

Near Infrared Spectroscopy as a Challenging Analytical Tool

O.Ye. Rodionova, A.L. Pomerantsev



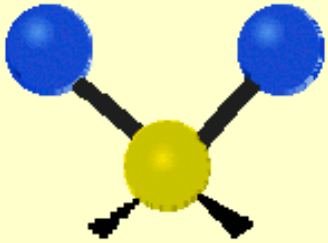
*Semenov
Institute of
Chemical
Physics RAS*



*Russian
Chemometric
Society*

mid-IR spectroscopy

(4000-400 cm^{-1} or 2500-25000 nm)

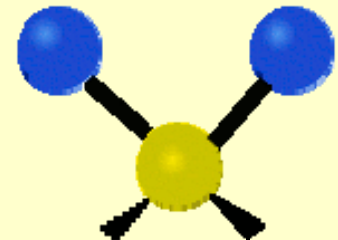


1. Well-known and widely used technique

2. Group frequencies are more or less constant for chemical groups independent on molecules containing these groups

3. Fingerprint frequencies are used for identification of unknown substances

Demand special sample preparation

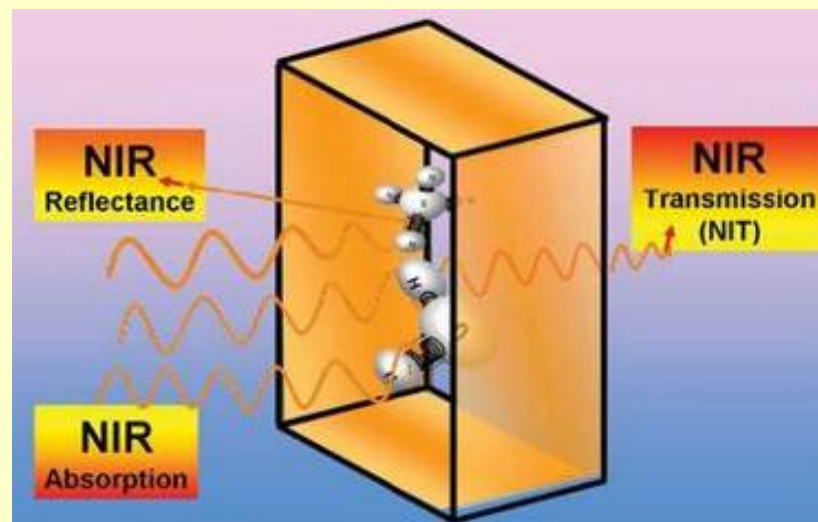


NIR spectroscopy (12500-4000 cm^{-1} or 800-2500 nm)

1. Based on overtone and combination vibrations of the investigated molecule

NIR spectra are much more complex than relatively easier for interpretation mid-IR spectra.

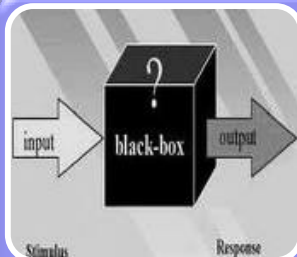
2. Minimal or no sample preparation



Delusions Regarding NIR-based approach



NIR is a magic box that can measure any component in any sample.

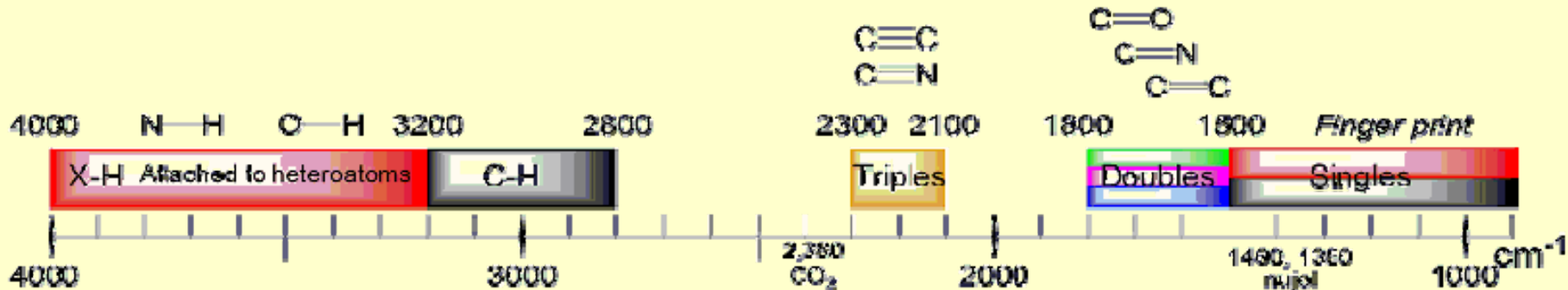


It is little to be gained by studying NIR spectroscopy due to complexity of NIR absorption

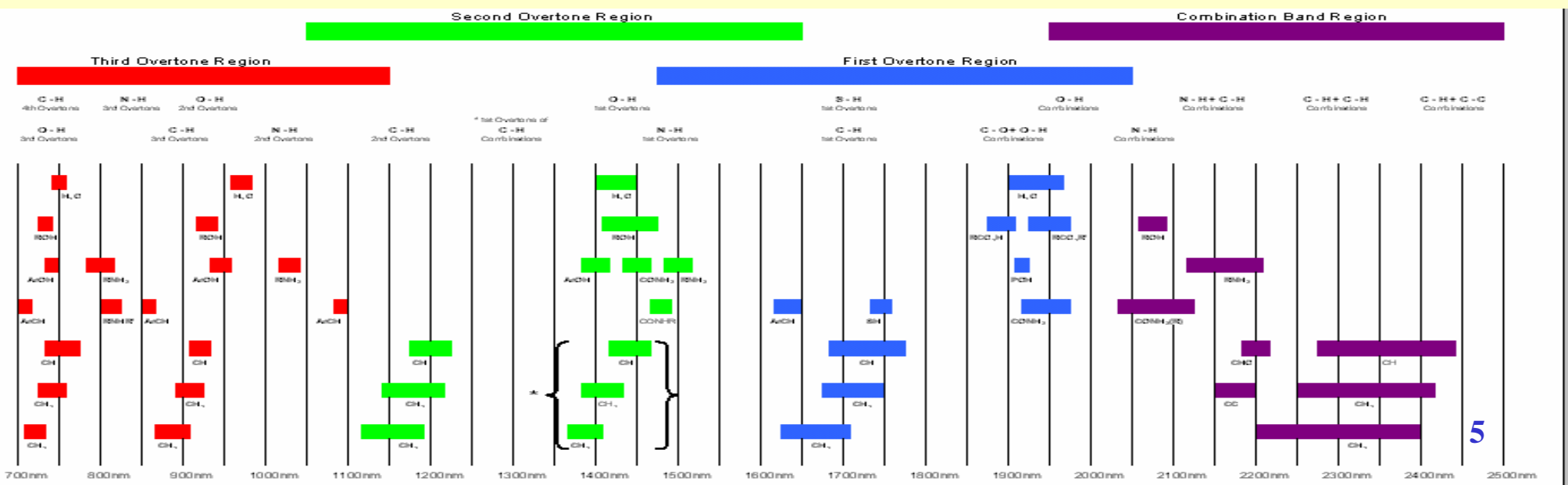
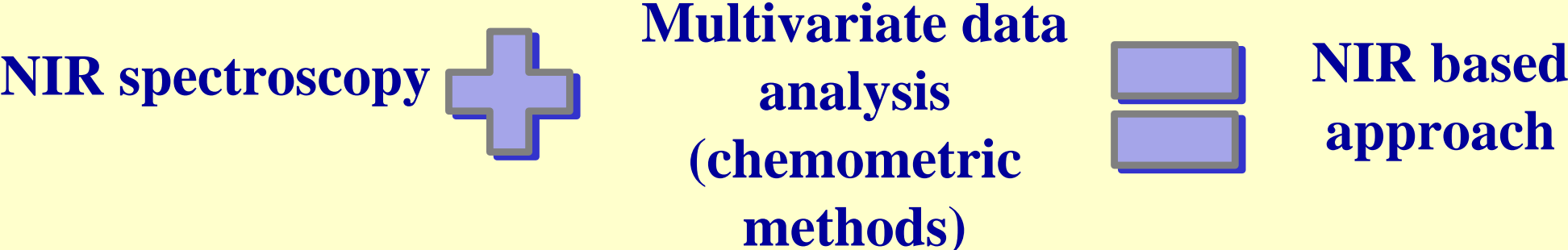


Overall, the method (PCR) seems to have few applications in the physical, engineering and biological sciences. It can sometimes be useful in the social sciences as a way of finding effective combination variables

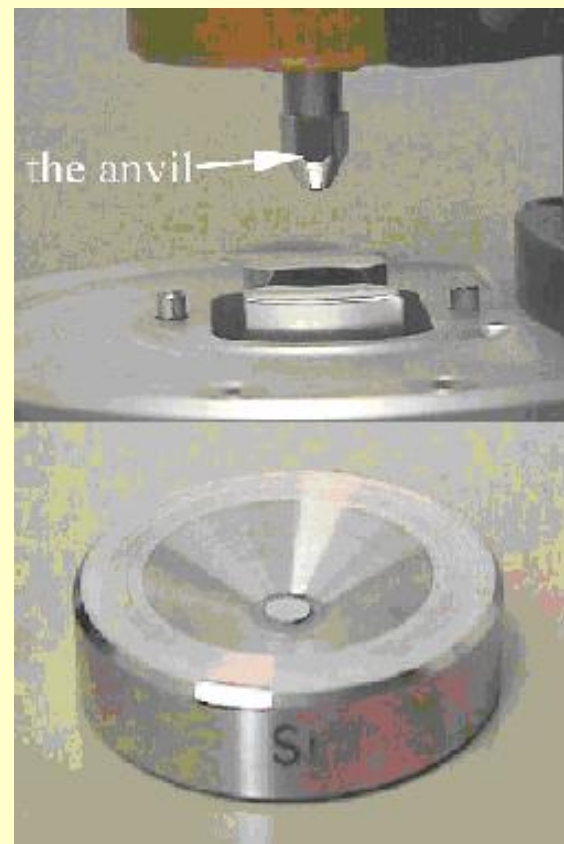
N.R. Draper, H. Smith, Applied regression analysis, 2-nd Edition, Wiley, N.Y,



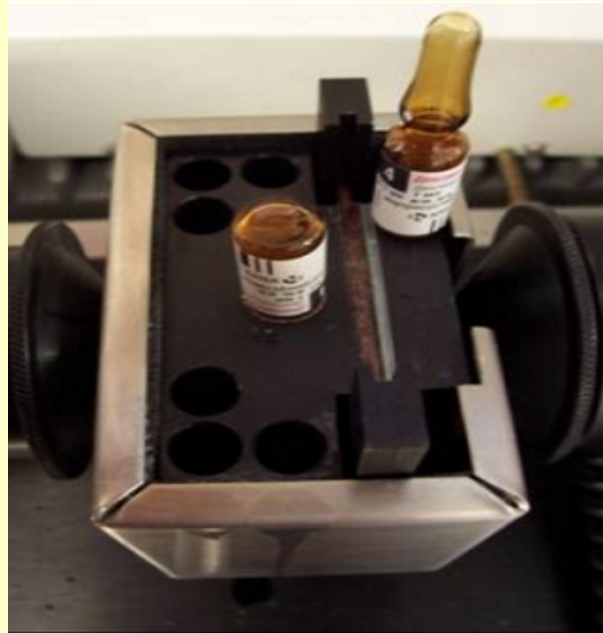
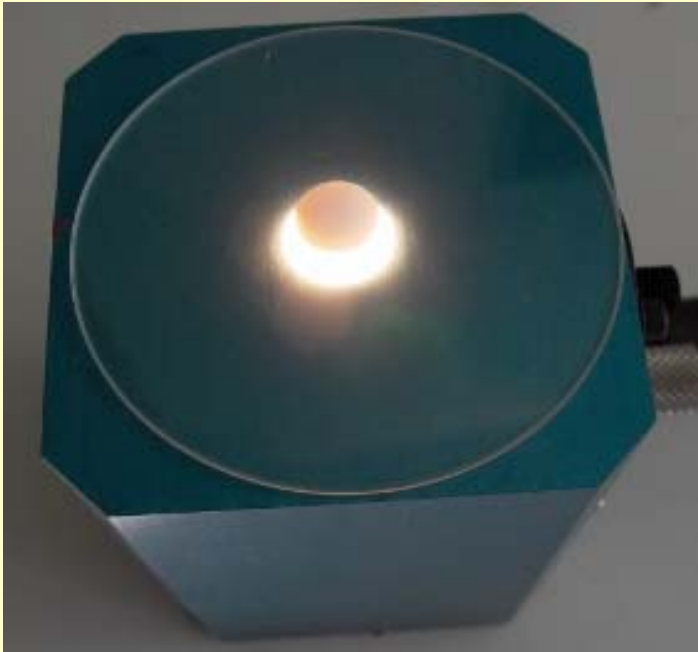
NIR spectra complexity ≠ Low-informative



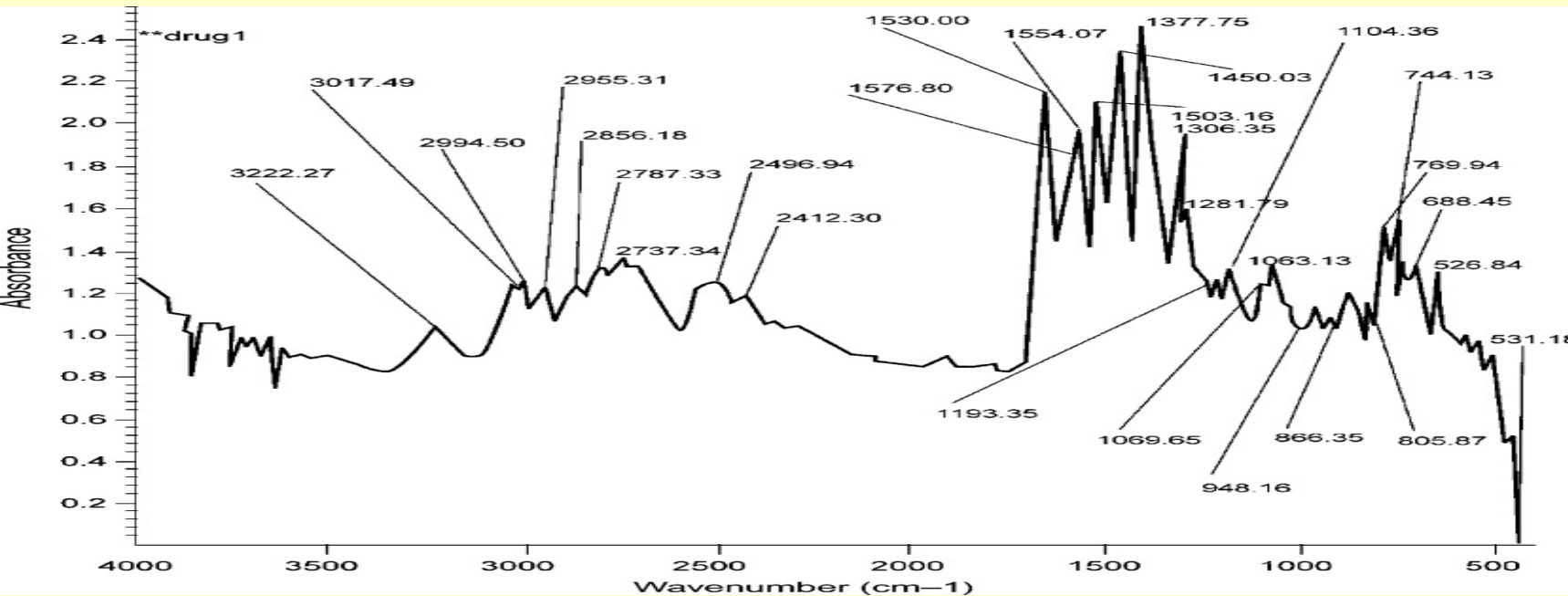
mid-IR: sample preparation



NIR: sample preparation

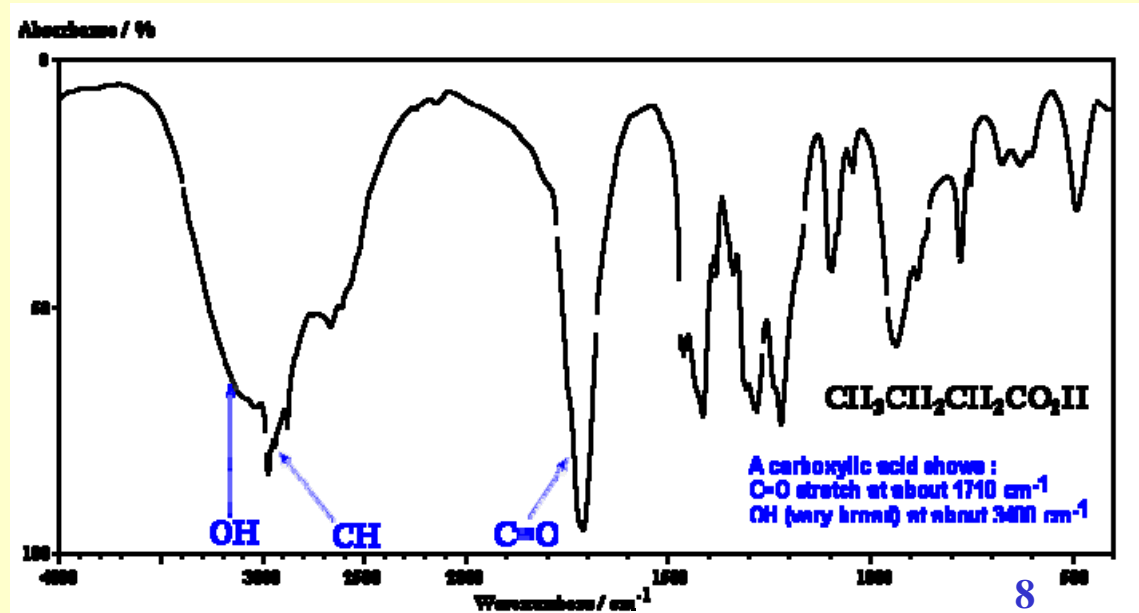


mid-IR: explorative analysis

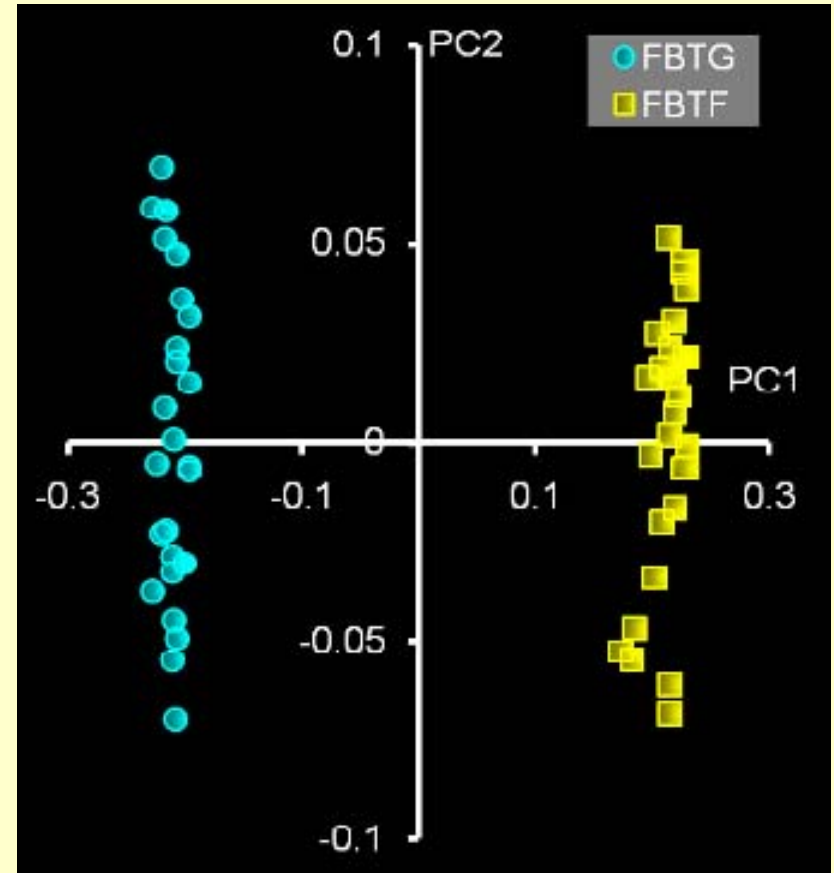
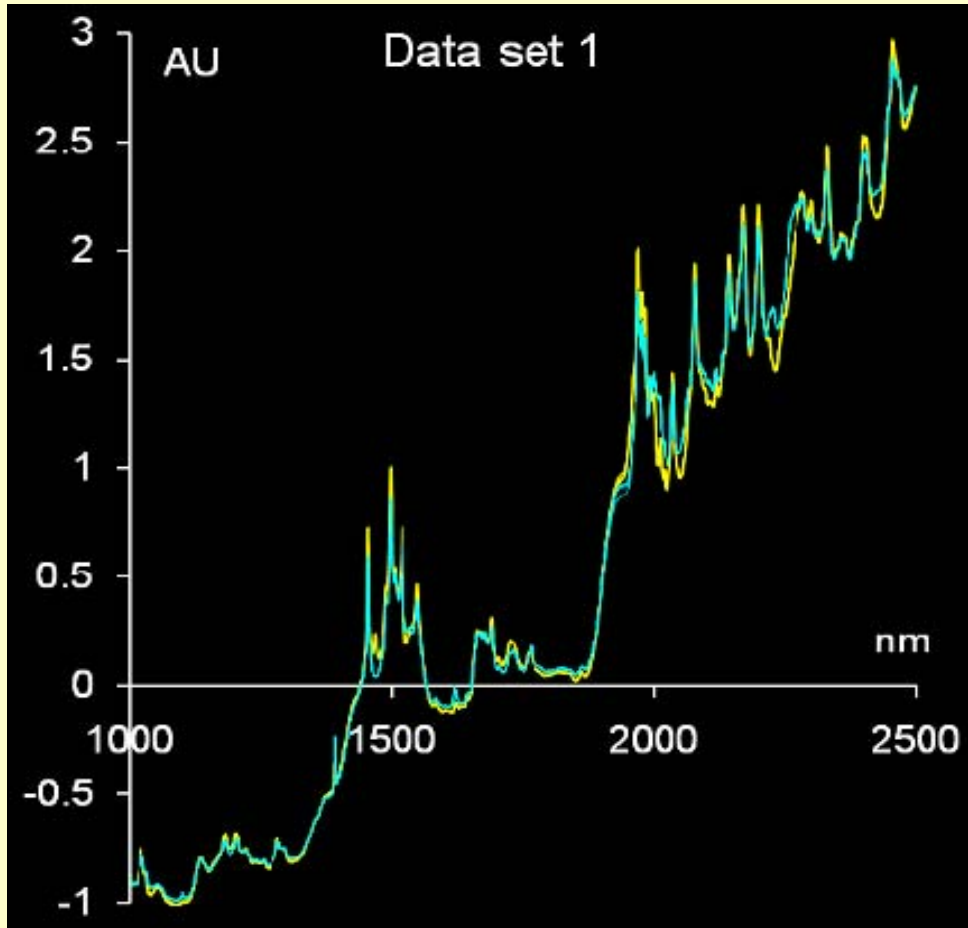


Diclofenac (API)

n-butyric acid



NIR: explorative analysis



Complex antibacterial drug
(2 APIs)

25 original tablets from 5 batches
25 counterfeit tablets from 5 batches

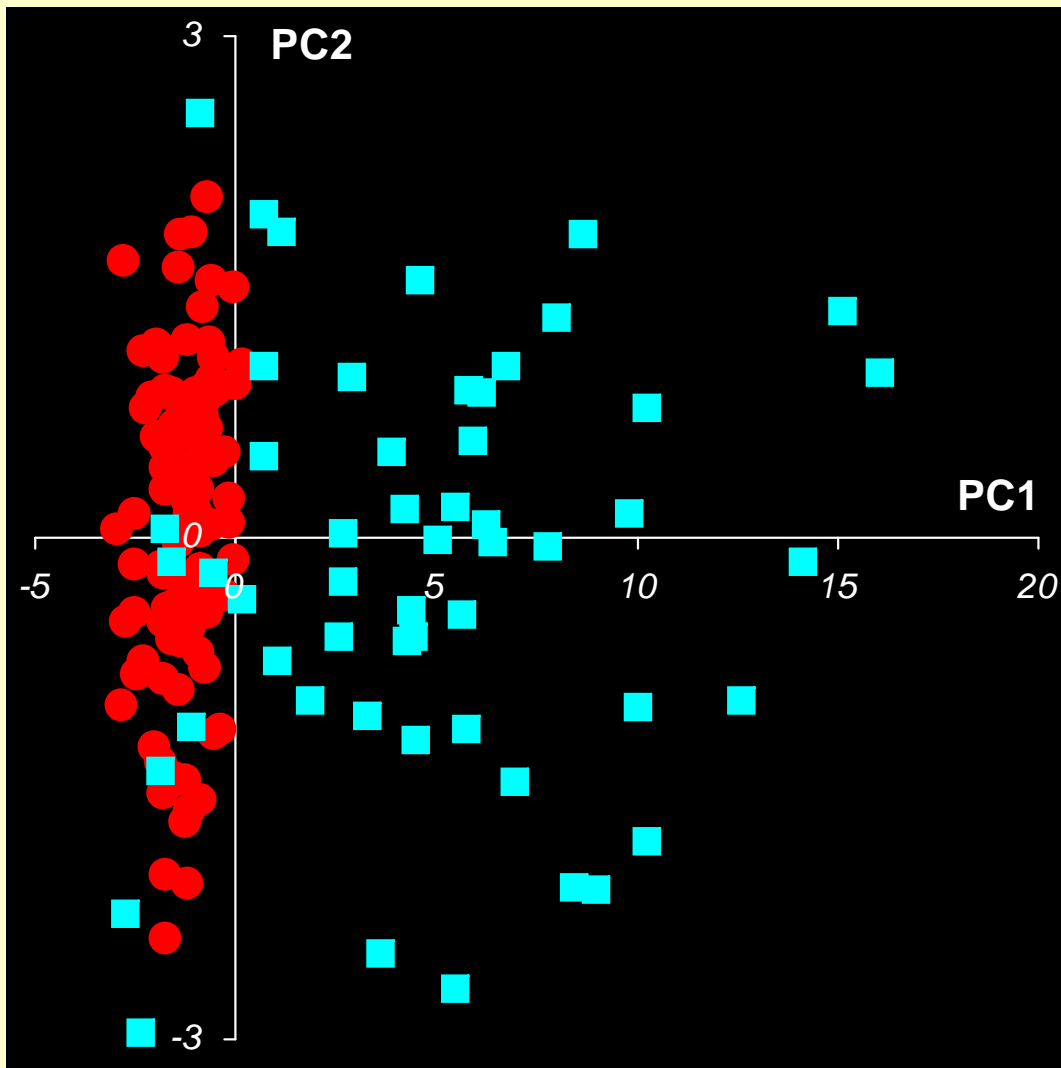
Influence of the employed spectral region & 2- stage classification procedure



Data acquisition with fiber-probe: NIR spectra in 4100 –10000 cm^{-1} region

Data set: Substance in the closed PE bags, 82 drums, each bag measured 3 times, totally: 246 spectra

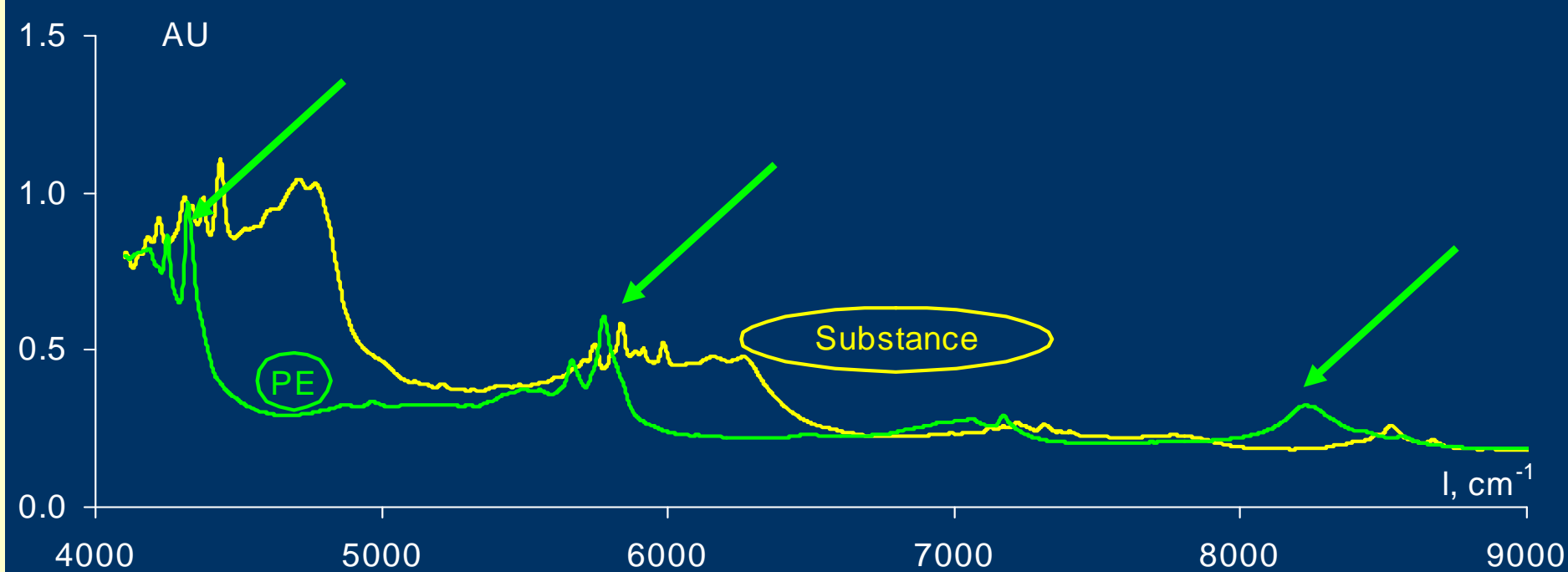
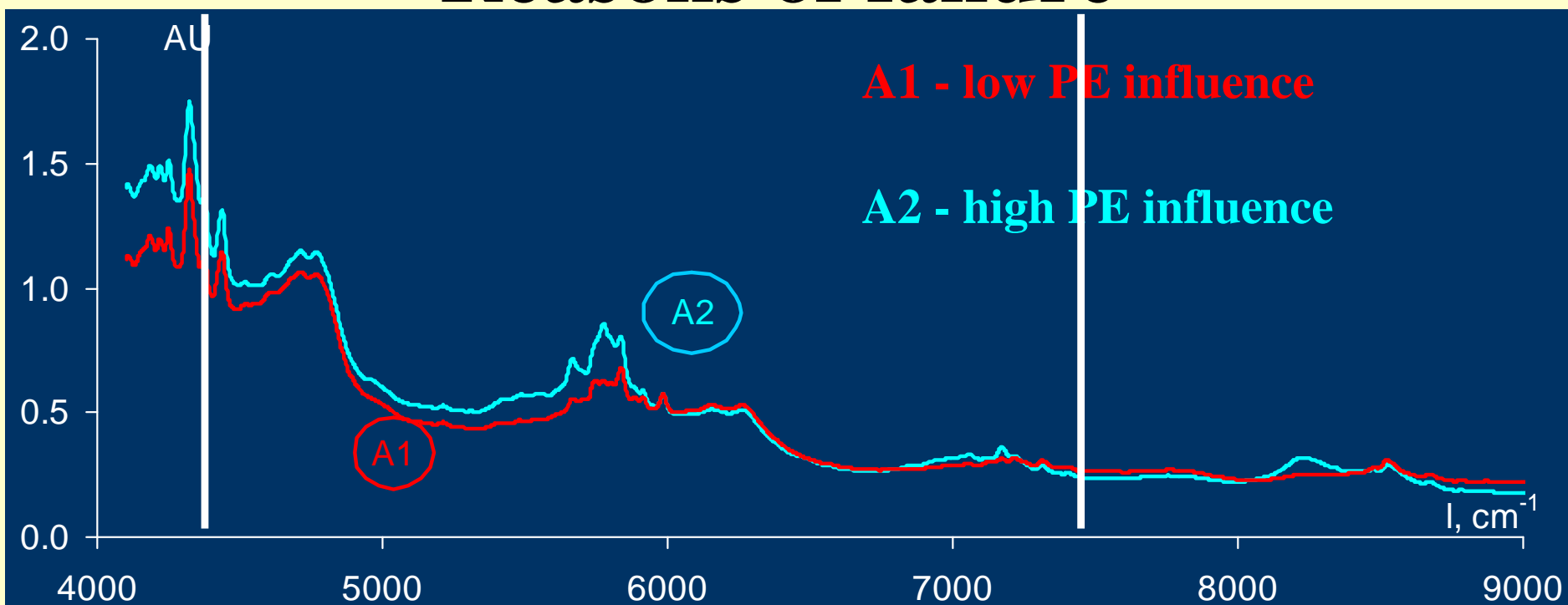
Explorative PCA



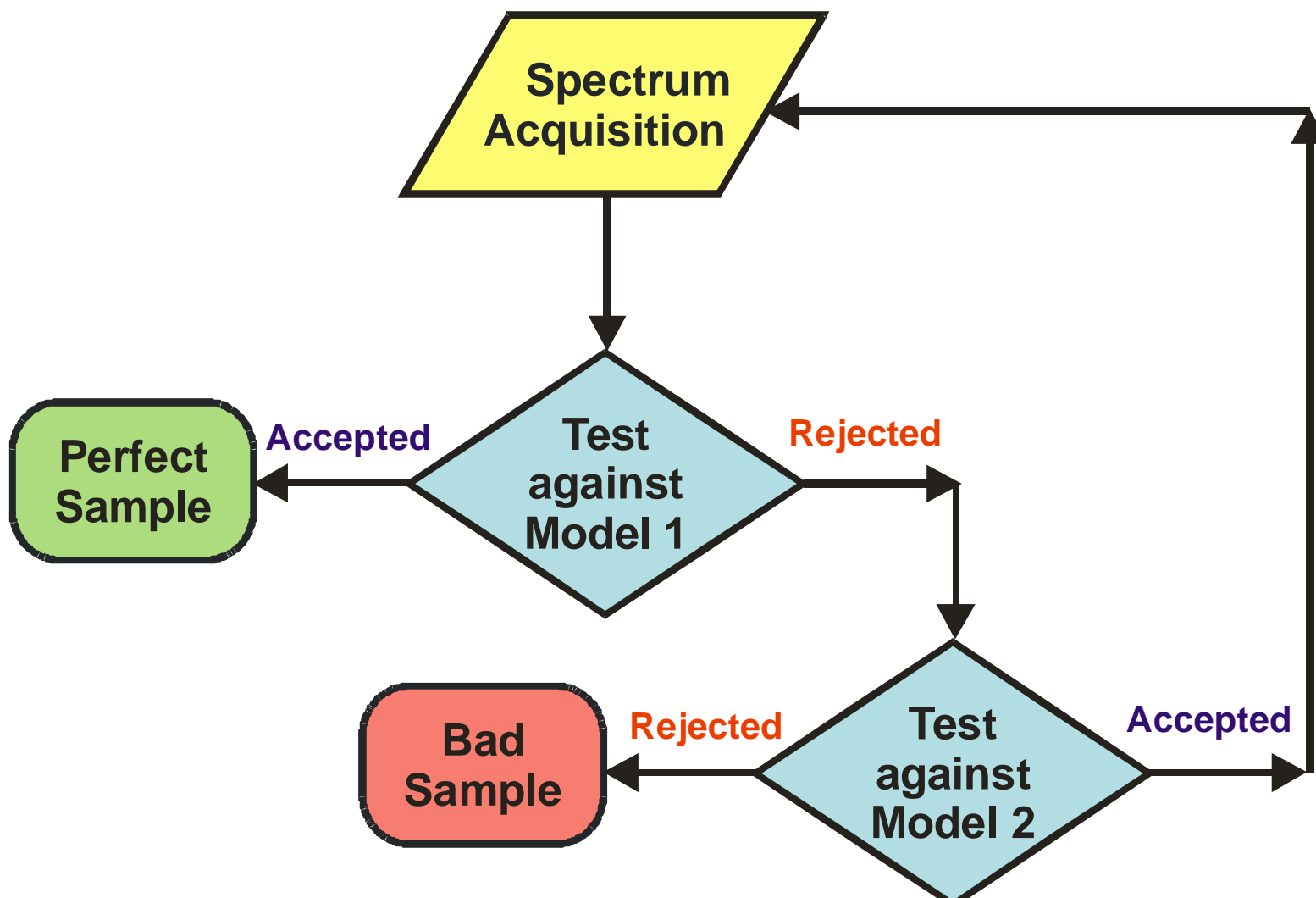
Challenge:

More than **60** out of **246** objects are treated as doubtless outliers

Reasons of failure



Routine testing procedure



$N=246$

$N_{G1}=184$

$N_{G2}=62$

$p=62/184 \approx 0.25$

$N_{\text{tries}} \approx 3$

Quality control of packed raw materials in pharmaceutical industry

O.Ye. Rodionova, Ya.V. Sokovikov, A.L. Pomerantsev, *Anal. Chim. Acta*, 642(1-2), 222-227 (2009)

NIR Sensitivity

NIR confirmed by the wet-chemistry results



G1

G2

F2

4% aqueous solution of
dexamethasone 21-phosphate
in closed transparent glass ampoules

Genuine objects

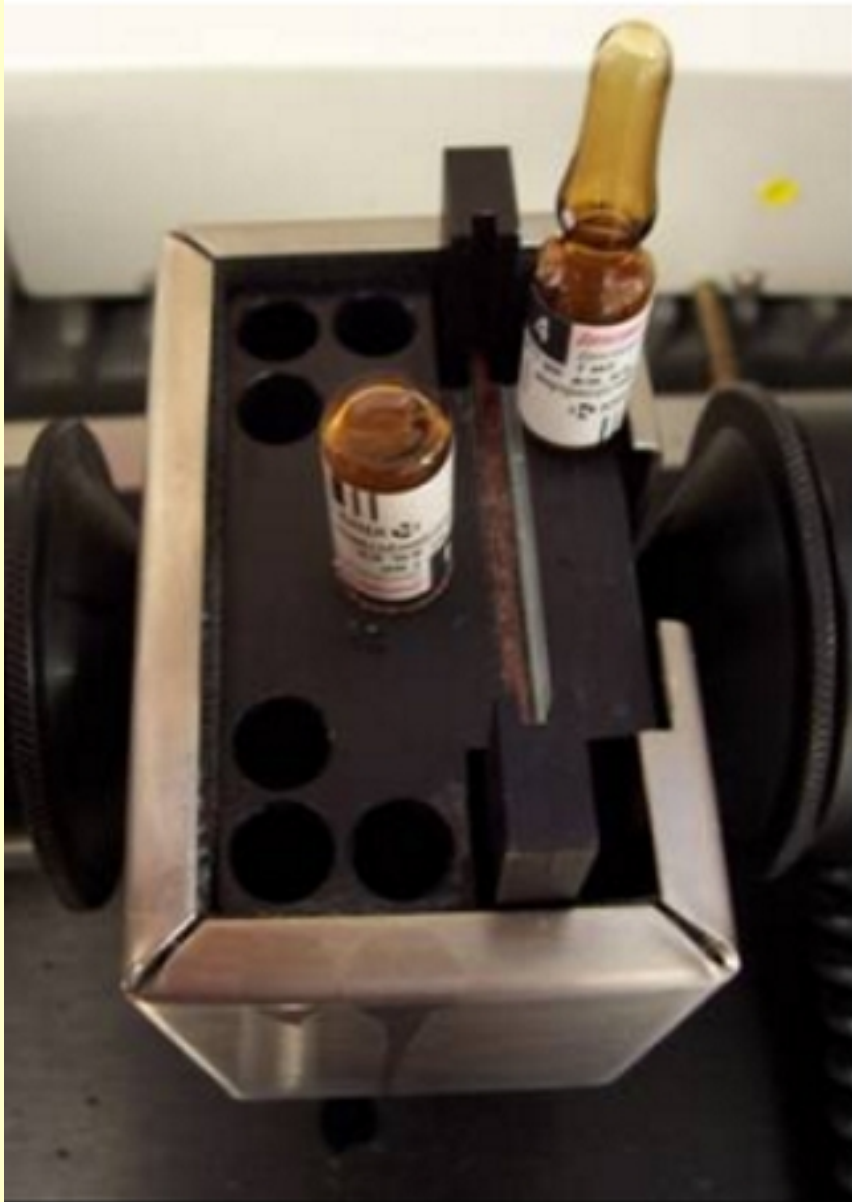
Batch G1: 15 ampoules

Batch G2 : 15 ampoules

Counterfeit objects

Batch F2: 15 ampoules

Measurements



Bomem 160 FT NIR

**spectral range 5500-
10000 cm^{-1} ,**

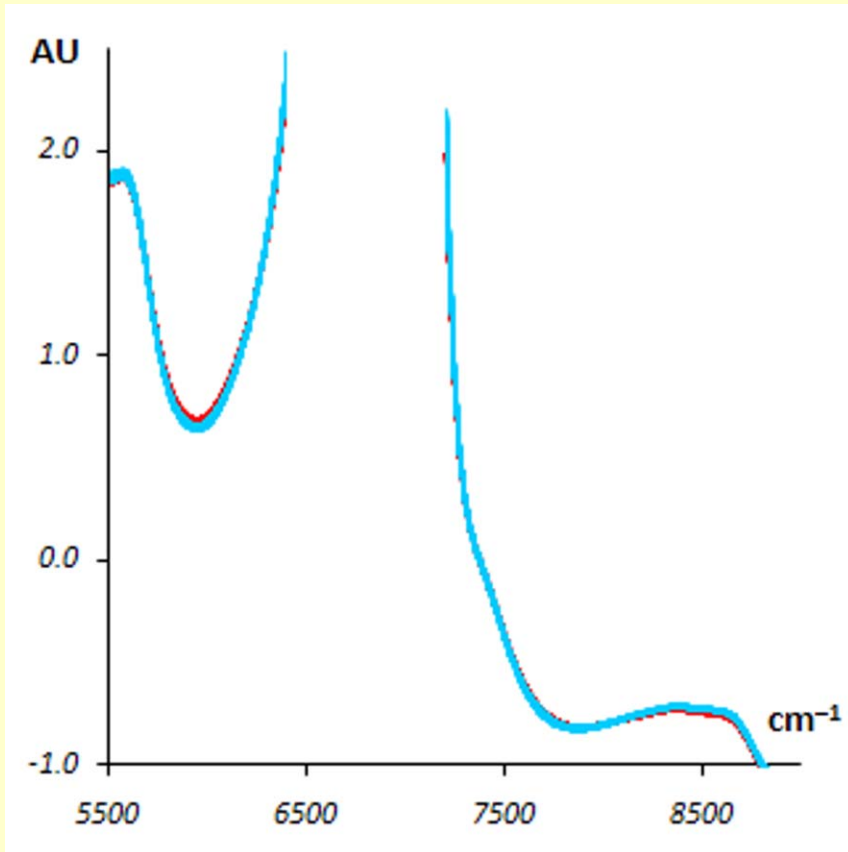
resolution 8 cm^{-1}

8 mm vial holder

T= 30°C

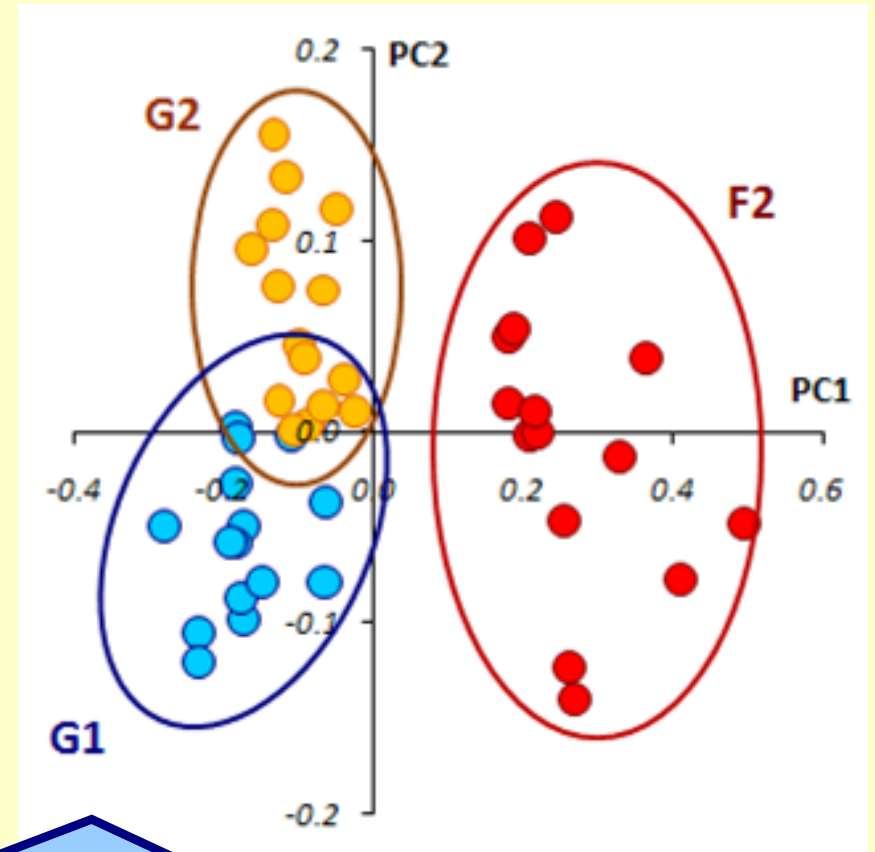
Explorative analysis

SNV pre-processing



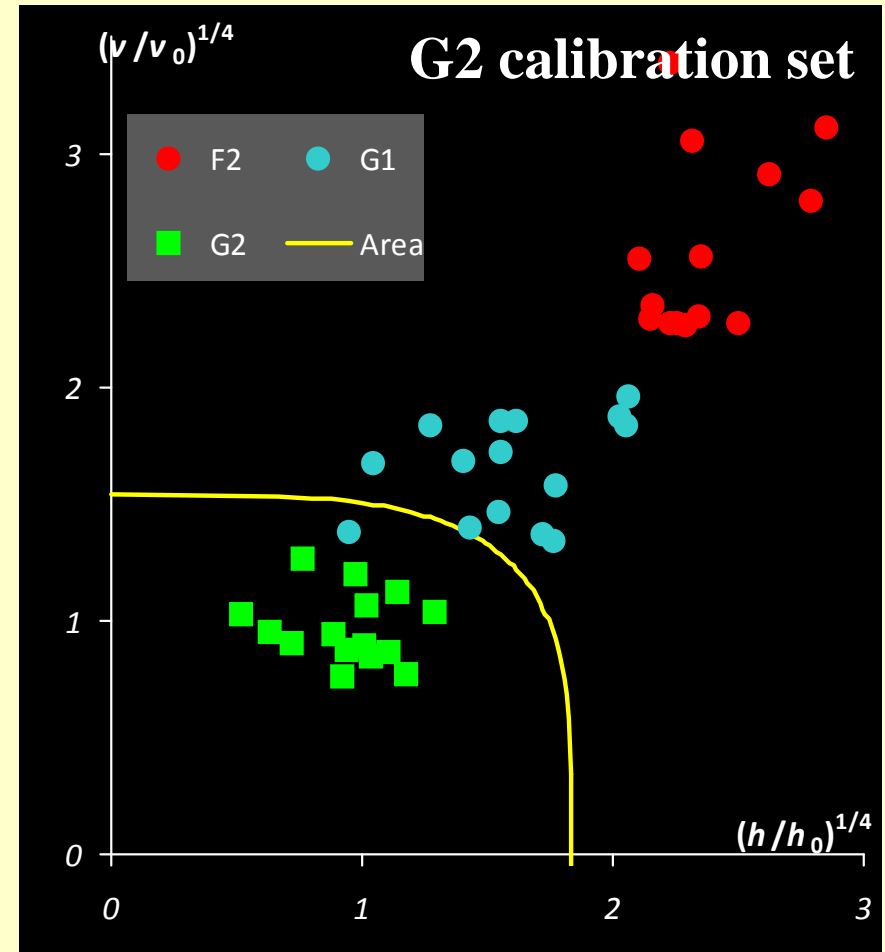
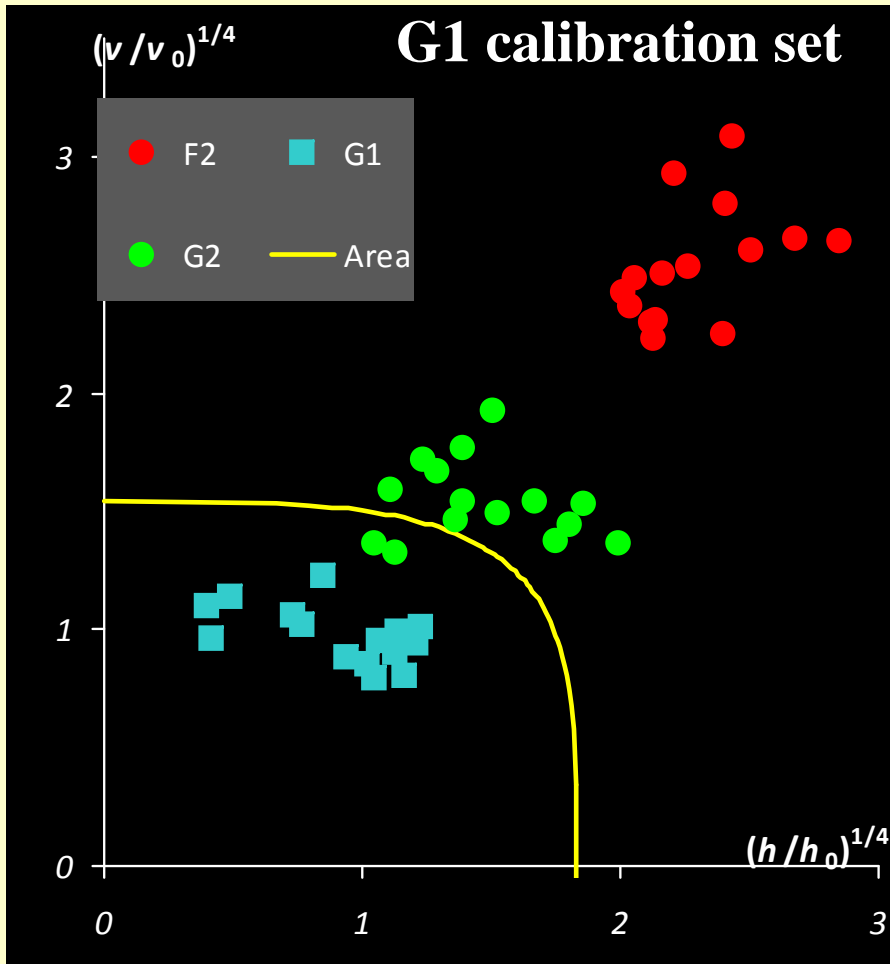
Selected spectral ranges

PCA



Scores plot

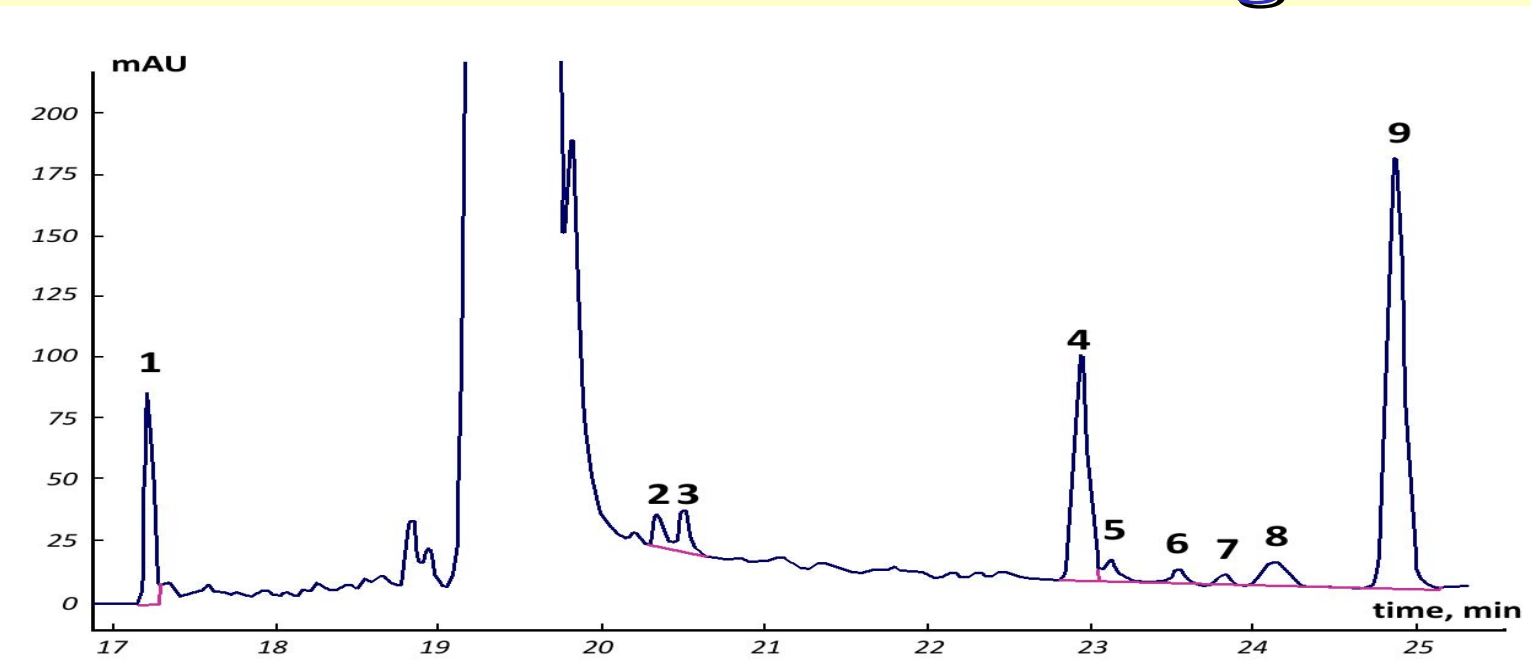
SIMCA classification



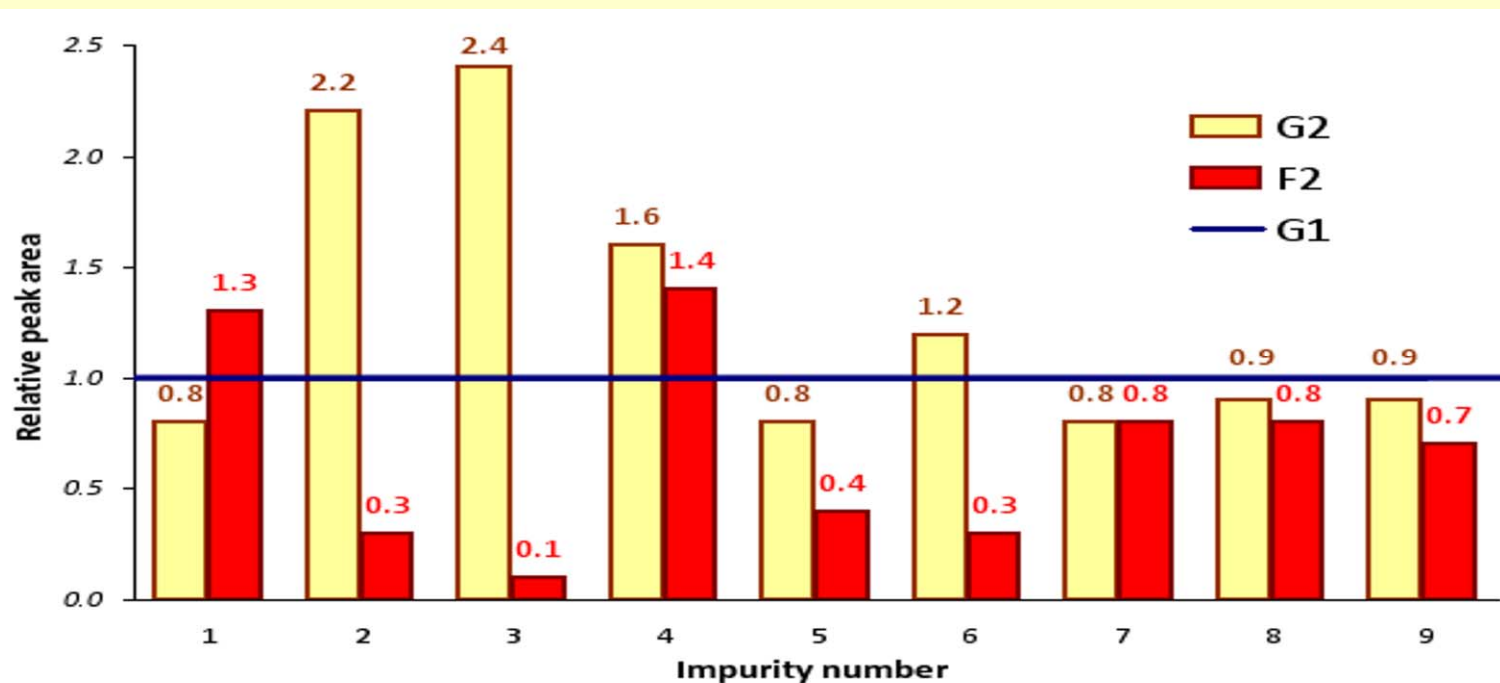
Conclusions:

1. Genuine sets G1 and G2 are similar but not identical
2. Set F differs greatly from the both genuine sets

HPLC-DAD Chromatograms for G1

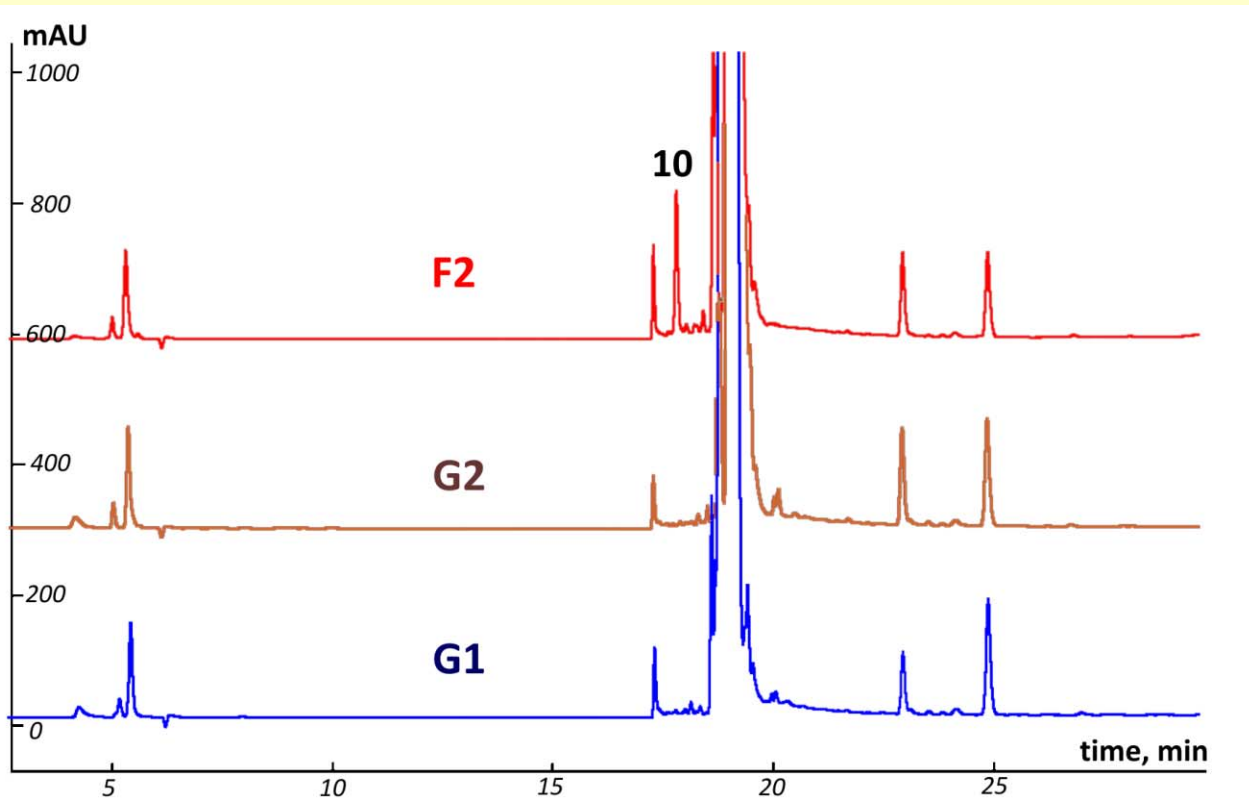


Micro-impurities in G1



**The genuine G1 sample is used as the reference
(HPLC-DAD, UV detection at 254 nm)**

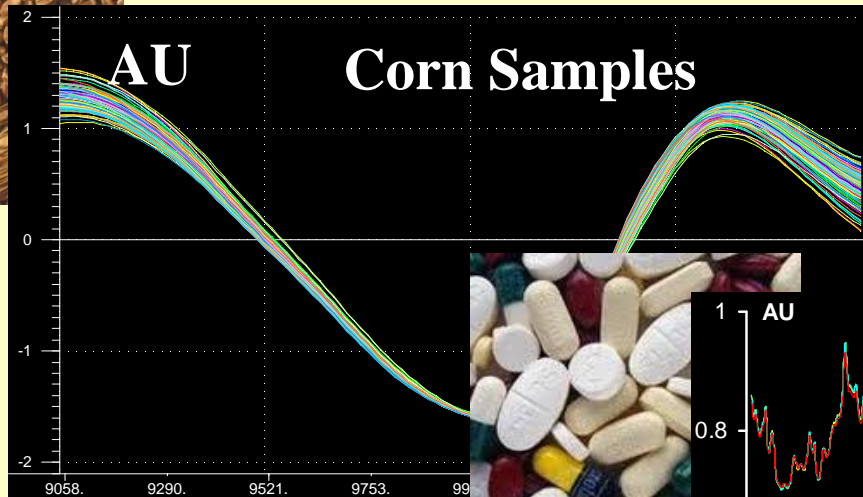
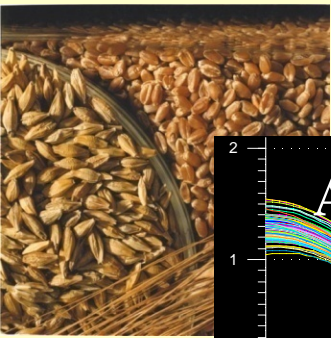
HPLC- DAD Chromatograms of Fake (F2) and Genuine (G1, G2) Samples



Conclusion 1. Peak positions for samples G1 and G2 are identical, but for impurities 2-4 peak areas differed notably.

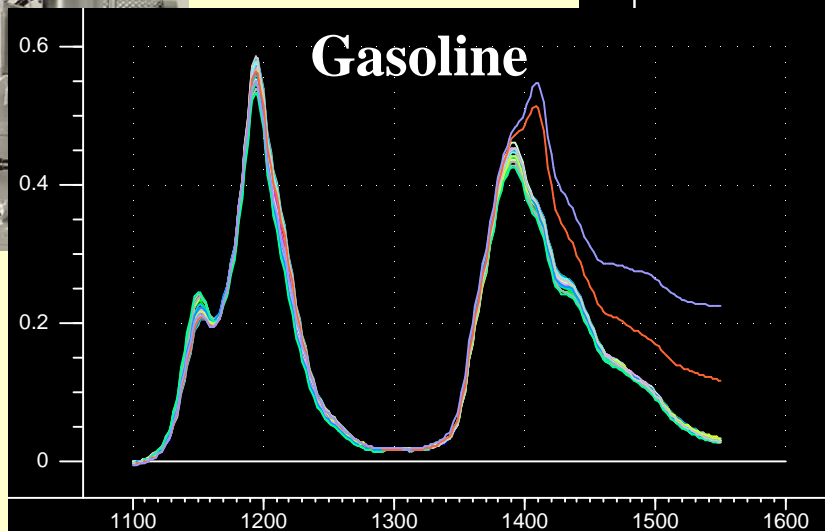
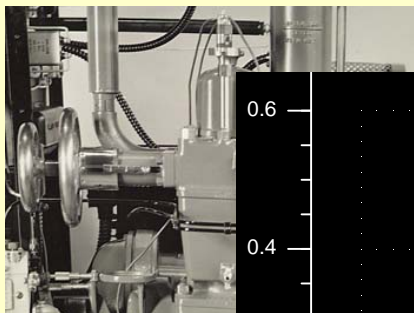
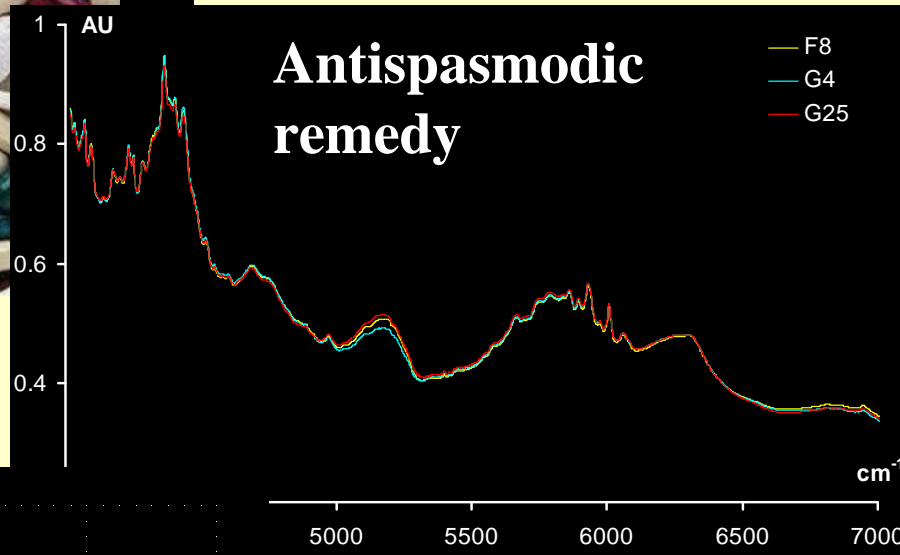
Conclusion 2. Large peak, corresponding to impurity 10, for the fake sample, which, together with the absence of impurities 2 and 3, makes it possible to detect forgery

NIR: quantitative analysis



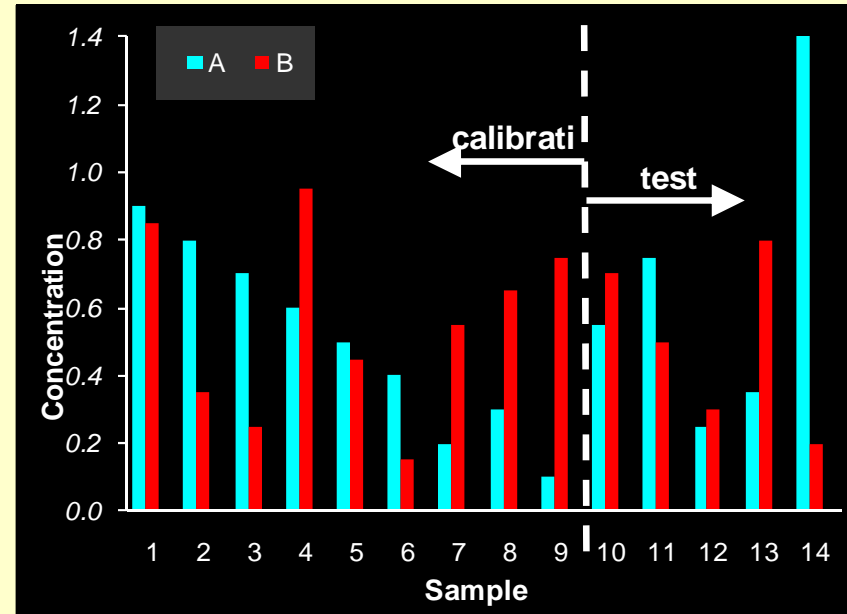
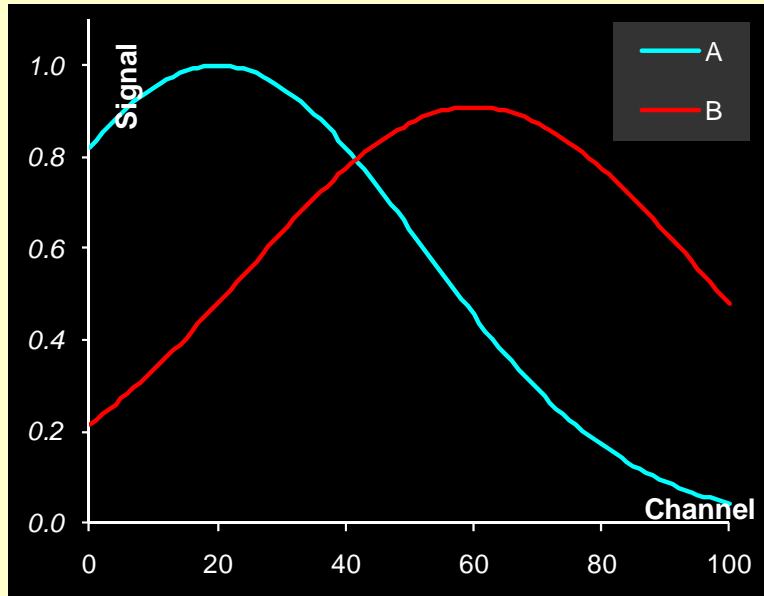
API concentration?
Excipient concentration?

Total protein content?
Moisture content?



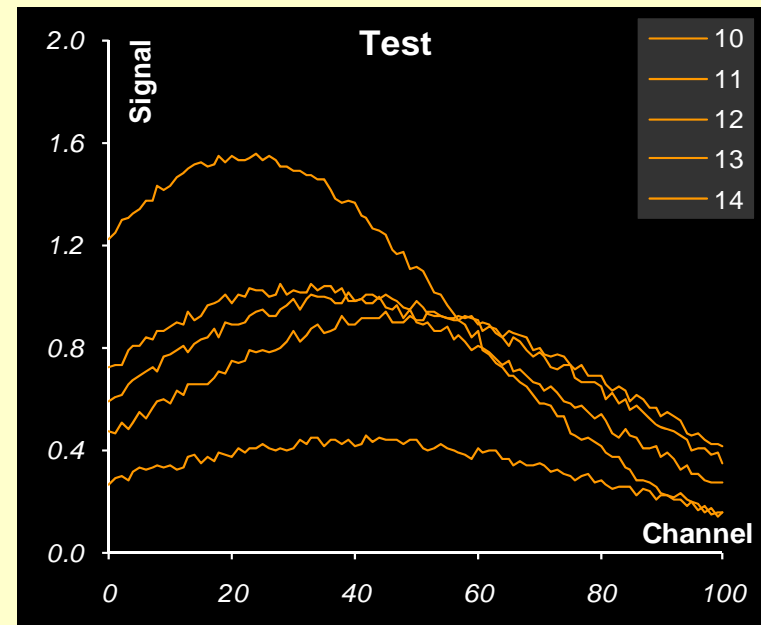
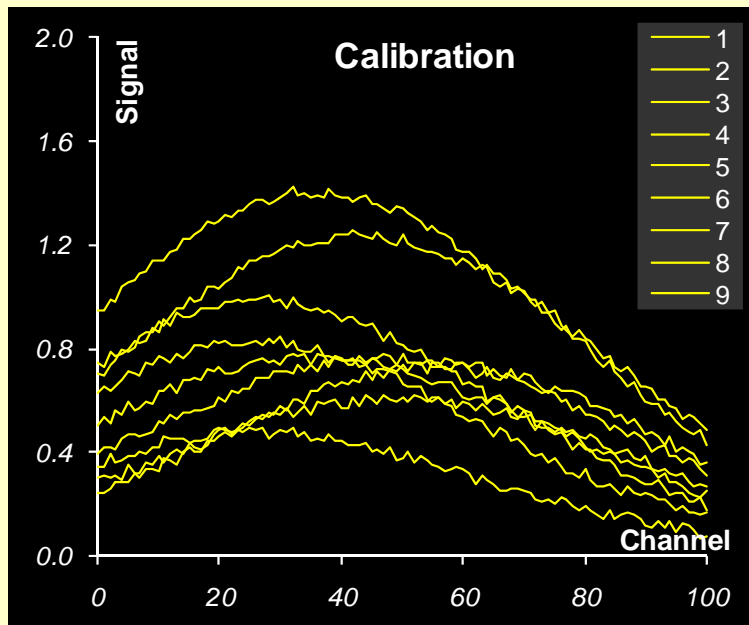
Octane number?

NIR spectra & Chemometrics

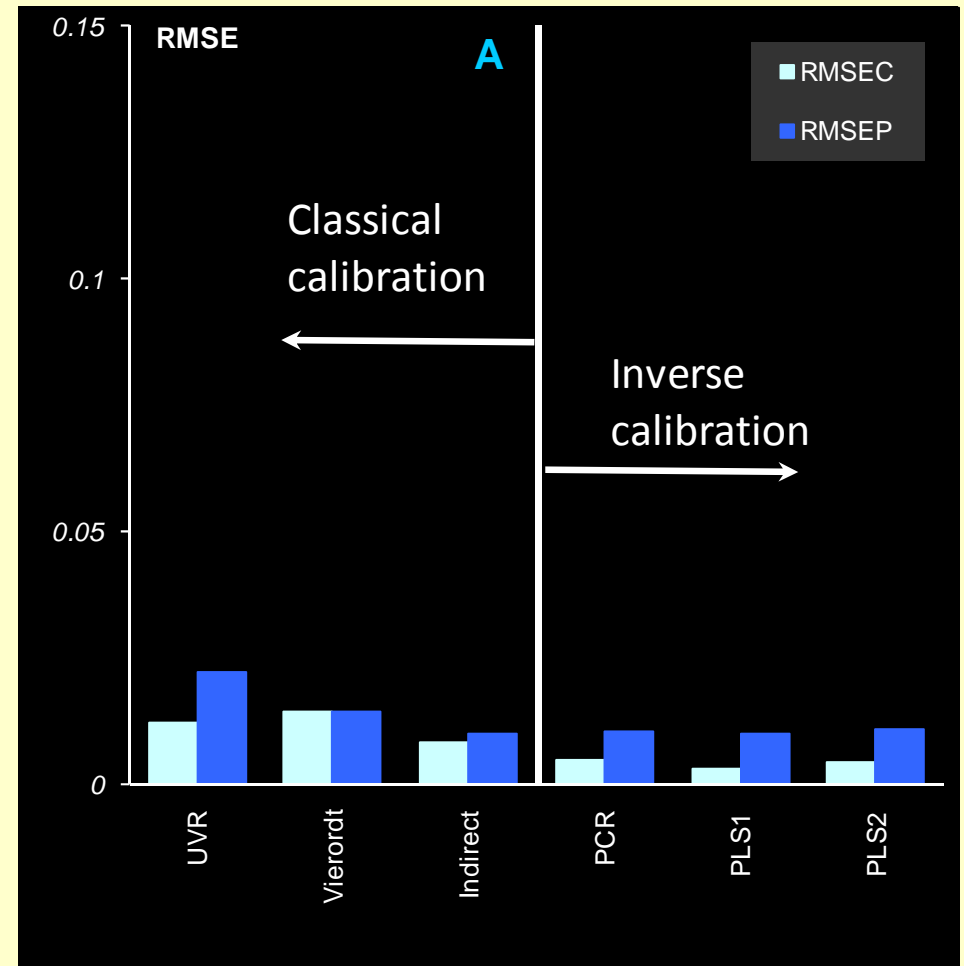
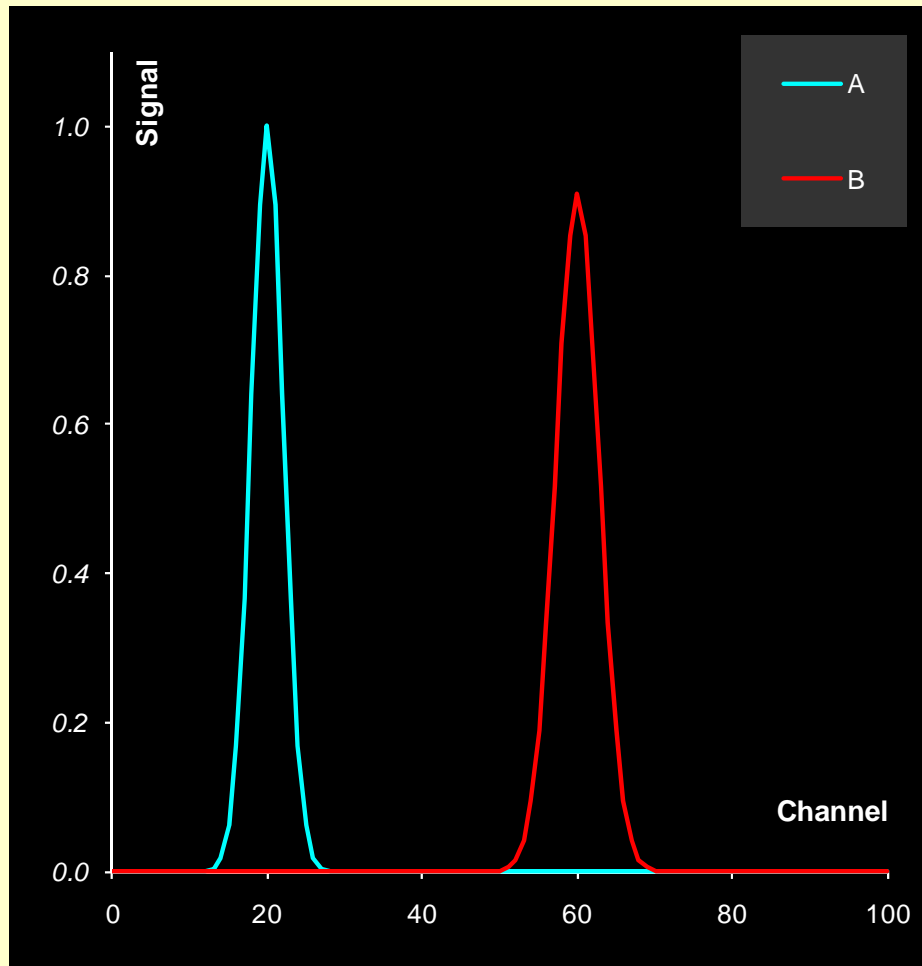


Simulated example

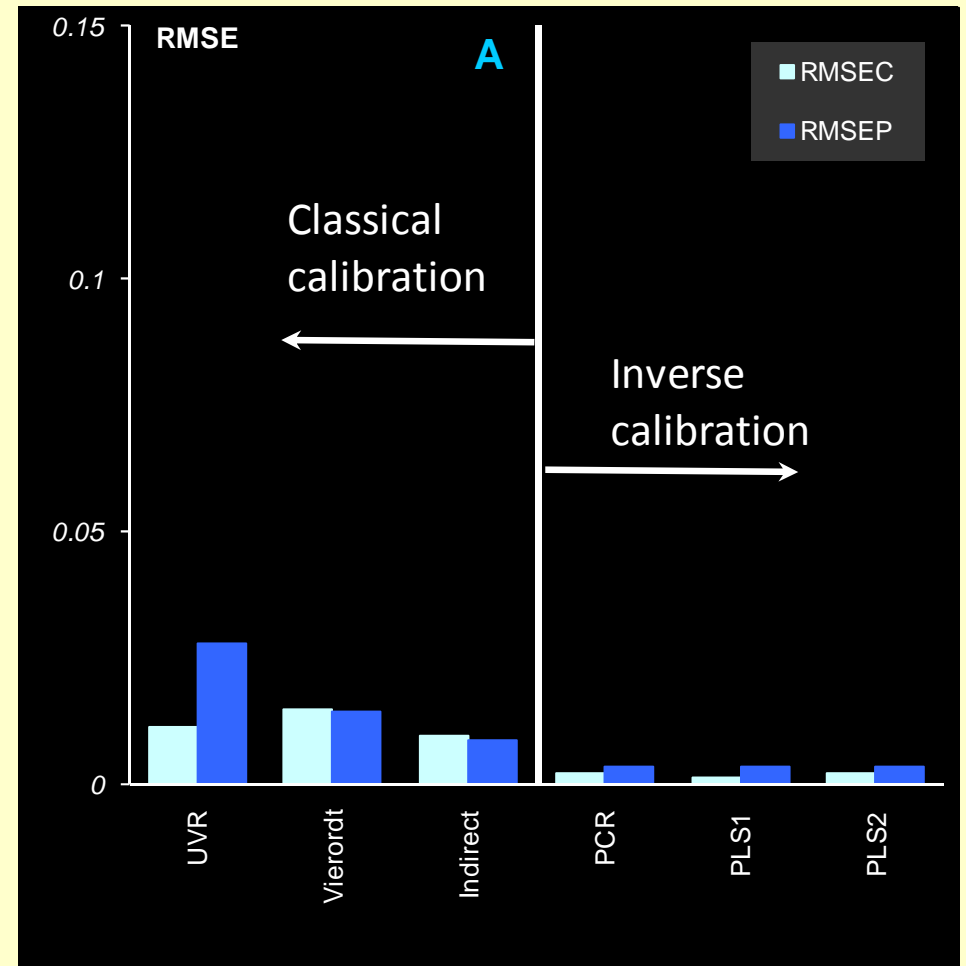
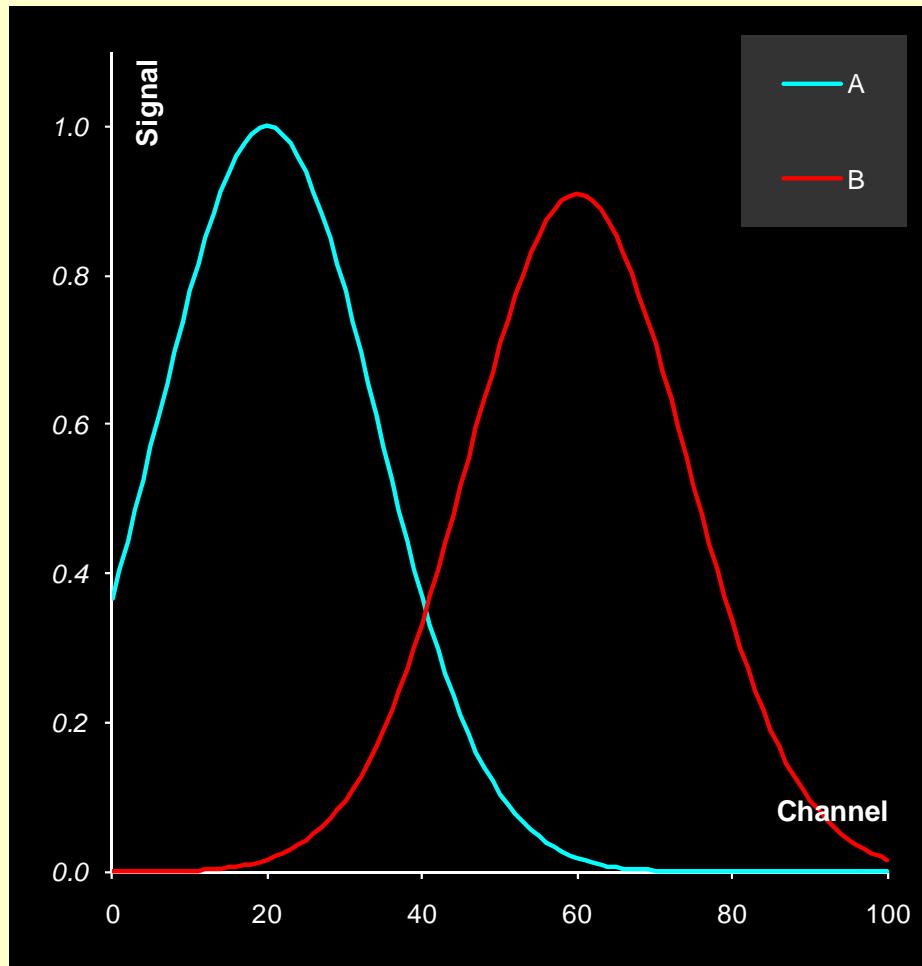
<http://rsc.chph.ras.ru/Tutorials/calibration/Calibration.xls>



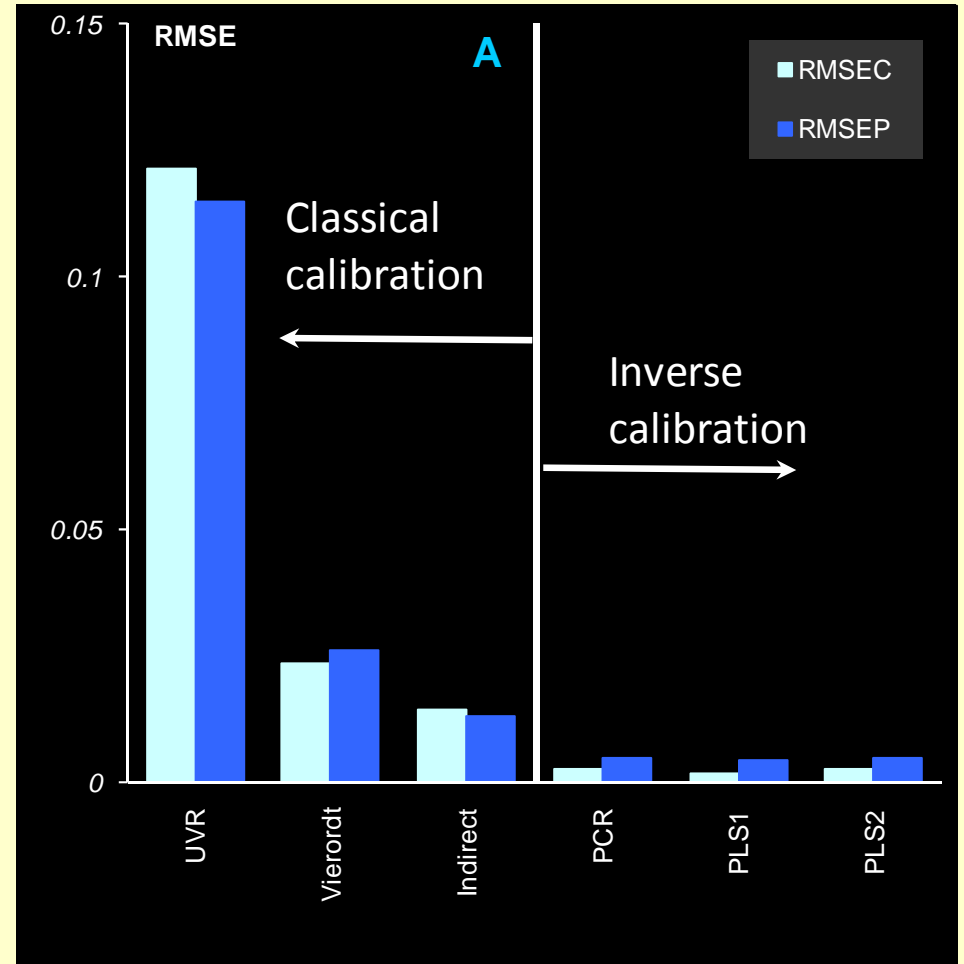
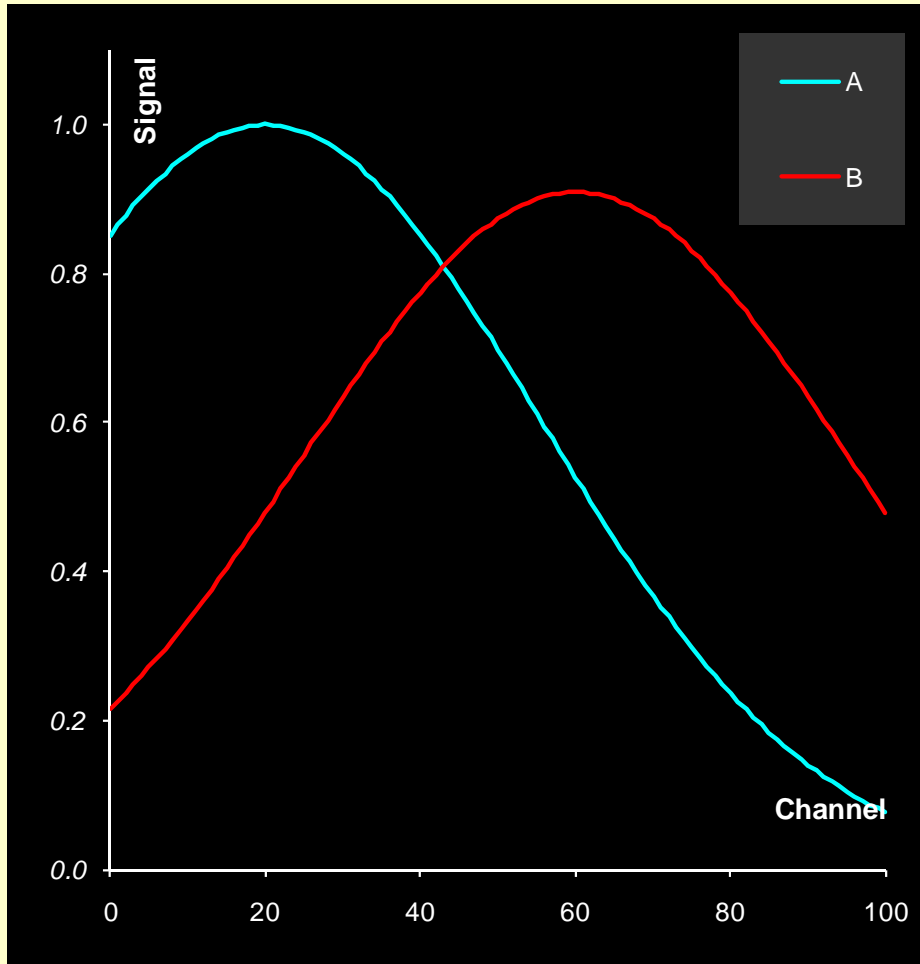
Well separated peaks



Half overlapped peaks



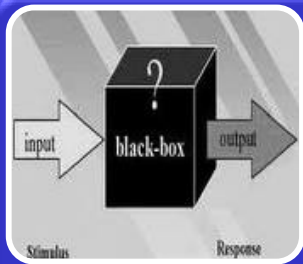
Overlapped peaks



Conclusions



NIR is a powerful tool for qualitative and quantitative analysis



With pertinent instrumentation set-up NIR spectra are sensitive to variations in micro-impurity composition



Multivariate (chemometric) data analysis is the inherent part of the NIR-based analysis

Collaborators



**Yaroslav
Sokovikov**

Scheltec
Russia



**Lars
Houmøller**

Arla Foods
Denmark



**Oleg
Shpigun**

MSU
Russia



February 27-March 2, 2012, near Moscow

<http://wsc.chemometrics.ru/wsc8/>

8th Winter Symposium on Chemometrics

