Near Infrared Spectroscopy as a Challenging Analytical Tool

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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

2. Minimal or no sample preparation

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

NIR spectra complexity ≠ Low-informative

NIR spectroscopy + Multivariate data analysis (chemometric methods)
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

A1 - low PE influence

A2 - high PE influence

Substance

A1 - low PE influence

A2 - high PE influence
Routine testing procedure

N = 246
N_{G1} = 184
N_{G2} = 62
p = 62/184 \approx 0.25
N_{tries} \approx 3

Quality control of packed raw materials in pharmaceutical industry
NIR Sensitivity

NIR confirmed by the wet-chemistry results

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= 30ºC
Explorative analysis

SNV pre-processing  PCA

Selected spectral ranges  Scores plot
Conclusions:
1. Genuine sets G1 and G2 are similar but not identical
2. Set F differs greatly from the both genuine sets
Micro-impurities in G1

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

Corn Samples

API concentration?
Excipient concentration?

Total protein content?
Moisture content?

Antispasmodic remedy

Gasoline

Octane number?
NIR spectra & Chemometrics

Simulated example

Well separated peaks

![Well separated peaks](image)

- **Signal** vs **Channel**
- **RMSE** for different methods:
  - Classical calibration
  - Inverse calibration

### Methods
- UVR
- Vierordt
- Indirect
- PCR
- PLS1
- PLS2
Half overlapped peaks

![Graph showing signal vs channel with half overlapped peaks for channels A and B.]

![Bar graph illustrating RMSE values for different techniques: Classical calibration, Indirect, PCR, PLS1, PLS2.]

- Classical calibration
- Inverse calibration

Techniques:
- UVR
- Vierordt
- Indirect
- PCR
- PLS1
- PLS2

Indices:
- RMSEC
- RMSEP
Overlapped peaks

- Classical calibration
- Inverse calibration
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 inherit part of the NIR-based analysis
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