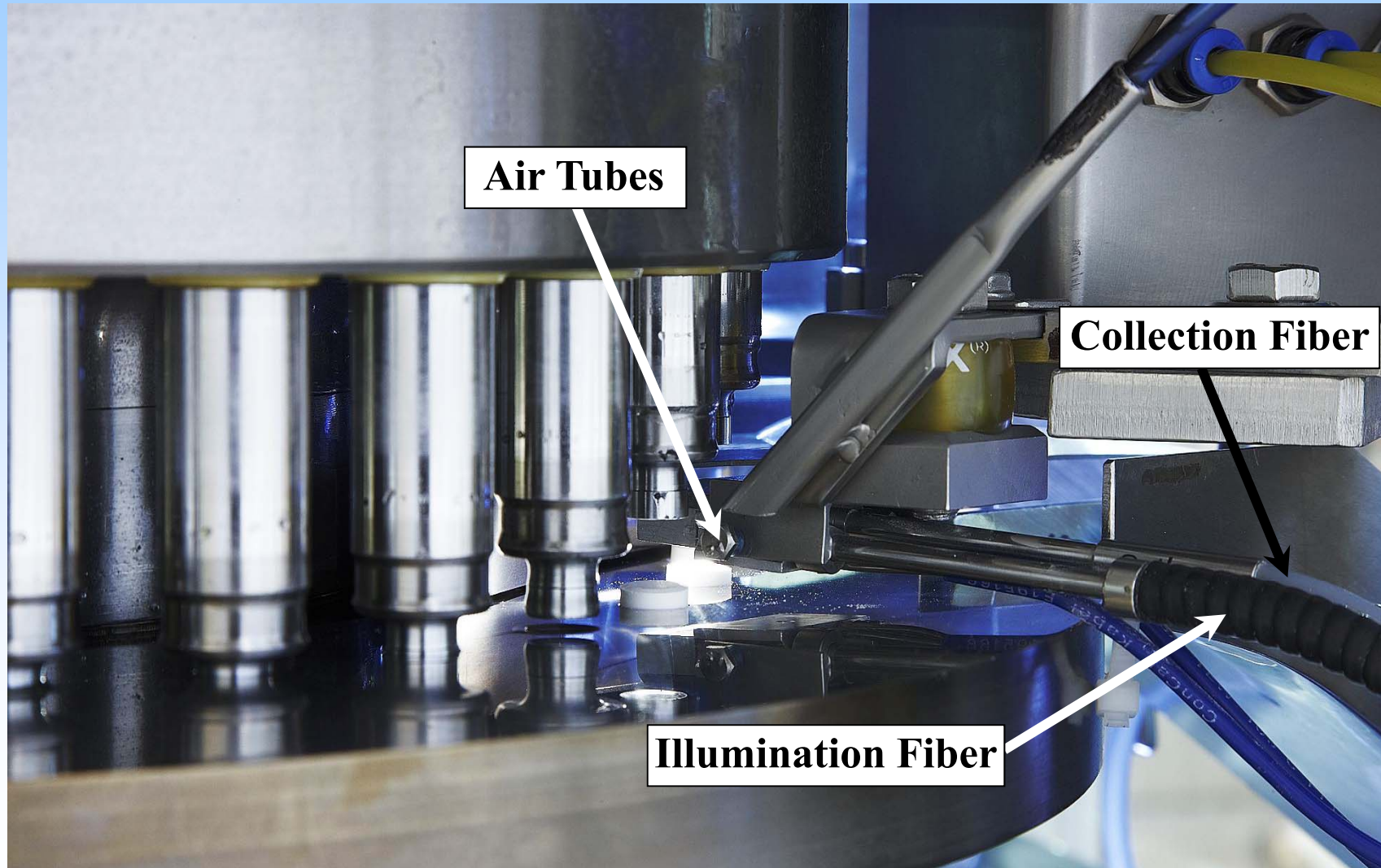
Total View



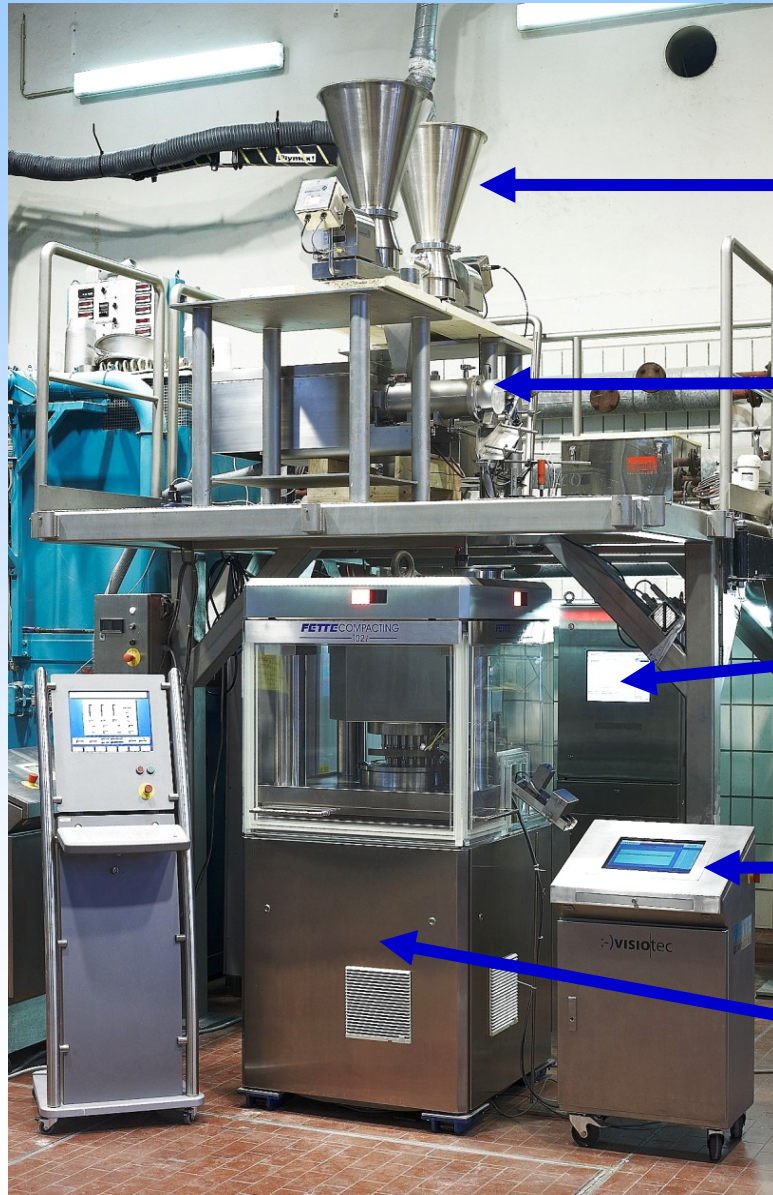
The VisioNIR Fiber Probe for the Tablet Press



Implementation of the VisionNIR Probe into the Tablet Press



The Overall Test Set-Up



Dosing Head (Schenk)

Continuous Mixer (Lödige)

VisioNIR for Mixer (VisioTec)

VisioNIR for Tablet Press (VisioTec)

Tablet Press (Fette)

Method Development for the Mixer

Investigated Formulation

25%
Paracetamol

74%
Lactose

1%
MgSt

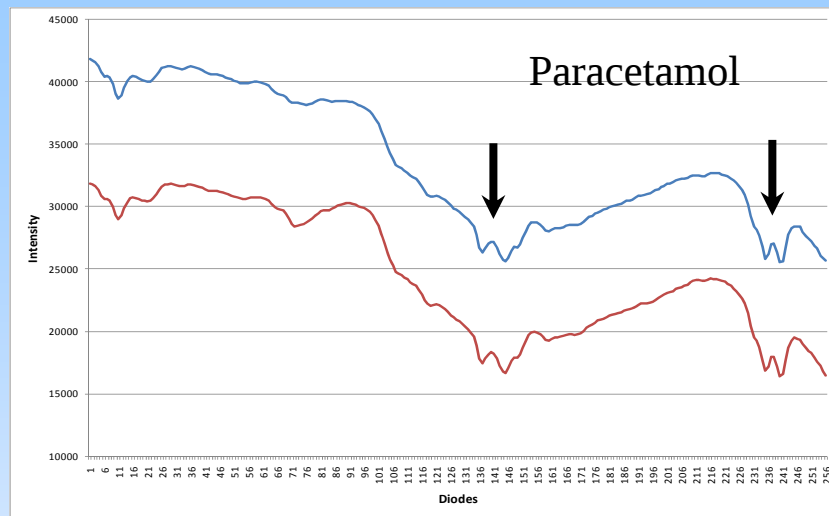
On-line monitoring of the mixed powders with the typical process variations

API content in the specified range (e.g. 20 - 30%, target content was 25%)

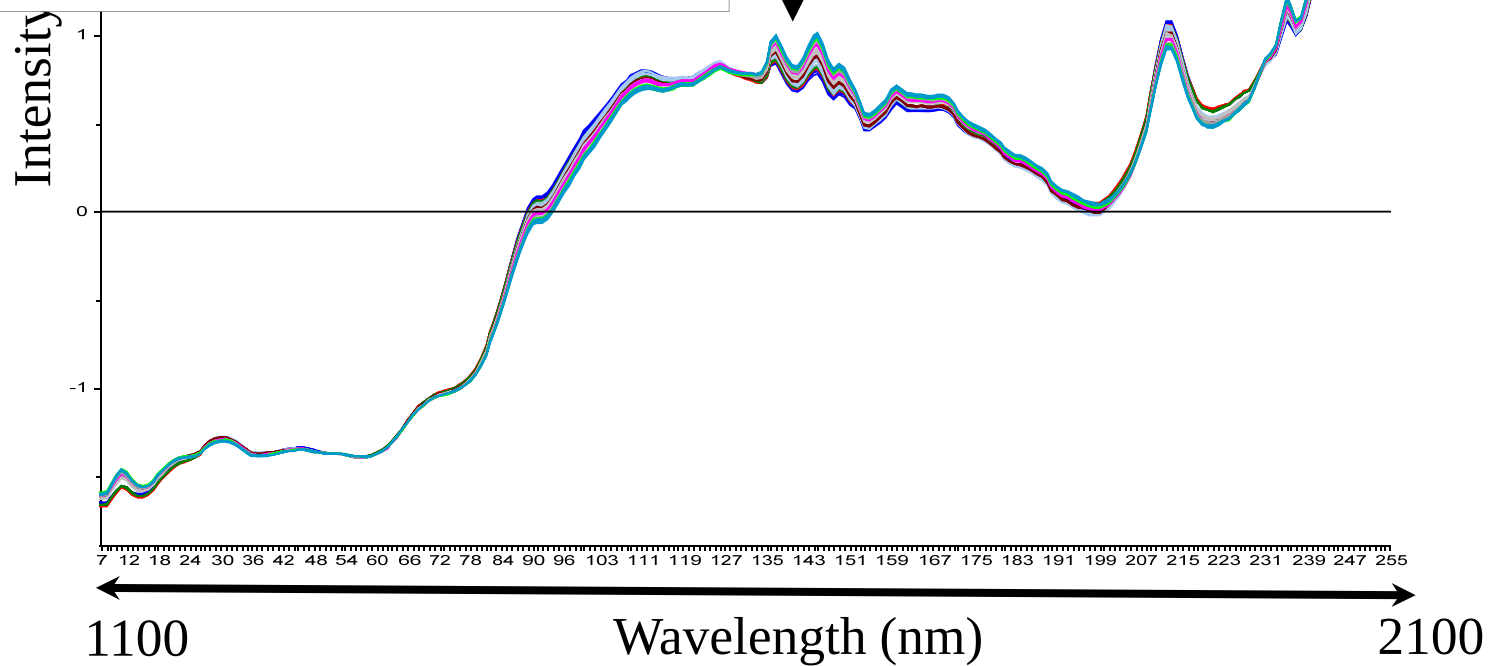
NIR spectra acquisition of the mixed product in 1% intervals (20 - 30%)

Sampling for Reference Analysis (UV)

NIR Spectra of the Powder from Mixer

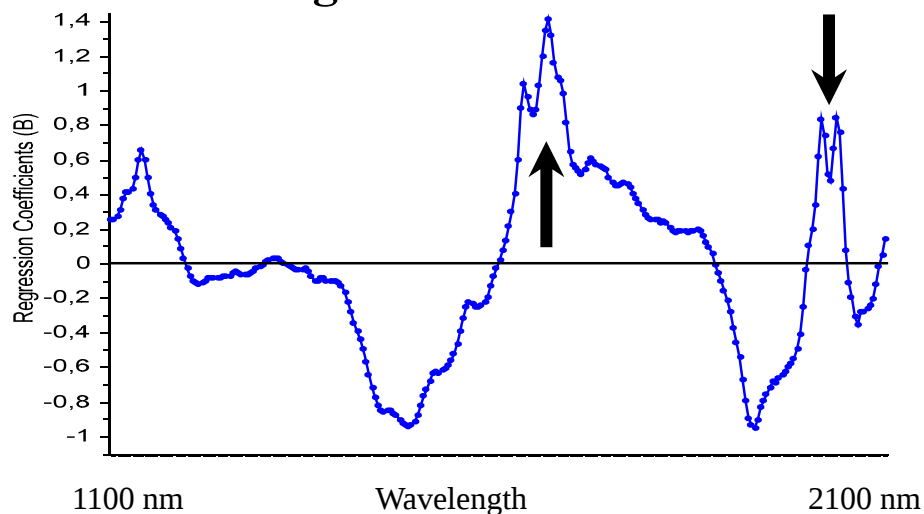


treatment: SNV

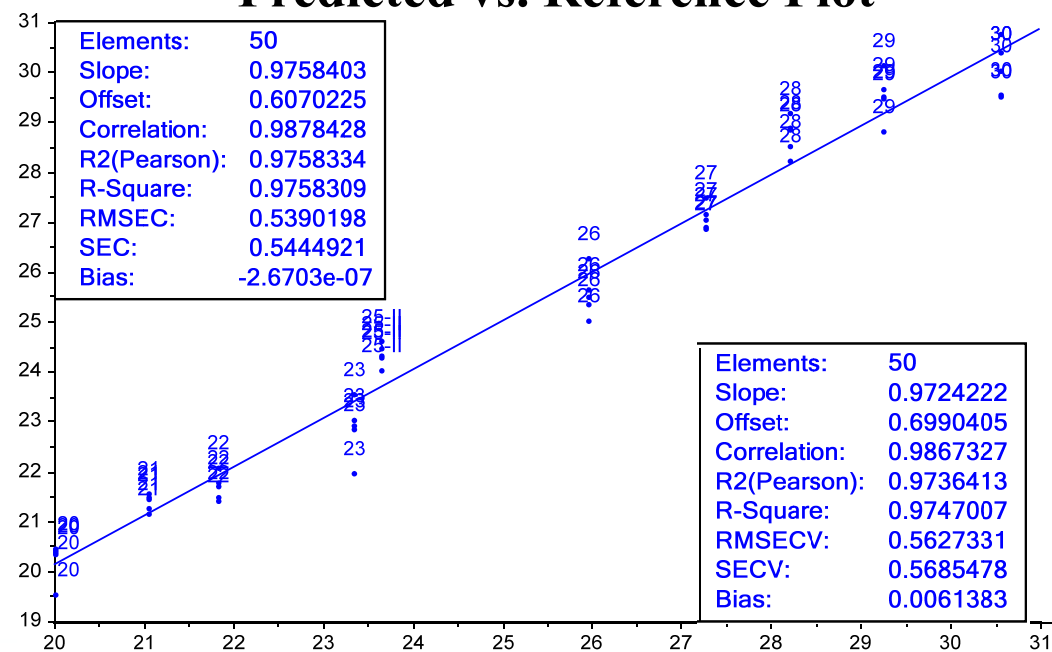


PLS Model for Active Ingredient (Mixer)

Regression Coefficient



Predicted vs. Reference Plot



Method Development for the Tablet Press

Investigated Formulation

25%
Paracetamol

74%
Lactose

1%
MgSt

On-line monitoring of the compressed tablets with the typical process variations and variation of the compression force and the tableting speed

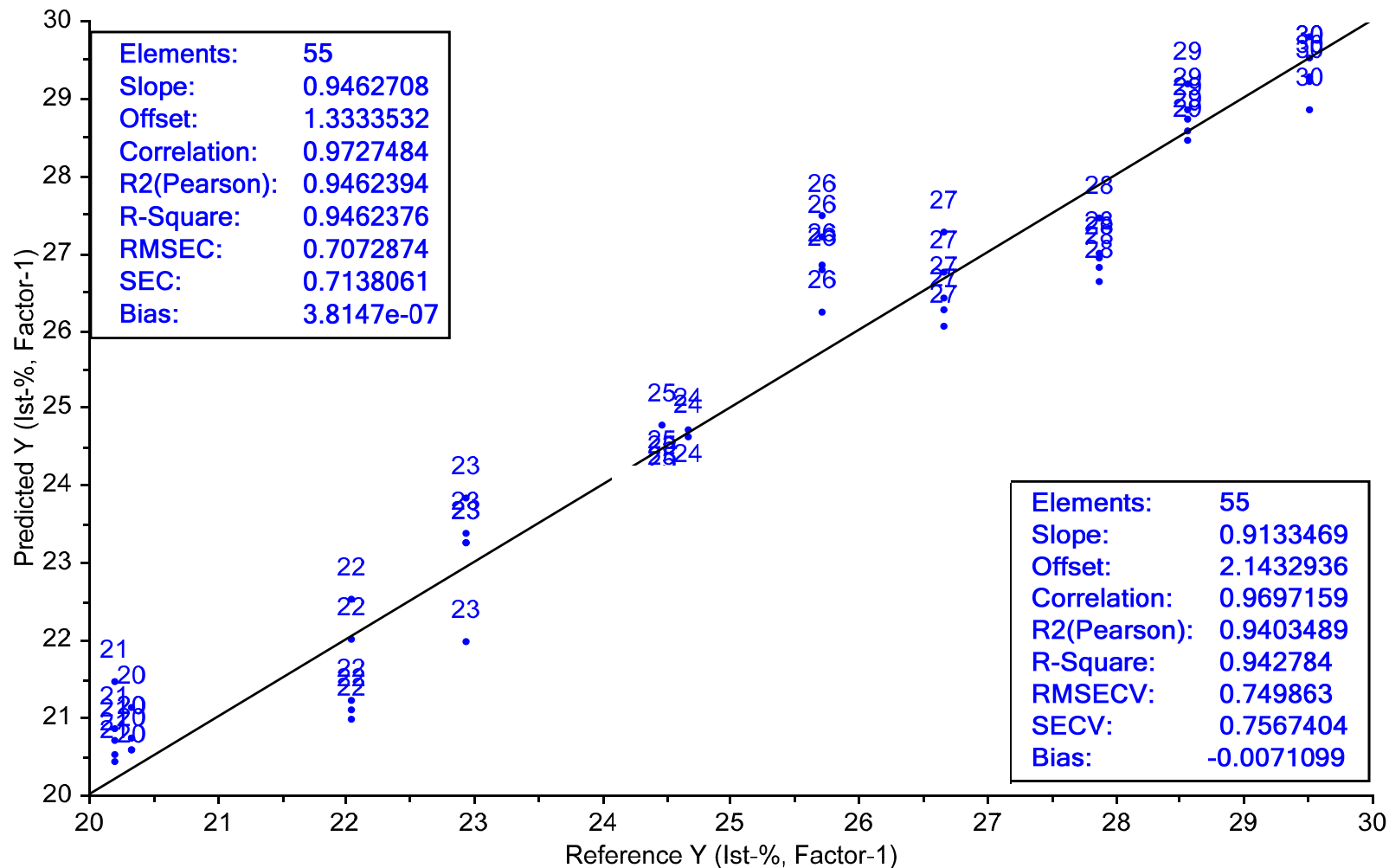
API content in the specified range between 20 - 30% (target content 25%)

NIR spectra acquisition of tablets with API contents 20 - 30% (1% intervals)

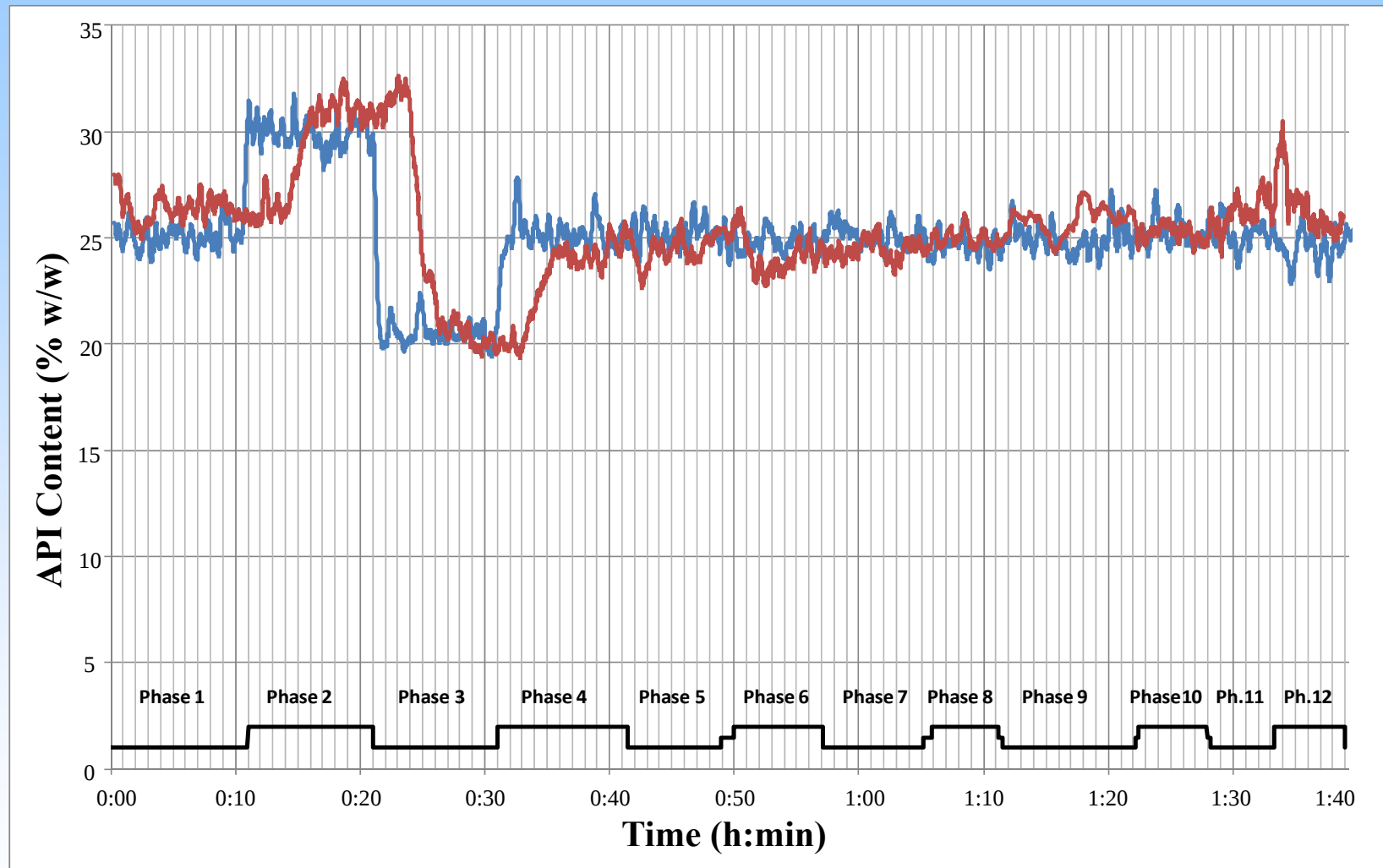
Sampling for Reference Analysis (UV)

PLS Model for Active Ingredient (Tablet Press)

Predicted vs. Reference Plot



Prediction of the API During the Test Run



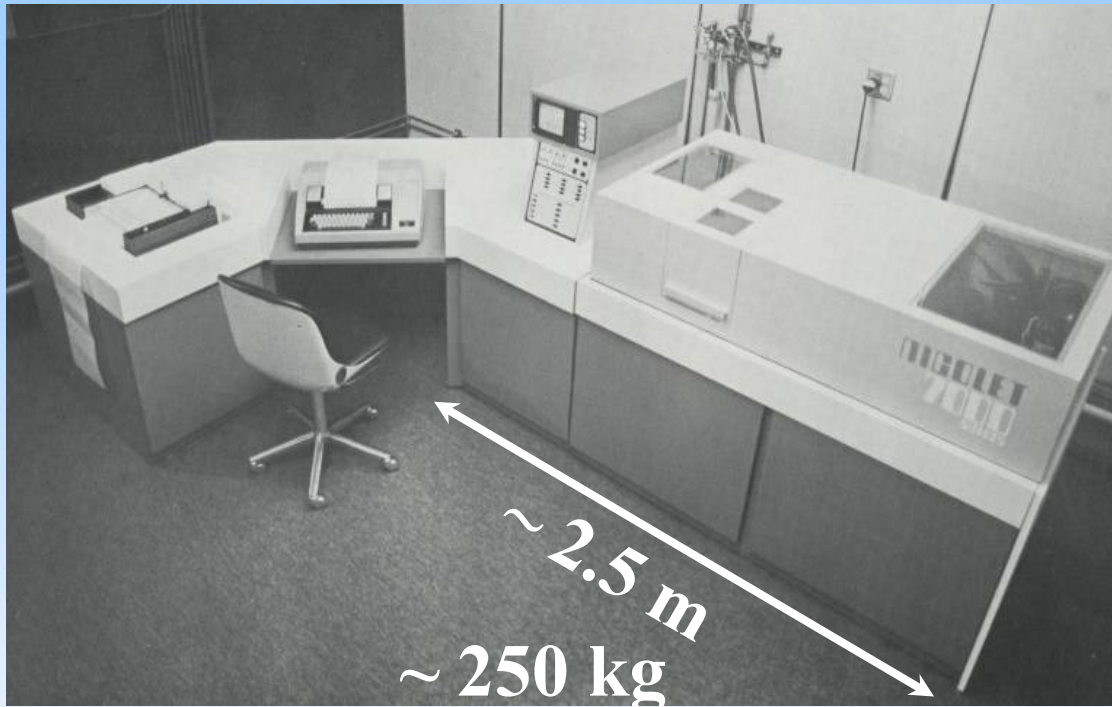
Continuous Mixer / Tablet Press

RMSEP > 1%

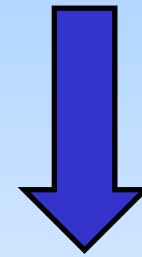
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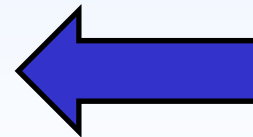
Miniaturization of IR/NIR-Spectrometers 1975 → 2015



**Nicolet FT-IR
1975**



**VIAVI Solutions
(formerly JDSU)
2015**



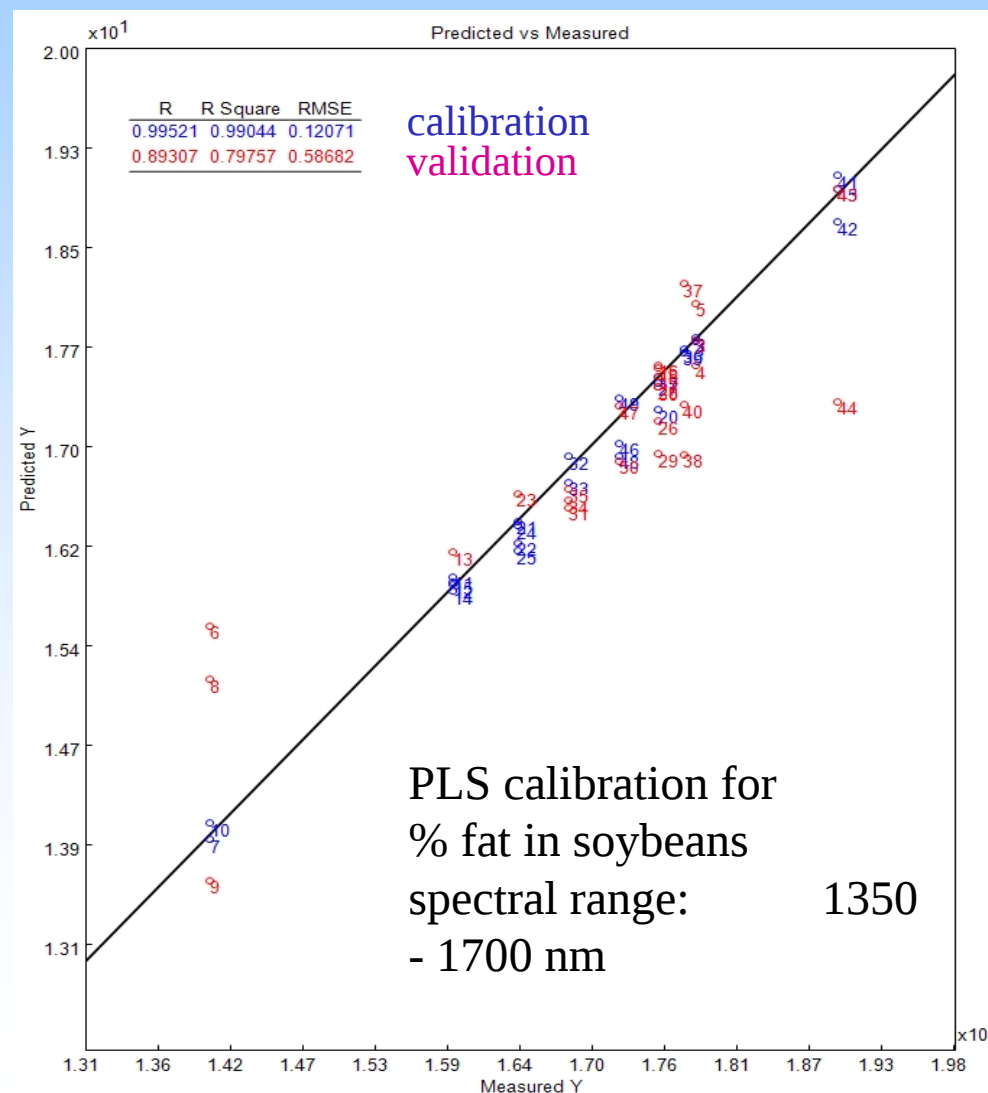
Further New Development



Preliminary Specifications

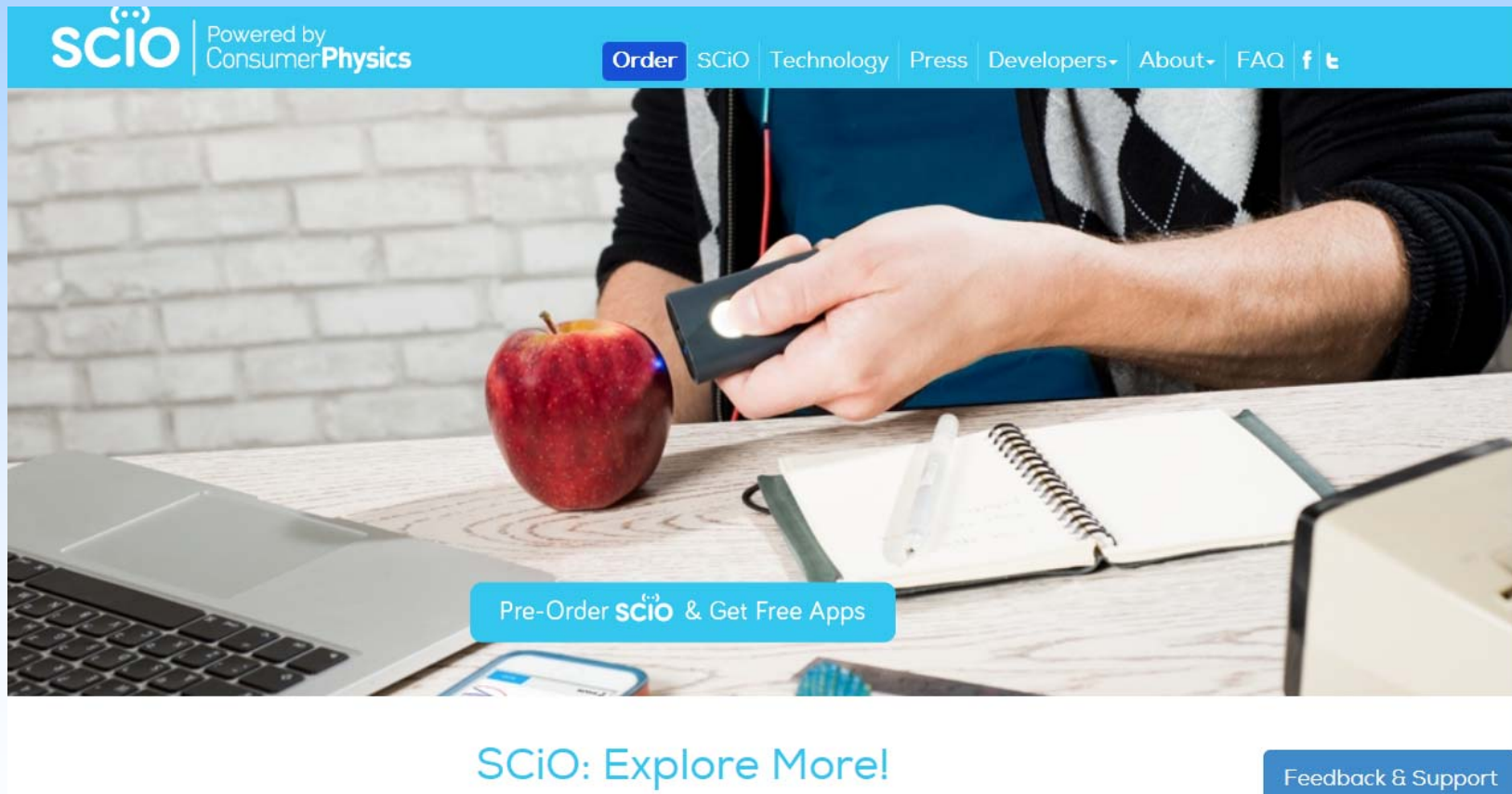
Wavelength Coverage	1.35-1.65 μ m 1.75-2.15 μ m
Noise of Absorption	< 50 μ A
Wavelength Accuracy	$\pm$ 0.2nm
Device-to-Device Repeatability	<0.3nm
Wavelength Repeatability	<0.01nm
Spectral Resolution (FWHM)	~1% of Central Wavelength
Stray Light Level	< 0.05%
Measurement Time	1-30s
Operating Temperature	5-40 $^{\circ}$ C

i-Spec Nano by B&W Tek



A Word of Caution

<https://www.consumerphysics.com/myscio/>



A Word of Caution

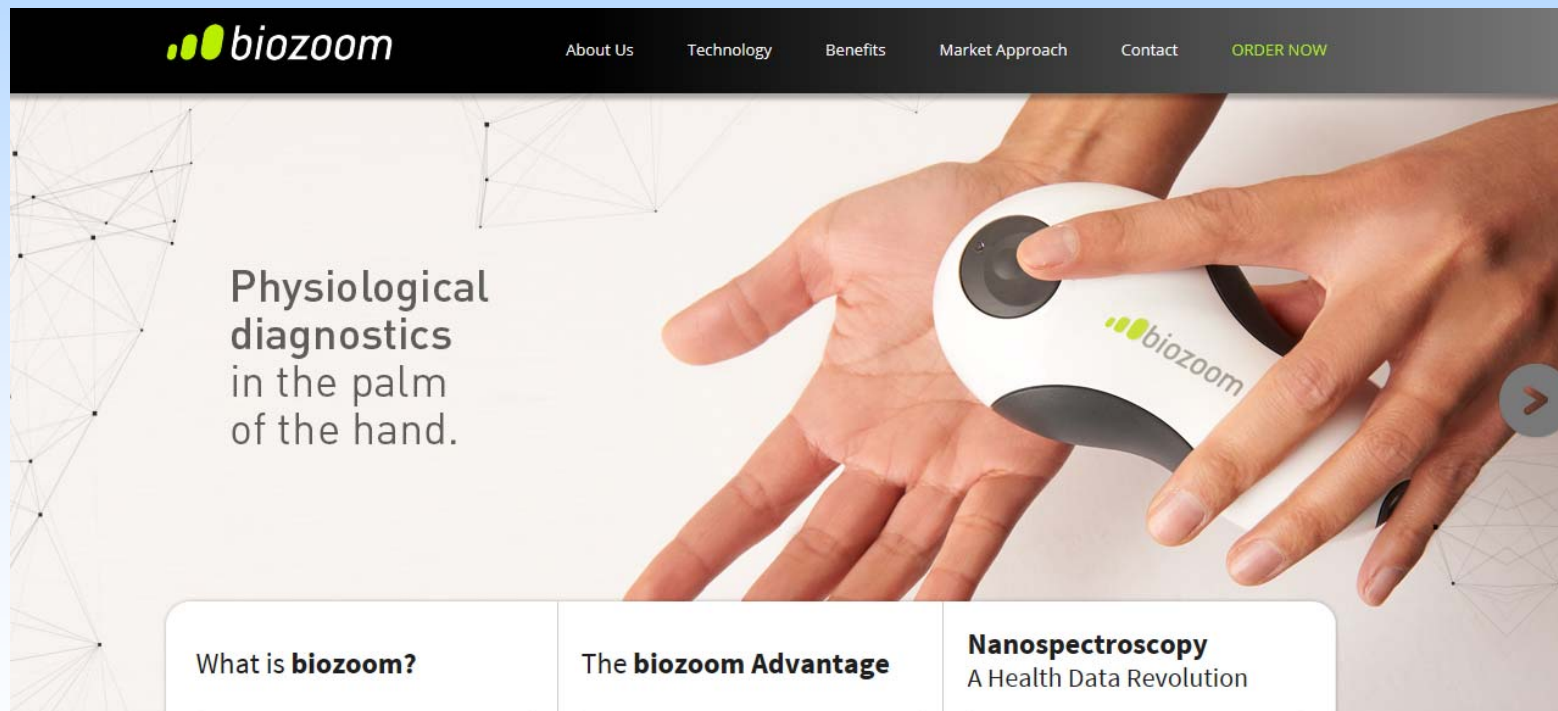
<http://tellspec.com/>



A Word of Caution

<http://biozoom.net/de/>

A Health Data Revolution



Conclusions

NIR spectroscopy has become a mature and extremely versatile technique that can be applied to solve a multiplicity of research and quality/process control problems.

Despite this positive development a further improvement of the acceptance and recognition of this technique can be achieved by:

- **intensified communication between spectroscopists, agro- and food-oriented users and chemometricians**
- **better understanding of the basic issues (band assignments, spectra pretreatments, use of alternative techniques, etc.).**

Acknowledgements

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M. Tondar, Glatt GmbH, Binzen, Germany

Fette Compacting, Schwarzenbek, Germany

Gebrueder Loedige Maschinenbau GmbH, Paderborn, Germany

ABB-Bomem, Quebec, Canada

Bruker Optik GmbH, Ettlingen, Germany

Büchi GmbH, Essen, Germany

Uhlmann VisioTec, Laupheim, Germany

VIAVI Solutions (formerly JDSU), Santa Rosa, USA