# DIRECT QUANTIFICATION IN THE PRODUCTION OF TABLETS

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## Introduction

Near Infrared Chemical Imaging (NIR-CI) is an attractive technique in pharmaceutical assessment of tablets. An important step in tabletting is the blending stage and NIR-CI can be used for assessing this.

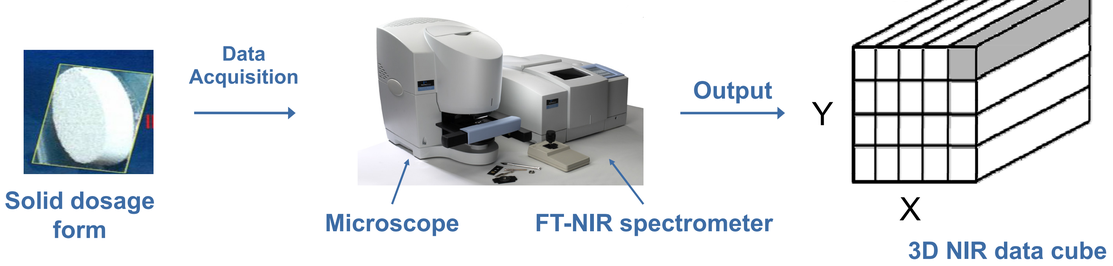
To model NIR-CI images, several chemometric methods, such as Partial Least Squares regression (PLS), are often used. PLS, though, requires a calibration phase. We study Classical Least Squares (CLS) and Multivariate Curve Resolution (MCR) that do not require access to a calibration data set.

We assess quantitative and spatial information in a complex blending mixture composed of five components. The homogeneity of the surfaces, as well as the local quantitative determination of the five components is studied and tested.

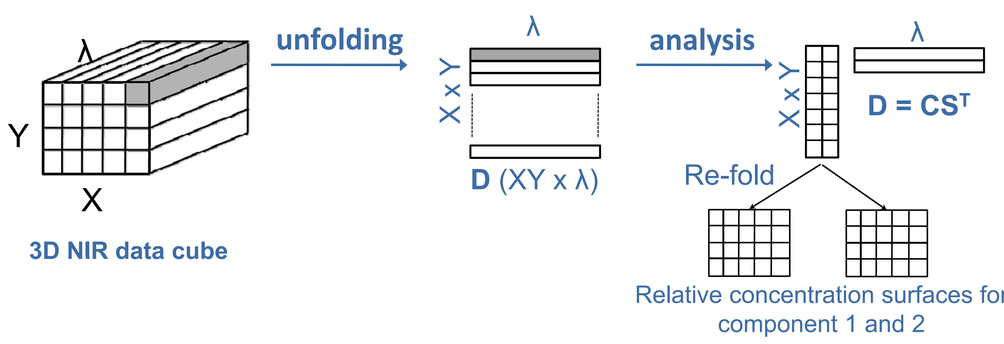
## Experimental

Composition of the tablets: Active Pharmaceutical Ingredient (API: 6.3% w/w), microcrystalline cellulose (MCC: 20.0% w/w), lactose (Lact: 71.5% w/w), magnesium stearate (MgSt: 0.75% w/w) and talc (talc: 1.5% w/w).

- Perkin Elmer Spotlight FT-NIR line imaging system.
- **CLS** (1) and **MCR-ALS** (2) models were applied by using MatLab.




## Background of CLS, MCR-ALS and augmented MCR-ALS




**CLS** ⟹ Direct regression of **D** by using the pure spectra to calculate **C**

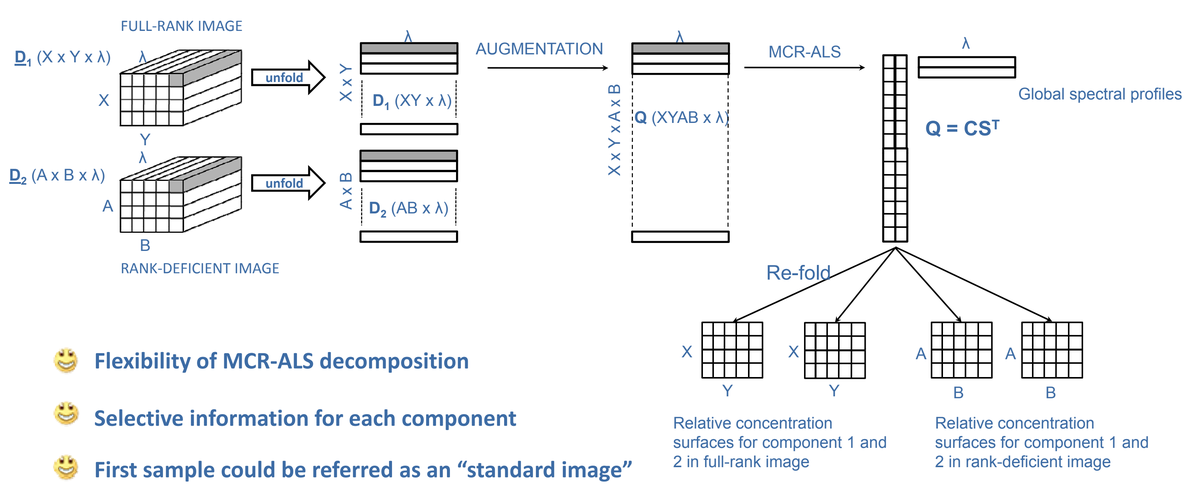
Highly affected by other sources of variability in the sample not reflected in the pure spectra

**MCR-ALS** ⟹ Iterative decomposition of **D** into two submatrices: **C** and **S**

$(\ )^2$ Highly dependent of areas with selective information for each pure component

Highly affected by the mutual similarity between spectra

**Augmented MCR-ALS:** MCR-ALS using two images: **The first one** containing selective information of each of the components of the mixture (Full-rank image), and **the second one** the tablet we want to study.




**Flexibility of MCR-ALS decomposition**

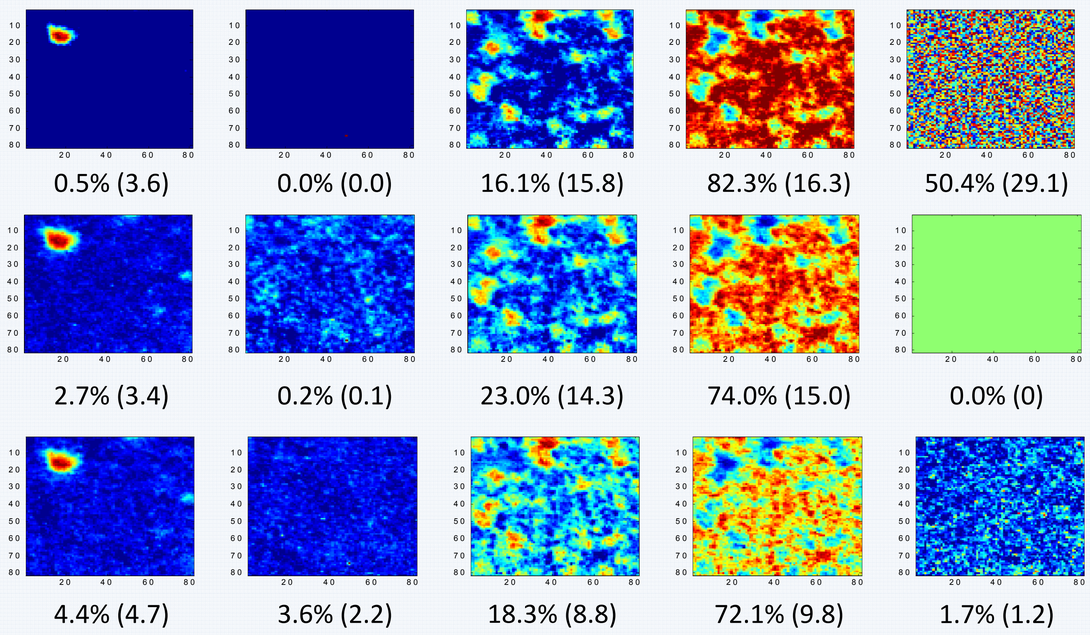
**Selective information for each component**

**First sample could be referred as an "standard image"**

**Of course, you need the "standard image"**

## Results and discussion

| | API | MgSt | MCC | Lact | Talc |
|---|---|---|---|---|---|
| **NOMINAL** | 6.2 | 0.75 | 20 | 71.49 | 1.5 |
| **CLS** | 0.5% (3.6) | 0.0% (0.0) | 16.1% (15.8) | 82.3% (16.3) | 50.4% (29.1) |
| **MCR-ALS** | 2.7% (3.4) | 0.2% (0.1) | 23.0% (14.3) | 74.0% (15.0) | 0.0% (0) |
| **Augmented MCR-ALS** | 4.4% (4.7) | 3.6% (2.2) | 18.3% (8.8) | 72.1% (9.8) | 1.7% (1.2) |



(standard deviation between pixels in brackets)

- **Preprocessing:**

  **SNV and smoothing (window size = 15)**

Not really good estimations of concentrations with CLS.

MCR-ALS encountered problems quantifying minor components.

The augmented version of MCR-ALS allows obtaining really good estimations of the concentrations

## Conclusions

Several methods for homogeneity testing and direct quantification of five components in pharmaceutical tablets have been tested. In general, good results have been obtained for the three methods in quantifying and visualization of homogeneity of major components of the tablet (MCC and Lact). Nevertheless, the problem is encountered in the minor components (API, MgSt and Talc). From the results, we can conclude that CLS and MCR-ALS do not offer robust and reliable information. Augmentation of MCR-ALS holds all the properties of MCR-ALS with the benefit of including one sample as "standard". This working methodology helps to minimize the drawbacks of MCR-ALS, obtaining the best results for the minor components quantification.

## References

(1) PLS-Toolbox. Eigenverctor Research, WA, USA.

(2) MCR-ALS home page: http://www.ub.es/gesq/mcr.htm

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