The invisible world
in my infrared eyes
MVDA aided (N)IR spectroscopy and imaging

Szilveszter GERGELY
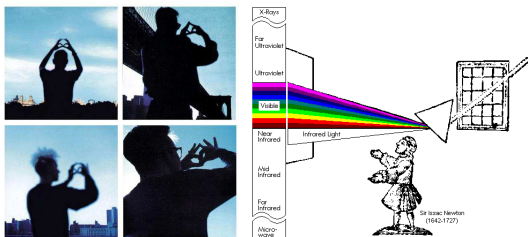
Department of Applied Biotechnology and Food Science

Budapest University of Technology and Economics

M Ú E G Y E T E M   1 7 8 2

Guest lecture at PCCL from BUTE NIR Spectroscopy Group

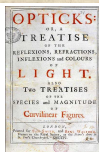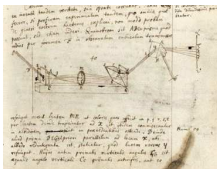**13th of September, 2018 ● Leoben, Austria**

The main topic of this lecture:
The invisible world in my infrared eyes

Newton's experiments
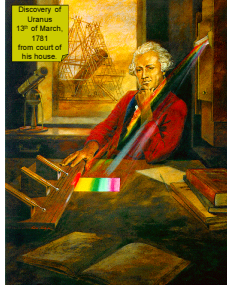## (over the white light)

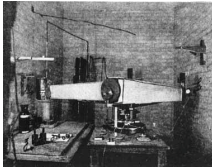It was known earlier, but he wrote it down...

OPTICKS:
OR, A
TREATISE
OF THE
REFLEXIONS, REFRACTIONS,
INFLEXIONS and COLOURS
OF
LIGHT,
ALSO
Two TREATISES
OF THE
SPECIES and MAGNITUDE
OF
Curvilinear Figures.

(1704)

Herschel's experiments
(below the red light)

Discovery of Uranus 13ᵗʰ of March, 1781, from court of his house.
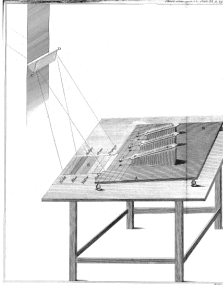
11ᵗʰ of February, 1800

4

Coblentz's experiments
(the IR fingerprint)

Ethanol CH₃–CH₂–OH Dimethyl ether H₃C–O–CH₃ C₂H₆O, but IR sp. ≠

(1905)

5

IR – heat – energy

Using IR against the fire-and-forget missiles

The small „stars" are more warm, than the engines

An AC-130U gunship fires flares to emit masses of infrared and confuse heat seeking missiles.
http://www.wired.com/dangerroom/2012/10/infrared-obscurant/

6

Developing of instruments:
from the military usage...

Aims today: smaller instrument; better resolution

A short movie?

DARPA: „Cheetah"

http://www.wired.com/dangerroom/2013/04/darpa-infrared-cameras/

7

Developing of instruments:
... to civil applications

NIR 2007 Umeå (S): painting „H₂O" on white paper by water

A short movie? (IDRC 2002 Baltimore, hospital ship)

http://www.newsweek.com/2015/01/16/making-blood-draws-easier-friendlier-needle-296317.html

8

Vibrations of molecules

NIR: molecule / vibrational spectro-scopy

That is why we can measure moisture content

Theory of Infrared Spectroscopy

The vibration can be broken up into three simpler motions, called **normal modes**. For water, these are the bend, symmetric stretch, and antisymmetric stretch. Every non-linear molecule has exactly **3N-6** normal modes (where N is the number of atoms in the molecule).

- bending (deformation)
  changes in **angle** of bonds

- symmetric stretching
  changes in **length** of bonds

- asymmetric stretching
  changes in **length** of bonds

PERKIN ELMER
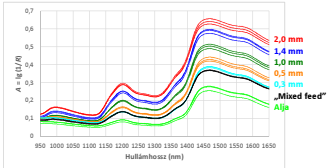IR Tutor Copyright © 1992-5 Charles B. Abrams | Main Menu | Help | Quit | ← →

Paradigm shift with changes of millennium

The spectrum is the sum total of changes of states:
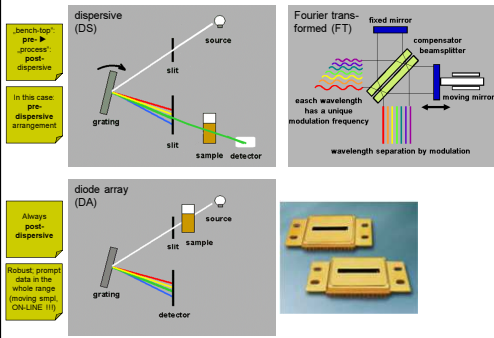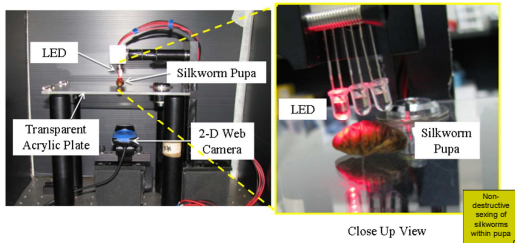**chemical AND physical „fingerprint"**

9

Moisture content below 0.5% vs. NIR (artificial fertilizer, 1st test)

Vibrations of molecules

Bonds have a vibrational "answer"

A quick example for NIR spectra

Water (H₂O)
10 mm
4 mm
1 mm

Many variables, small differences ► MVDA

Ethanol (CH₃–CH₂–OH)
10 mm
4 mm
1 mm

Wine
10 mm
4 mm
1 mm

Gergely S., Farkas K., Forgács A., Salgó A.: Quantitative and qualitative differentiations of alcoholic beverages by near infrared spectroscopy[13]
In *Near Infrared Spectroscopy: Proceedings of the 11th International Conference,*
Ed by Davies A.M.C., Garrido-Varo A. NIR Publications, Chichester, pp. 569–572 (2004).

»chemical and physical „fingerprint"«

A   B   C

Plate 1. Pulverized green bottle glass. Particle sizes in the respective containers are **A**, less than 0.125 mm; **B**, 0.25–0.50 mm; and **C**, 1.0–2.0 mm.

Dahm D.J, Dahm K.D.: The Physics of Near-Infrared Scattering.
In *Near-Infrared Technology in the Agriculture and Food Industries,*
Ed by Williams P., Norris K., Association of Cereal Chemists Inc., St. Paul, pp. 1–17 (2004).

»chemical and physical „fingerprint"«

A   B   C

This is only glass + air / water / oil. What are inside a grain?

Plate 2. All three containers have pulverized glass with particles less than 0.125 mm. The media surrounding the particles are **A**, air, $n_1 = 1.0$; **B**, water, $n_1 = 1.33$; and **C**, mineral oil, $n_1 = 1.48$.

Dahm D.J, Dahm K.D.: The Physics of Near-Infrared Scattering.
In *Near-Infrared Technology in the Agriculture and Food Industries,*
Ed by Williams P., Norris K., Association of Cereal Chemists Inc., St. Paul, pp. 1–17 (2004).

Particle size vs. NIR

How we can measure? – 3-in-1

How we can measure? – NIR LEDs

How we can measure? – NIR LEDs

Sumriddetchkajorn S., Chakkrit Kamfongdee C.:
Optical penetration-based silkworm pupa gender sensor structure.
Appl. Optics 51(4), 409–412 (2012)

19

How we can measure? – NIR lasers (tunable)

Non-destructive sorting of watermelon

Pál MAÁK / Dept. of Atomic Physics, BME

20

How we can measure? – NIR lasers (tunable)

Pál MAÁK / Dept. of Atomic Physics, BME

21

Step by step – (IQ)Q = IQ^2

- **I**dentification
  - Who are you?
    - searching for sharp spectral differences
    - correlation, Euclidean distances etc.
- **Q**ualification
  - Where do you belong to?
    - define subpopulation based on more fine differences
    - principal component analysis (PCA), Mahalanobis distance etc.
- **Q**uantification
  - How many?
    - calibrations with reference parameters
    - partial least squares (PLS) method etc.

22

Overview of calibration and validation

- Main elements:
  - well-defined sample sets
  - accurate reference methods
  - reliable spectroscopic tools
  - exact mathematics and chemometry

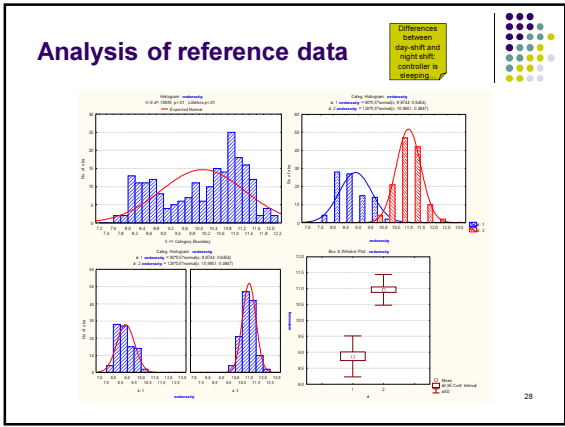The Un...

23

Overview of calibration and validation

- Calibration
  - to find multivariate correlation between spectroscopic and reference data sets

- Validation
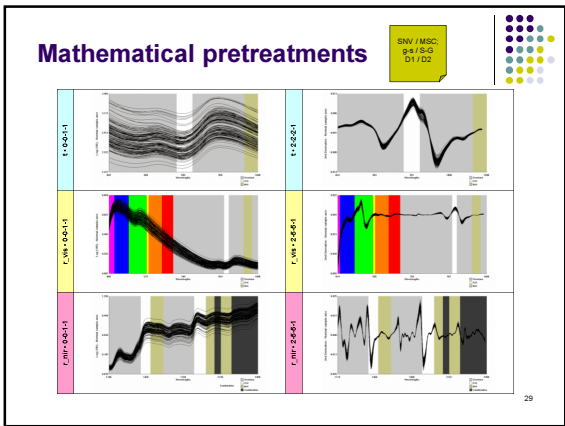 - to estimate the performance of the calibration model using independent sample set or cross-validation

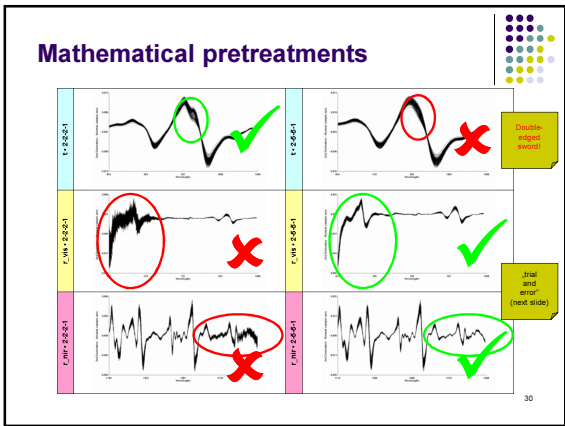24

Analysis of reference data

Differences between day-shift and night shift: controller is sleeping...

28

Mathematical pretreatments

SNV / MSC; g-s / S-G D1 / D2

29

Mathematical pretreatments

Double-edged sword!

„trial and error" (next slide)

30

10

Drugs – building spectrum library

65 products, 390 batches

Drugs – searching for patterns (PCA)

65 products, 390 batches

Alcoholic/hard drinks – searching for patterns (PQS)

From „off-line" to „in-/on-line"

Because NIR is quick and non-destructive

on-line
in-line
at-line
off-line

Guidance for Industry
PAT — A Framework for
Innovative Pharmaceutical
Development, Manufacturing,
and Quality Assurance

„[...] These measurements can be:

at-line:
Measurement where the sample is removed, isolated from,
and analyzed in close proximity to the process stream.

on-line:
Measurement where the sample is diverted from the manufacturing process,
and may be returned to the process stream.

in-line:
Measurement where the sample is not removed from the process stream
and can be invasive or noninvasive [...]"

The Process Analytical Technology (PAT) tools
& within it: research fields of our academic group

In order to implement a successful PAT project, a combination of three main PAT tools is essential

- **Multivariate** data acquisition and **data analysis (MVDA)** tools
  - Usually advanced software packages which 1) aid in **design of experiments (DoE)**, 2) collection of raw data and 3) statistically analyzing this data in order to determine what parameters are Critical Process Parameters (CPP).
- Process analytical chemistry (PAC) tools
  - In-line and on-line analytical instruments used to measure those parameters that have been defined as CPP. These include mainly **near infrared spectroscopy (NIRS)**; but also include biosensors, Raman spectroscopy etc.
- Continuous improvement and/or knowledge management tools
  - Software packages which accumulate Quality Control data acquired over time for specific processes with the aim of defining process weaknesses and implementing and monitoring process improvement initiatives.
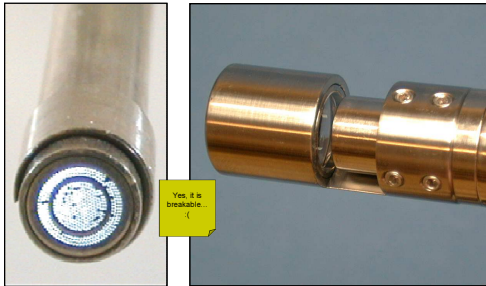

ICH Q10 approach of PAT
& within it: research fields of our academic group
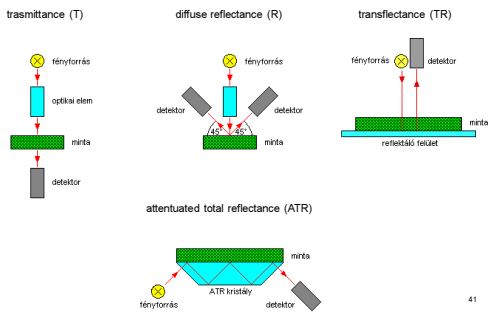

Summary:
time is money,
so we need
PAT.

multivariate
data analysis
(MVDA)
[calculating, solving]

DATA HISTORIAN

The Unscrambler

SIEMENS
Optimal
ABB

is it any faster
than the light?
No. So the NIR
light is good
enough for us.

**near-infrared
spectroscopy
(NIRS)
[off-line testing]**

SiPAT, SynTQ, ABB, Symbion, etc

Spectroscopic
Analysers

Process Inputs
and Outputs

Environmental
Outputs

Process Interface

**design of
experiments
(DoE)
[planning, projecting]**

Raw
Materials

Granulation
and Drying

Blending
and Milling

Compression
and Coating

The tool of in-/on-line – the fiber probe

How we can collect spectra?
The theory ...

trasmittance (T)　diffuse reflectance (R)　transflectance (TR)

attentuated total reflectance (ATR)

How we can collect spectra?
... and the practice (with probes)
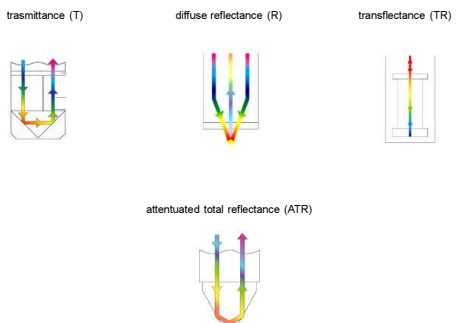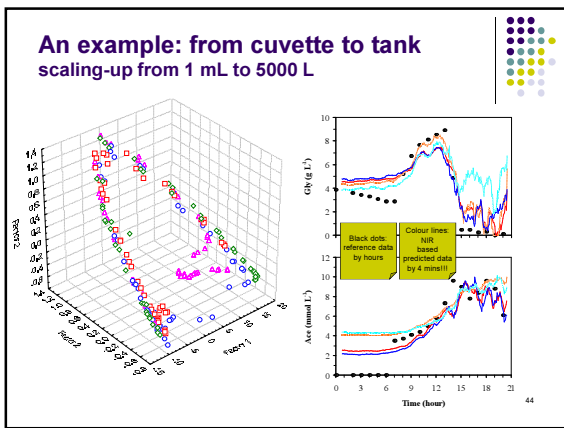
trasmittance (T)　diffuse reflectance (R)　transflectance (TR)

attentuated total reflectance (ATR)

An example: from cuvette to tank
scaling-up from 1 mL to 5000 L

An example: from cuvette to tank
scaling-up from 1 mL to 5000 L

From „off-line" to „in-/on-line"

From „off-line" to „in-/on-line"

Industrie 4.0

1st	2nd	3rd	4th
Mechanikus gépek Víz és gőzgépek	Futószalag, Tömegtermelés, Elektromosság	Számítógépek és automatizáció	Kiber - fizikai rendszerek, Smart eszközök

Industrie 1.0 – Győr / Raab / Arrabona

Industrie 2.0 – Győr / Raab / Arrabona

Textile factory

id. Konok Tamás (1951, képszám: 43348)
http://www.fortepan.hu

49

Industrie 3.0 – Győr / Raab / Arrabona

Vending machine

Bauer Sándor (1975, képszám: 109843)
http://www.fortepan.hu

50

Industrie 4.0 – Győr / Raab / Arrabona
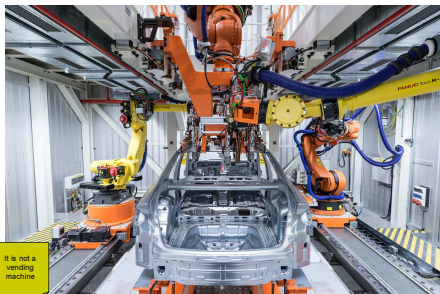
It is not a vending machine

AUDI AG (2015, képazonosító: 146eaa22)
https://images.audi.hu/gallery/fin2/146eaa22.jpg

51

Industrie 4.0 – here we are

52

Industrie 4.0 – resulting...

Macro/micro imaging

54

Tablets – NIR microscopy

- Genuie steroid tablet
- Fake steroid tablet

Abs.

PCA

Package materials – „as is"

Package materials – light microscopy
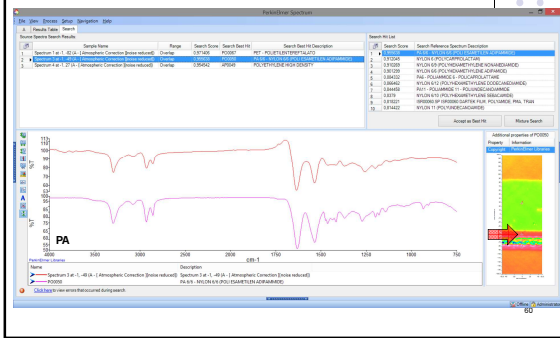
metal layer
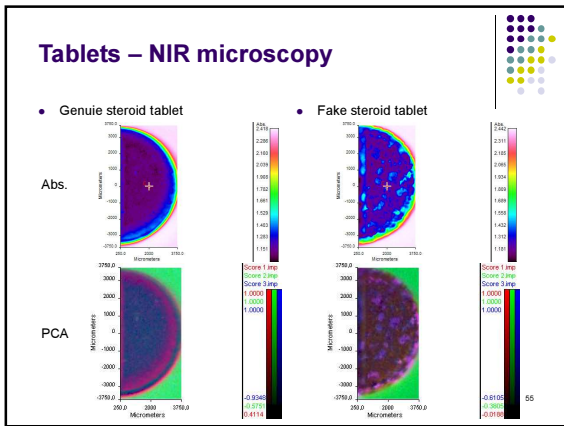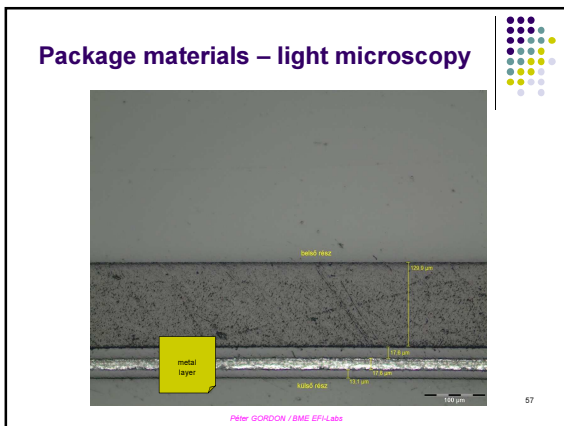
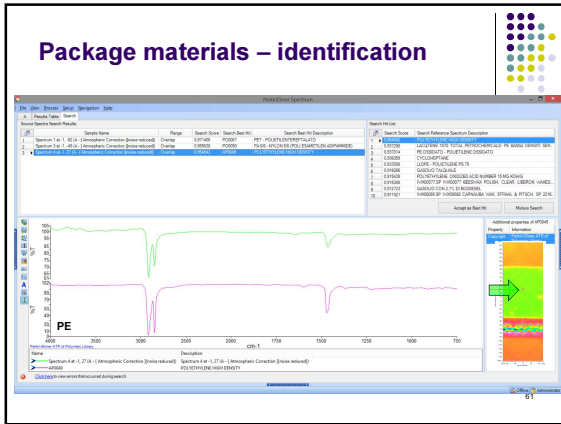**Package materials – IR microscopy**
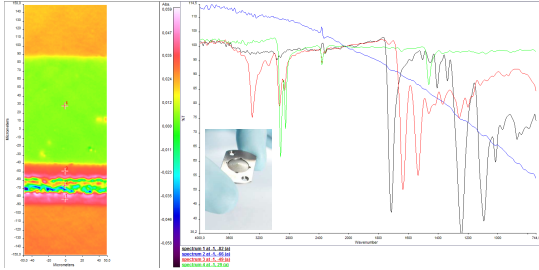
Package materials – identification
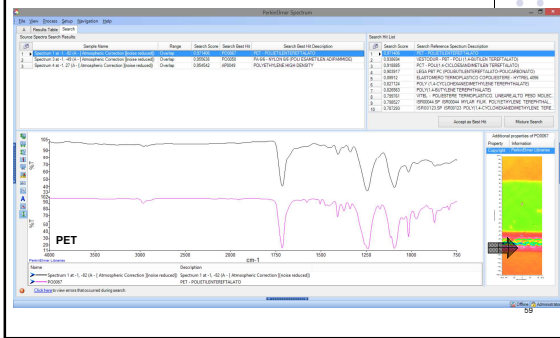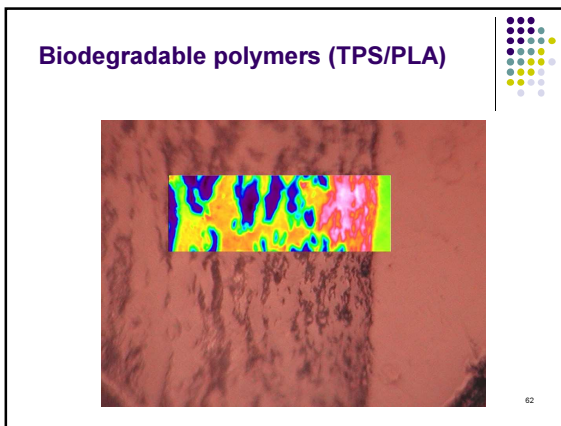
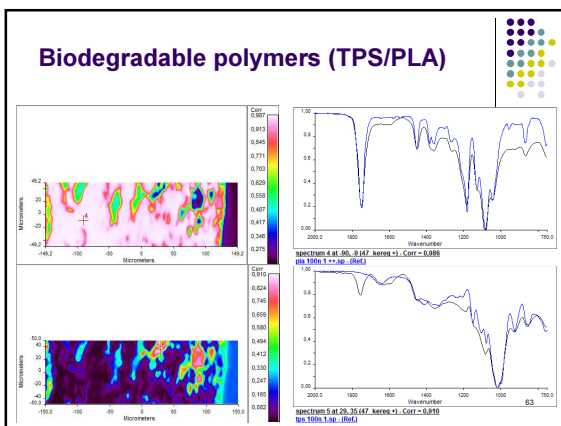

Package materials – identification

Package materials – identification

Biodegradable polymers (TPS/PLA)

Biodegradable polymers (TPS/PLA)

**Thank you
for your kind attention**

Szilveszter GERGELY

Department of Applied Biotechnology and Food Science

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