Analysis of heterogeneity distribution in powder blends using hyperspectral imaging

Dr Juan Antonio Fernández — Walloon Agricultural Research Centre (CRA-W), Belgium

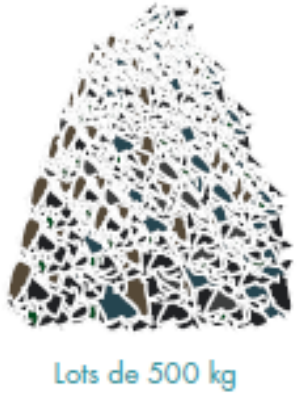
Dr Vincent Baeten

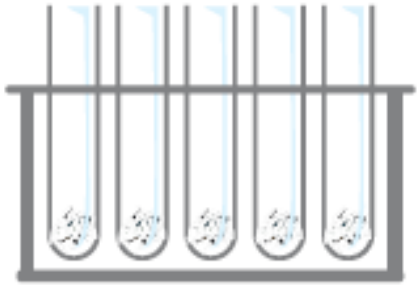
Guanghui Shen — China Agricultural University (CAU), China

Dr Anna de Juan — Universitat de Barcelona, Spain

Rodrigo R. de Oliveira

The context
Theory Of Sampling (TOS)





http://www.aliapur.fr/media/files/RetD_new/Conferences_Publications/Aliapur_-_Prelevement_et_echantillonnage_des_granulats.pdf

The context
TOS – Distributional Heterogeneity (DH)

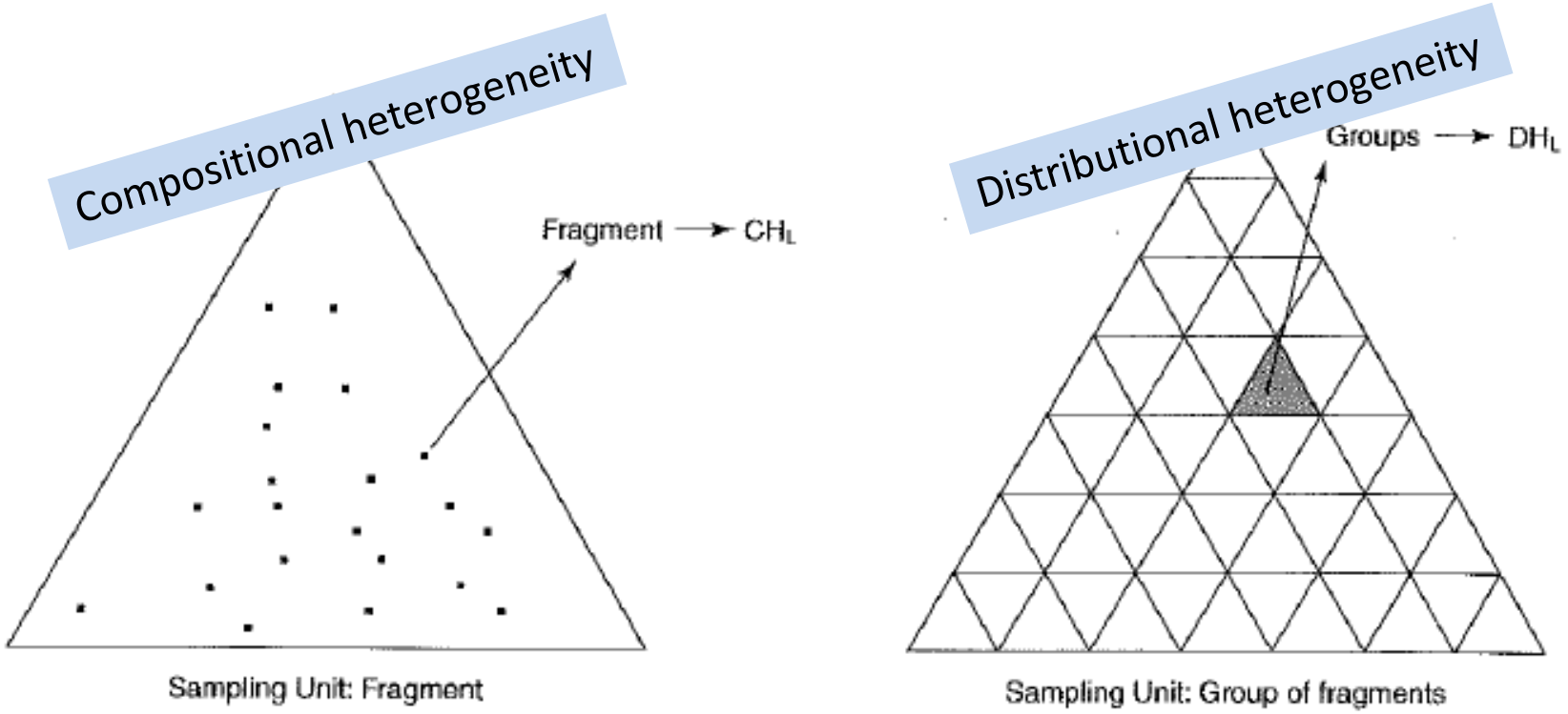


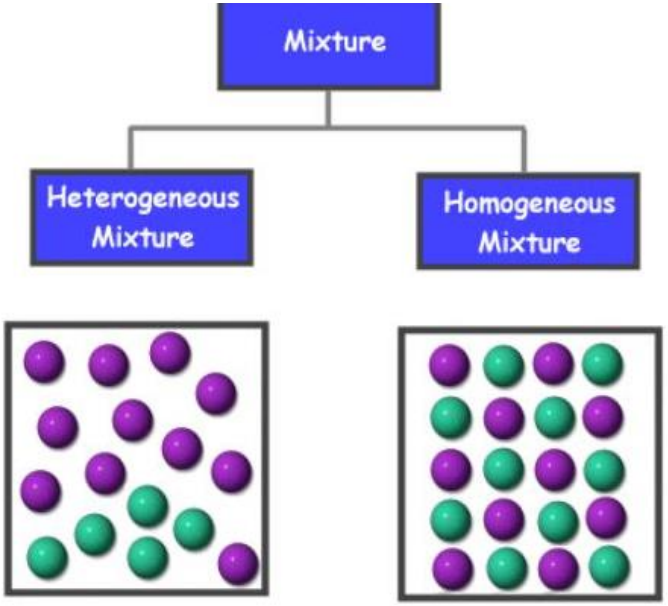
Figure 3.1 *Principle illustration of scale-related concepts of constitutional and distributional heterogeneity. The constitutional heterogeneity, CHL, expresses all between-fragment compositional differences in the entire lot, while the distributional heterogeneity, DHL, reflects all between-increment (between-group) compositional differences, which can be seen as covering the entire spatial geometry of the lot.*

Source : Esbensen and Paasch-Mortensen. Process sampling – the missing link in Process Analytical Technologies PAT. *In Process Analytical Technology (Ed. K.A. Bakeev), Wiley, 2010, 557p.*

The context

TOS – Distributional Heterogeneity (DH)

The assessment of heterogeneity/homogeneity is a critical step for obtaining high quality and uniform mixtures.



Homogeneous mixture: components are uniformly distributed throughout

The context

Powder mixing is a crucial unit operation required for the production of all solid products. In the blending process, blend uniformity analysis (BUA) is an important aspect that needs to be controlled during the manufacturing of solid dosage forms, since only a homogeneous mixture can be subdivided into individual doses.

The current approach for ensuring homogeneity of a powder blend is based on collecting samples at different powder bed locations within the vessel at predefined time intervals. Collected samples are then analysed off-line by time-consuming and laborious procedures – e.g., UV–VIS spectroscopy or high-performance liquid chromatography (HPLC).

Method: vibrational spectroscopy

Classical spectroscopic techniques, such as mid-infrared (MIR), near-infrared (NIR) and Raman spectroscopy, which could provide chemical information of the samples have been used to monitor powder blending process. However, these spectroscopy methods can not provide spatial distribution of the components of mixtures.

Method: Hyperspectral imaging

Hyperspectral imaging technology provides spectral and spatial information at the same time.

Applications of hyperspectral imaging for homogeneity analysis of the blending process have increased significantly in the past few years usually based on:

Colour segmentation

This method can not differentiate the samples with same colour; or need characteristic wavelength imaging.

Binarization

Supervised methods for the binarization pro-cessing of hyperspectral images will inevitably bring errors.

Histogram parameters

Mean, standard deviation, skewness and kurtosis are useful to assess homogeneity, However, two maps may have exactly the same constitutional homogeneity while being spatially totally different.

Distributional heterogeneity in images

MCR-ALS and external calibration based tools:

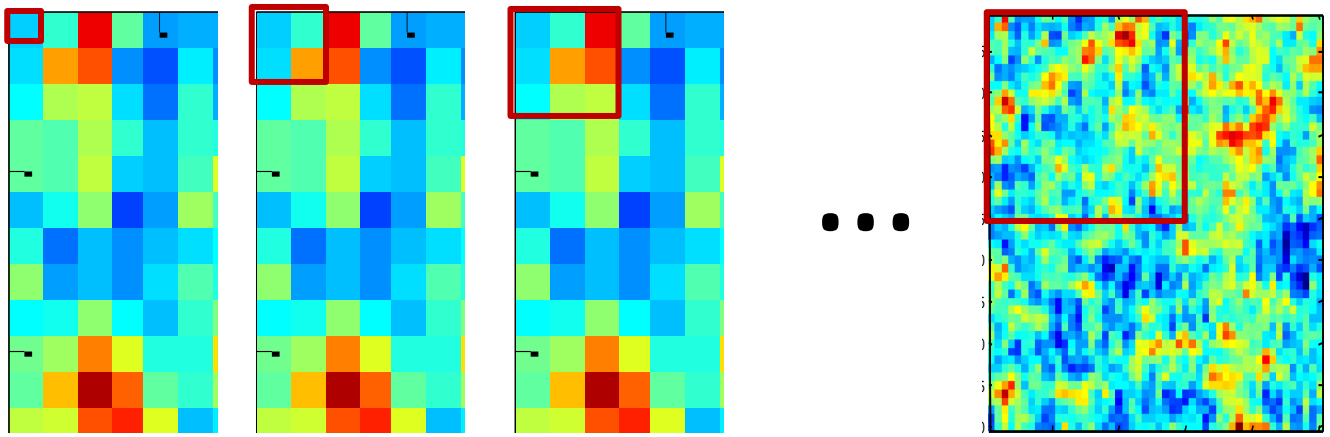
- Variation in composition among pixel areas as a function of image area size (**heterogeneity curves**, *macropixel analysis*).
- Extent of compositional correlation as a function of distance between pixels (**image variograms**).

PCA and PLS-DA based tools:

- Variation in composition among pixel areas as a function of image area size (**heterogeneity curves**, *macropixel analysis*).

Heterogeneity curves

Display **relative variance** or **standard deviation** with respect to pixel neighbourhood size.



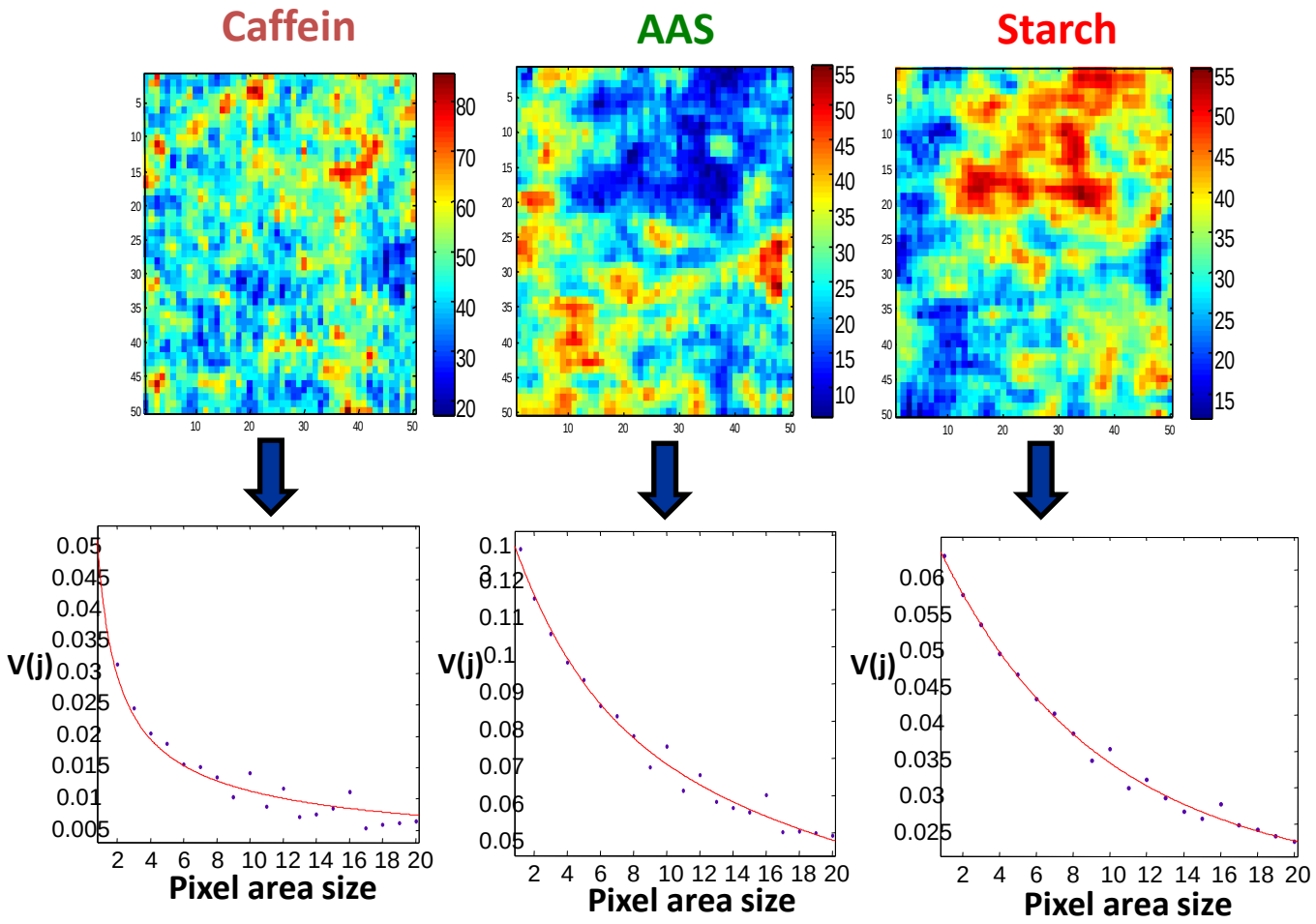
$$V(j) = \frac{\sum_i \left(c_{ij} - \bar{c}\right)^2}{n\bar{c}^{-2}}$$

$\bar{c}$ average concentration in the distribution map

c_{ij} 'concentration' value for pixel i, estimated averaging neighbouring pixel concentrations in an area of a particular size.

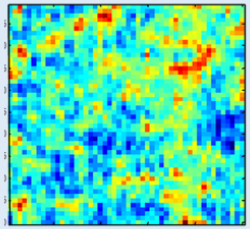
n number of pixel areas of a certain size.

Heterogeneity curves



Fast decrease of heterogeneity curves indicates lower heterogeneity.

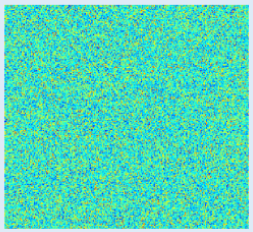
Heterogeneity curves – MCR-ALS based method



Component distribution map

Macropixels → Mean, Mean, Mean, ⋮, Mean → Standard deviation SD_{SM}

Randomization

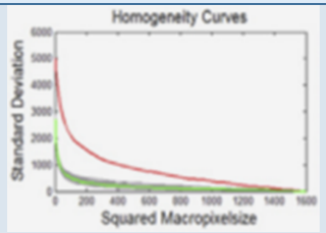


Macropixels → Mean, Mean, Mean, ⋮, Mean → Standard deviation SD_{RM}

Macropixel size: 2 ⟶ M

SD_{SM} against macropixel size ⇨ AUC_{SM}

SD_{RM} against macropixel size ⇨ AUC_{RM}

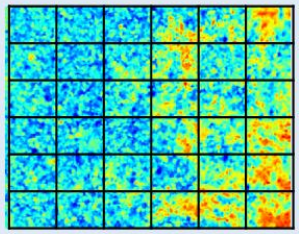


Distributional Heterogeneity Index

$$DHI = \frac{AUC_{SM}}{AUC_{RM}}$$

Sacré, P.; Lebrun, P.; Chavez, P.; Bleye, C. D.; Netchacovitch, L.; Rozet, E.; Klinkenberg, R.; Streel, B.; Hubert, P.; Ziemons, E. Analytica Chimica Acta 2014, 818, 7-14.

Heterogeneity curves – PCA based method



PCA score map

Randomization

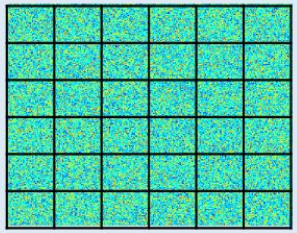
Macropixels

Mean SD_1
Mean SD_2
Mean SD_3
⋮
Mean SD_m

$GMSD_{original}$

$$SD_i = \sqrt{\frac{\sum_{j=1}^{n}(S_{ij} - \bar{S}_i)}{n-1}}$$

$$Mean\ SD = \frac{\sum_{i=1}^{h} SD_i}{h}$$



Macropixels

Mean SD_1
Mean SD_2
Mean SD_3
⋮
Mean SD_m

$GMSD_{random}$

Macropixel size: 5*5 10*10 25*20 50*40

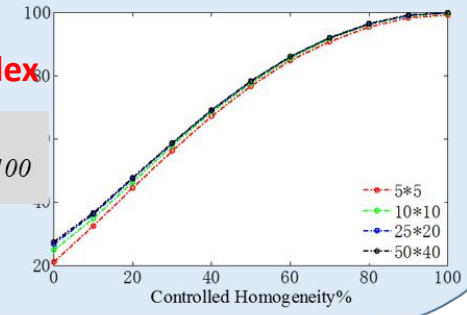
$$GMSD = \frac{\sum_{l=1}^{m} Mean\ SD_l}{m}$$

$GMSD_{original}$

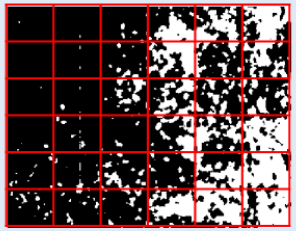
$GMSD_{random}$

Poole Heterogeneity Index

$$H\%_{poole} = \frac{GMSD_{original}}{GMSD_{random}} * 100$$

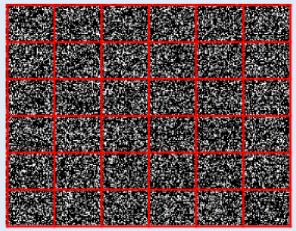


Heterogeneity curves – PLS-DA based method



Binary PLS-DA prediction map

Randomization



Macropixels → SD_1, SD_2, SD_3, ⋮, SD_m → $GMSD_{original}$

$$SD = \frac{\sum_{i=1}^{n} S_i}{n}$$

Macropixels → SD_1, SD_2, SD_3, ⋮, SD_m → $GMSD_{random}$

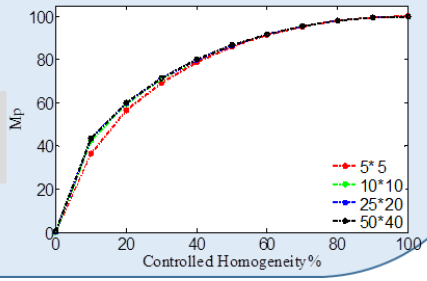
Macropixel size: 5*5 10*10 25*20 50*40

$$GMSD = \frac{\sum_{l=1}^{m} SD_l}{m}$$

$GMSD_{original}$, $GMSD_{random}$

Poole Heterogeneity Index

$$H\%_{poole} = \frac{GMSD_{original}}{GMSD_{random}} * 100$$



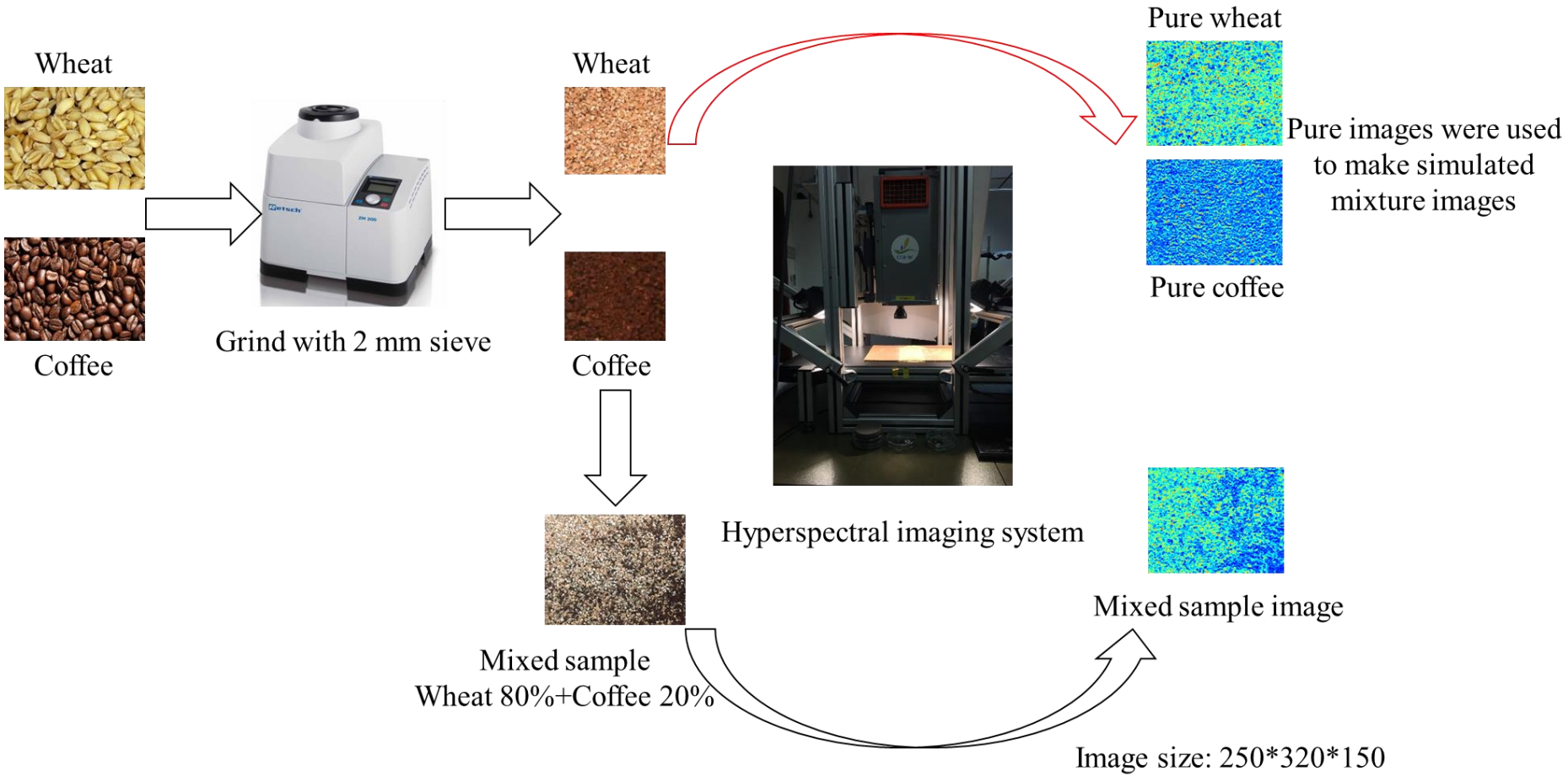
Rosas, J. G.; Blanco, M. Journal of Pharmaceutical and Biomedical Analysis 2012, 70, 691-699.

Data

Simulated hyperspectral images with different mixing proportion of wheat and coffee

Blends of Soybean and corn at different mixing proportions

Sample preparation and image acquisition

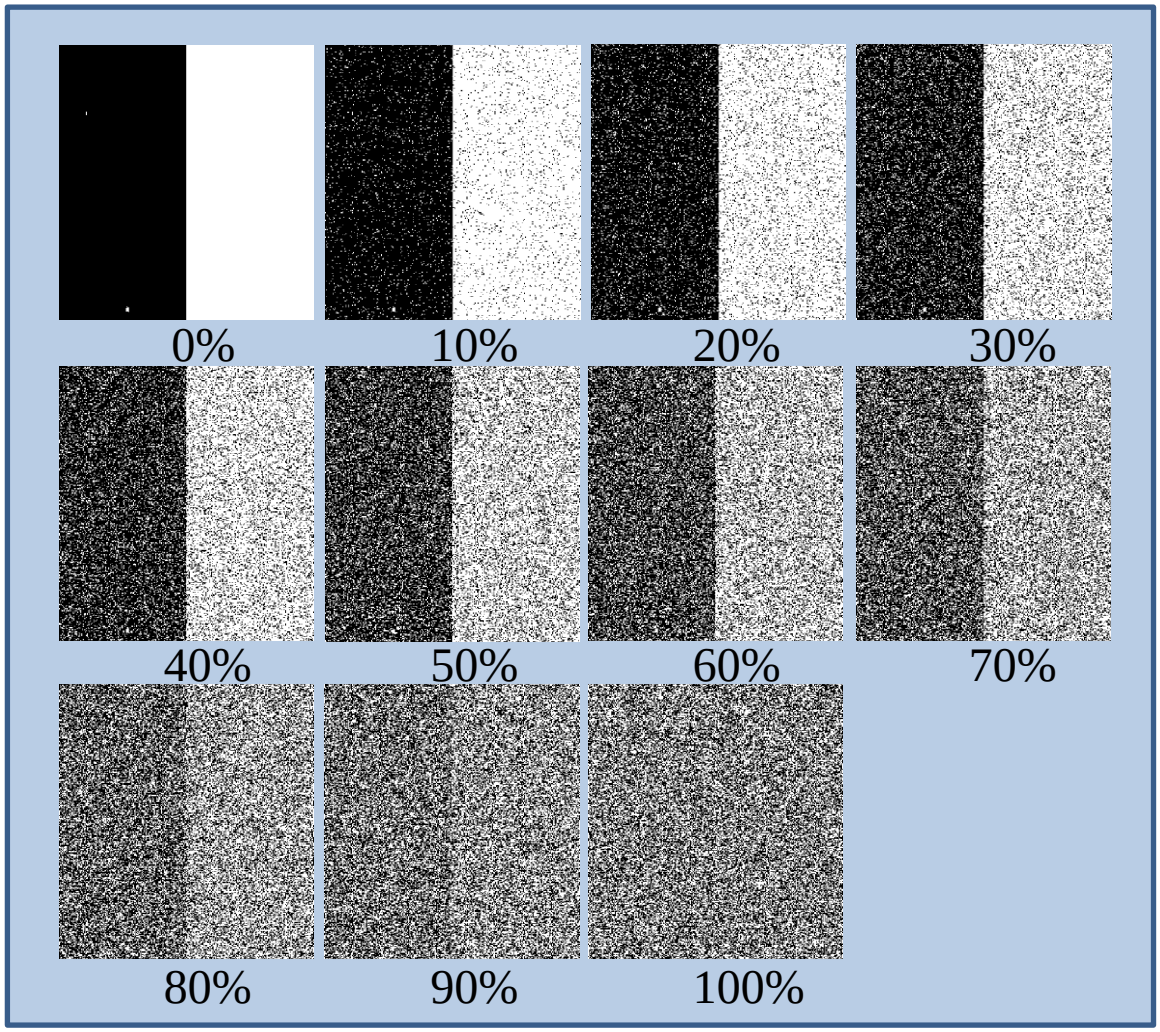


Results on simulated images

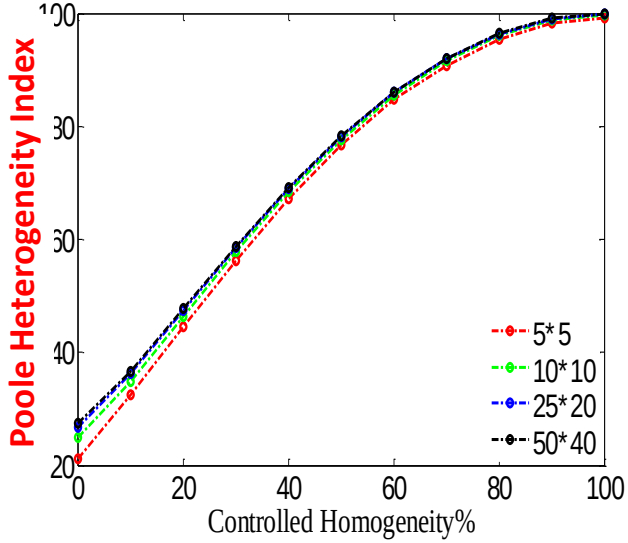
Heterogeneity curves – simulated images

(50% wheat + 50% coffee) with desired homogeneity from 0% to 100%.

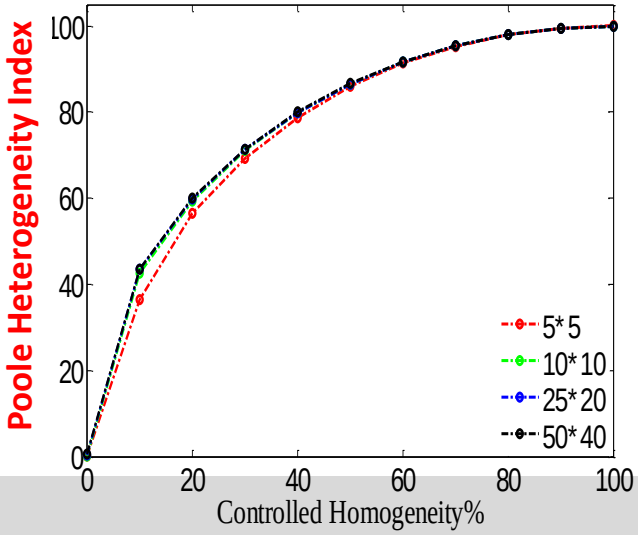
Single-pixel mixture



PCA based method



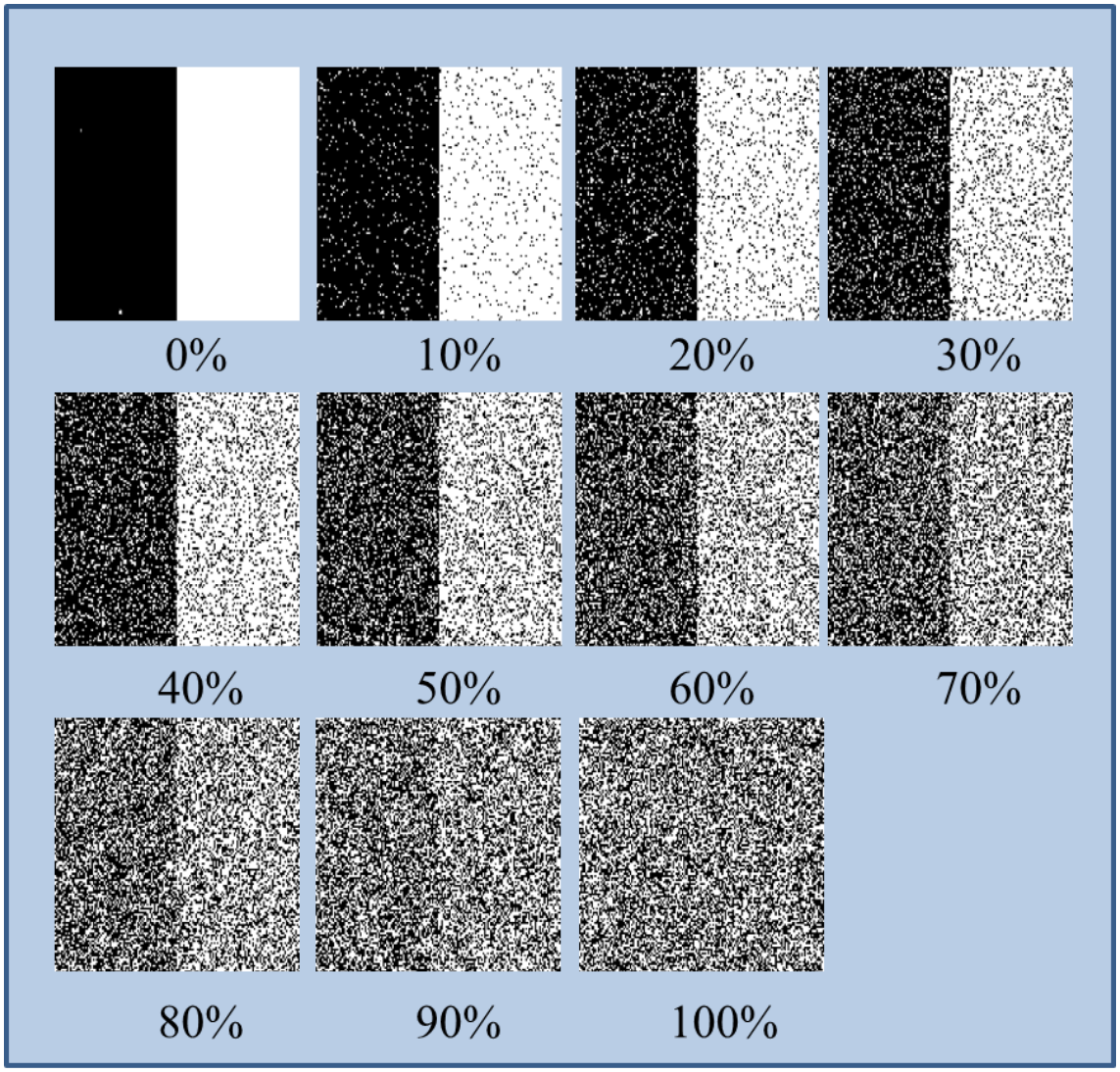
PLS-DA based method



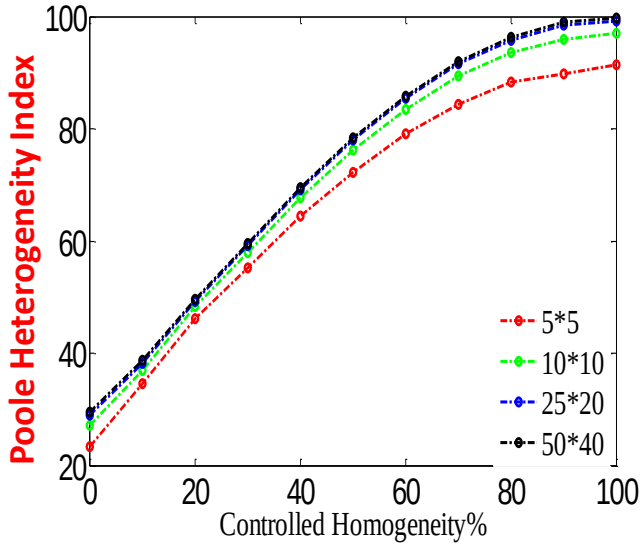
Heterogeneity curves – simulated images

2*2-pixels mixture

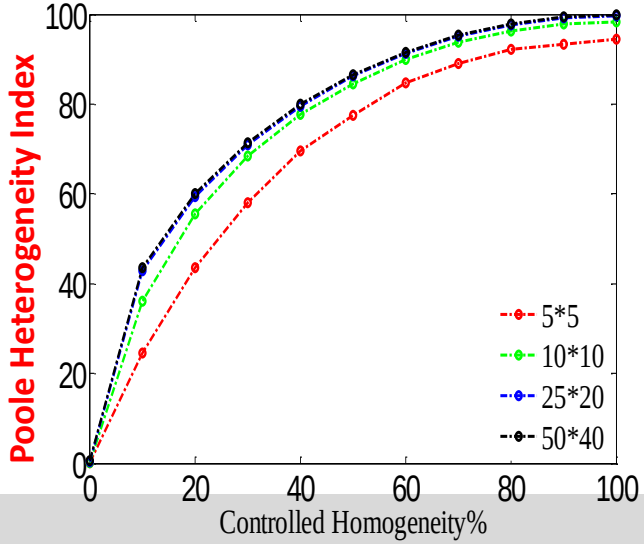
(50% wheat + 50% coffee) with desired homogeneity from 0% to 100%.



PCA based method



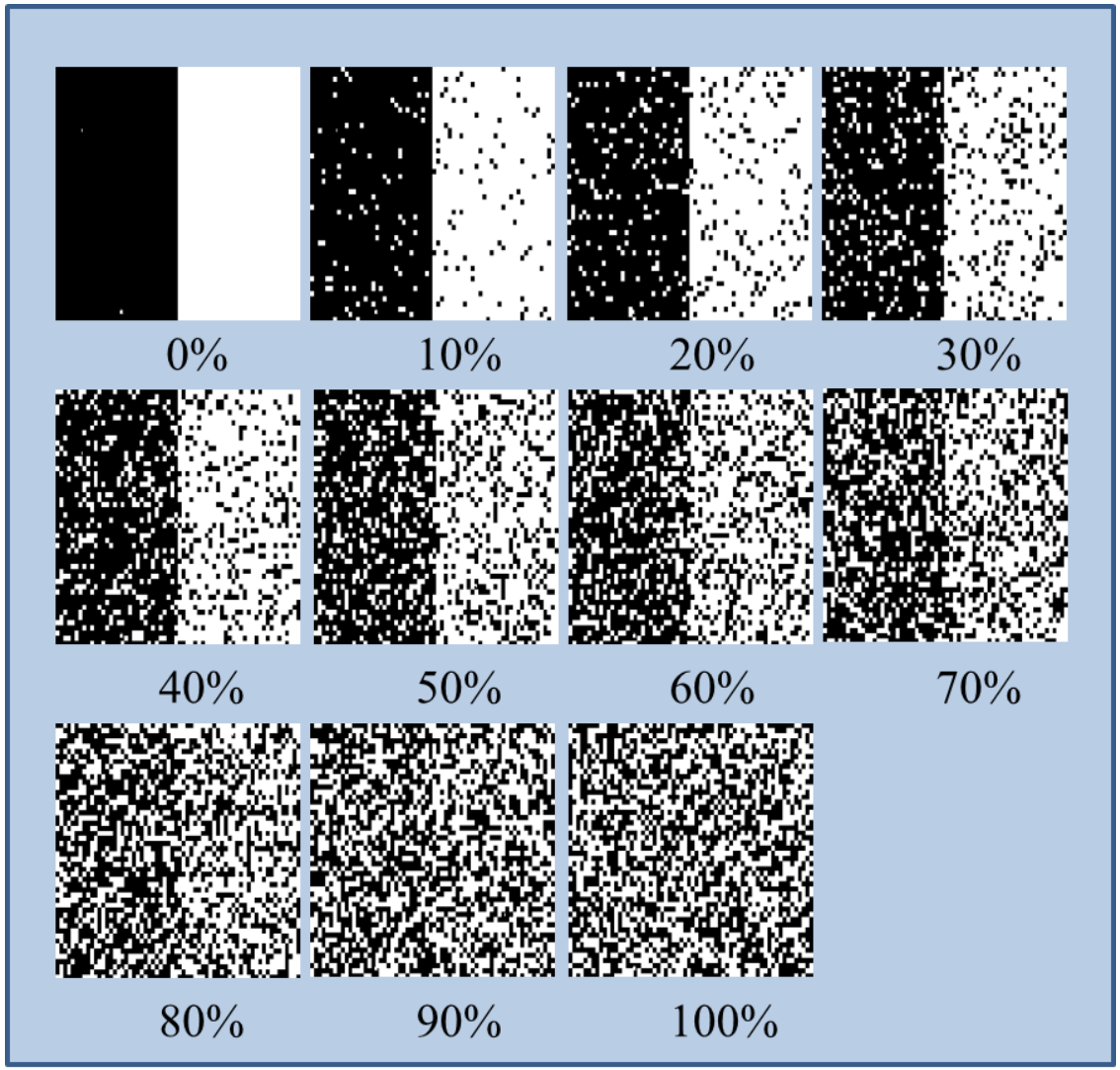
PLS-DA based method



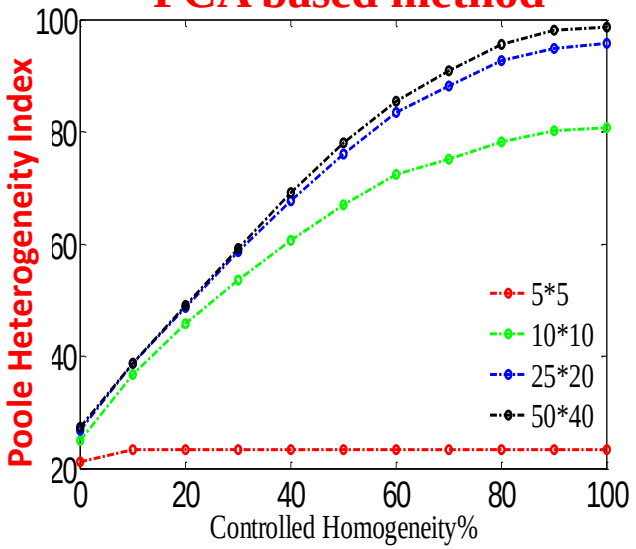
Heterogeneity curves – simulated images

(50% wheat + 50% coffee) with desired homogeneity from 0% to 100%.

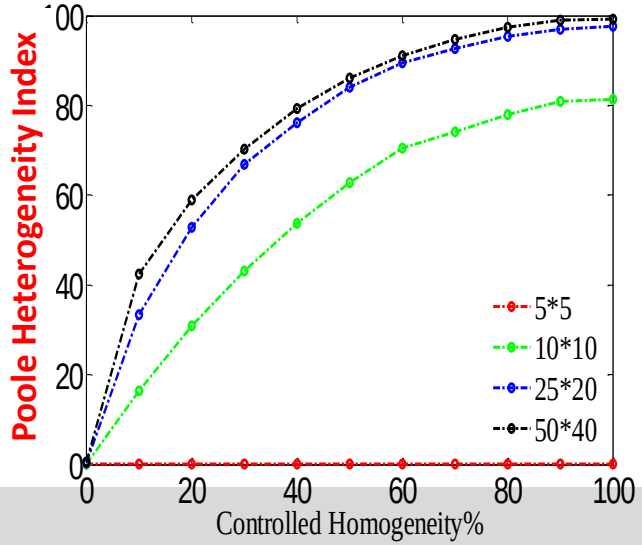
5*5-pixels mixture



PCA based method



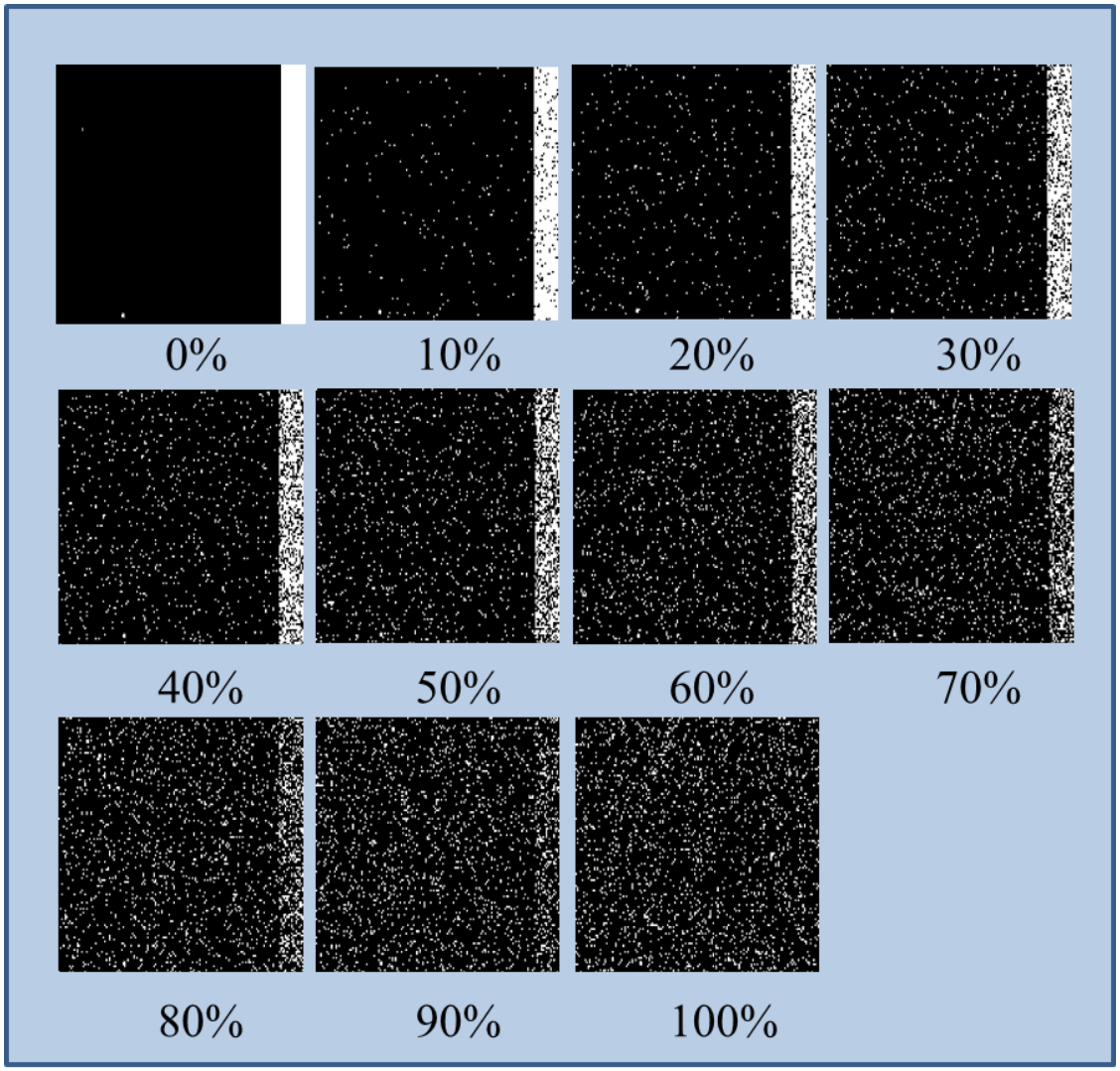
PLS-DA based method



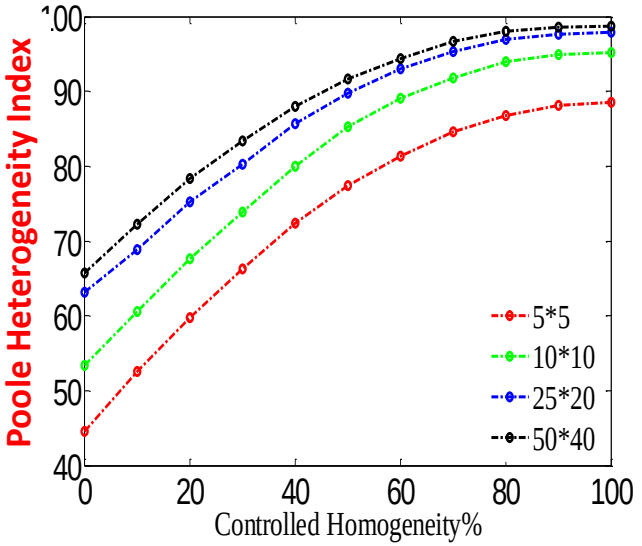
Heterogeneity curves – simulated images

2*2-pixels mixture

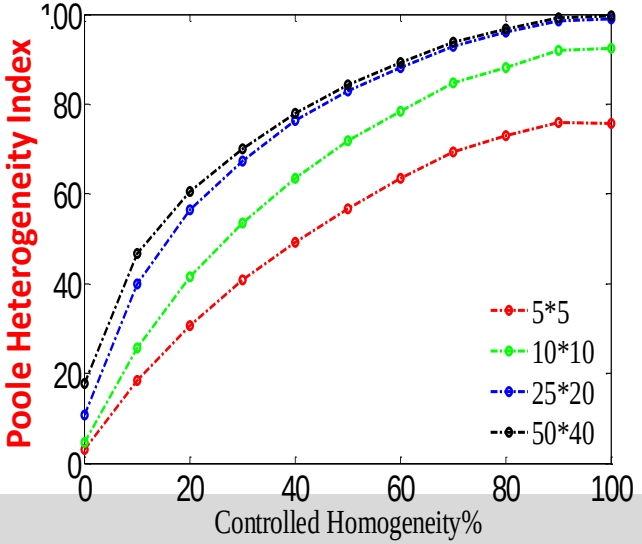
(90% wheat + 10% coffee) with desired homogeneity from 0% to 100%.



PCA based method



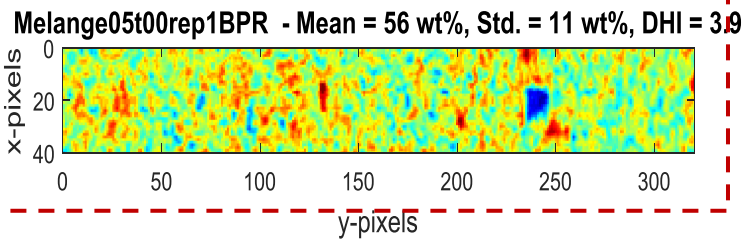
PLS-DA based method



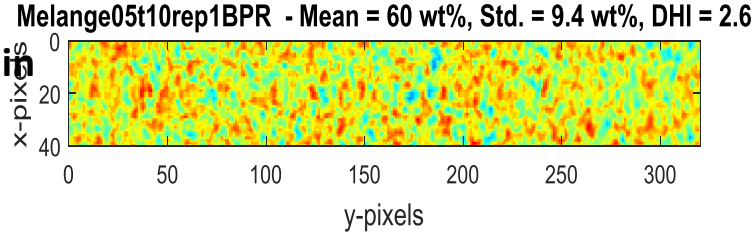
Results on real images

Heterogeneity curves – soya map

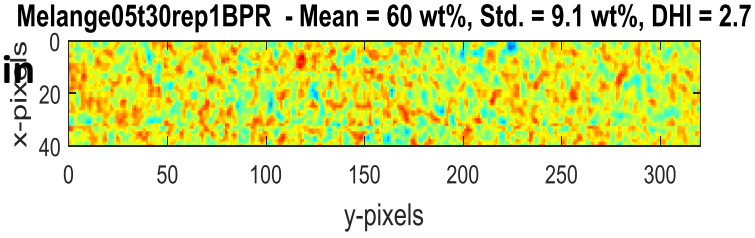
t = 0



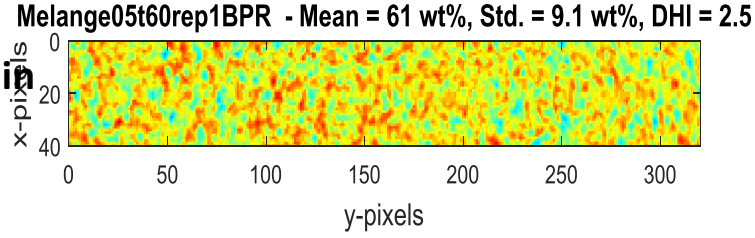
t = 10 min



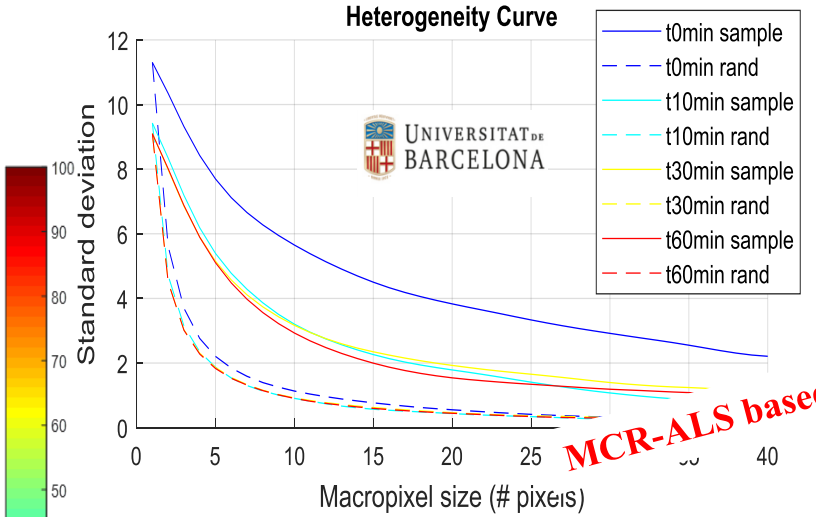
t = 30 min



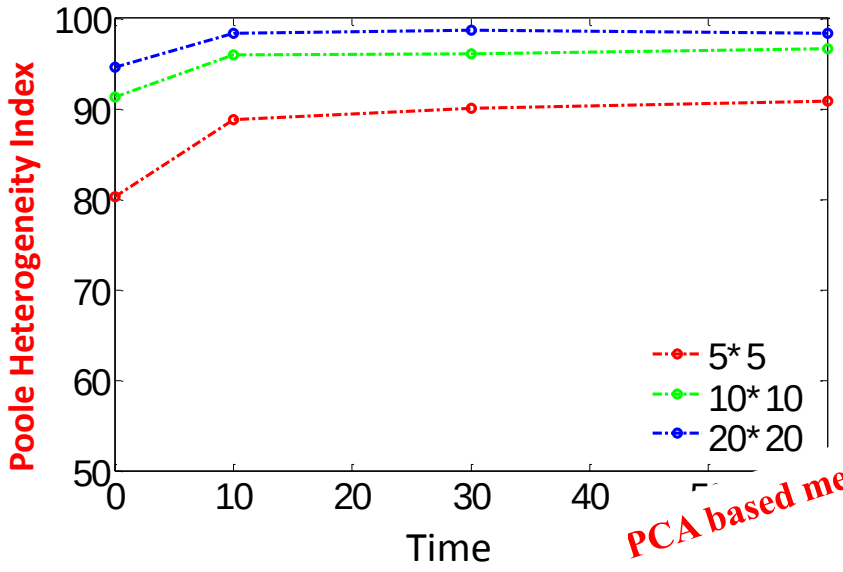
t = 60 min



60%Soya / 40%Corn



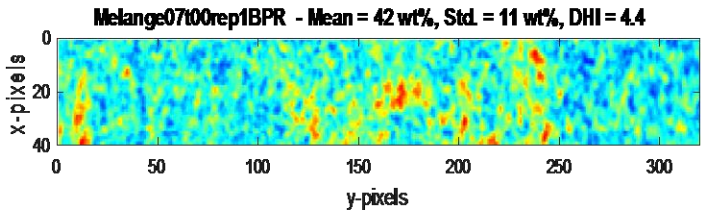
MCR-ALS based method



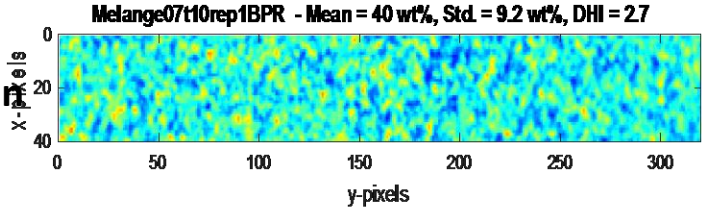
PCA based method

Heterogeneity curves – soya map

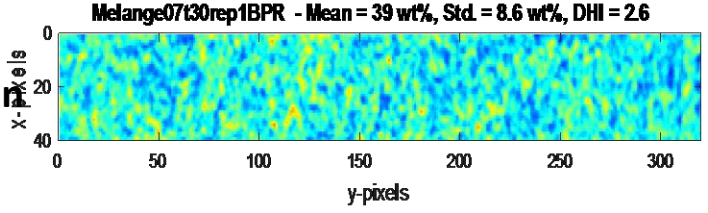
t = 0



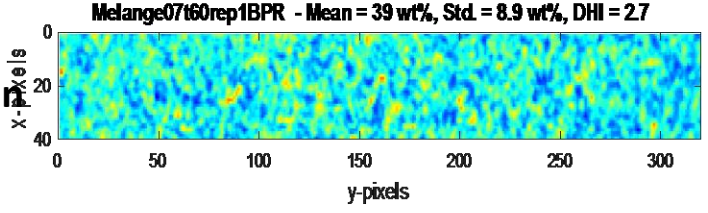
t = 10 min

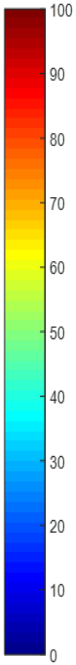


t = 30 min

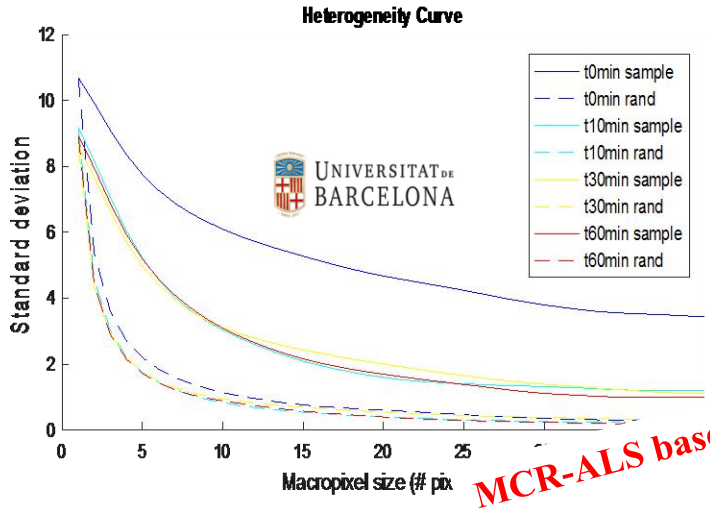


t = 60 min

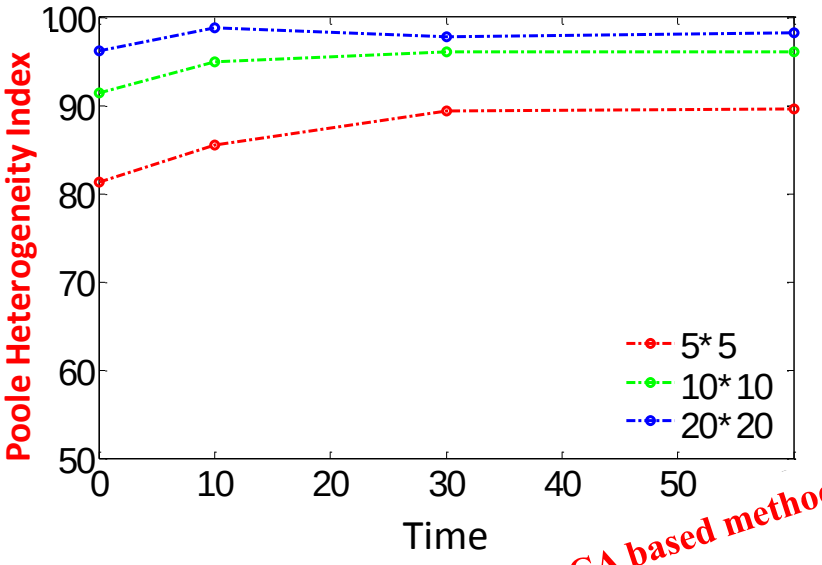




40%Soya / 60%Corn



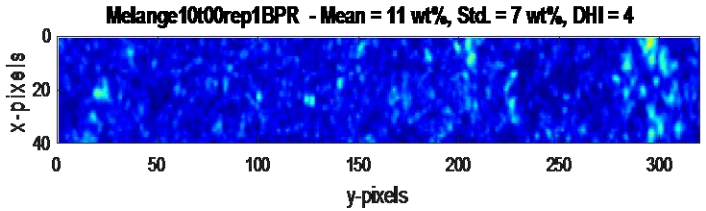
MCR-ALS based method



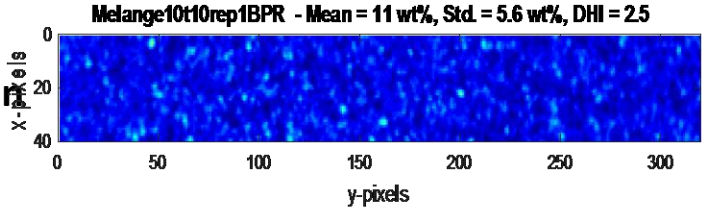
PCA based method

Heterogeneity curves – soya map

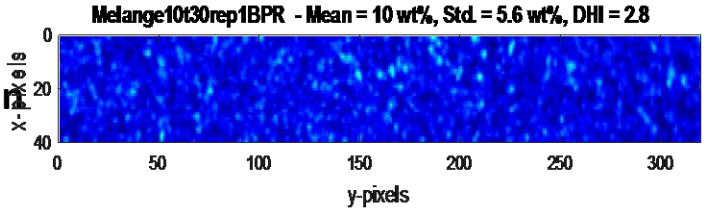
t = 0



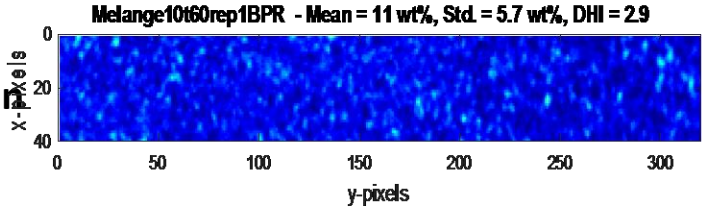
t = 10 min

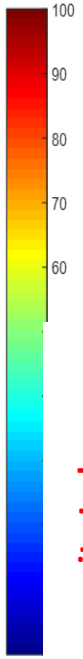


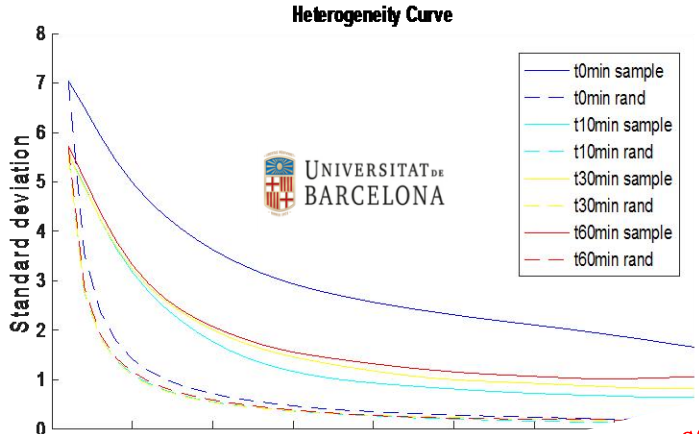
t = 30 min



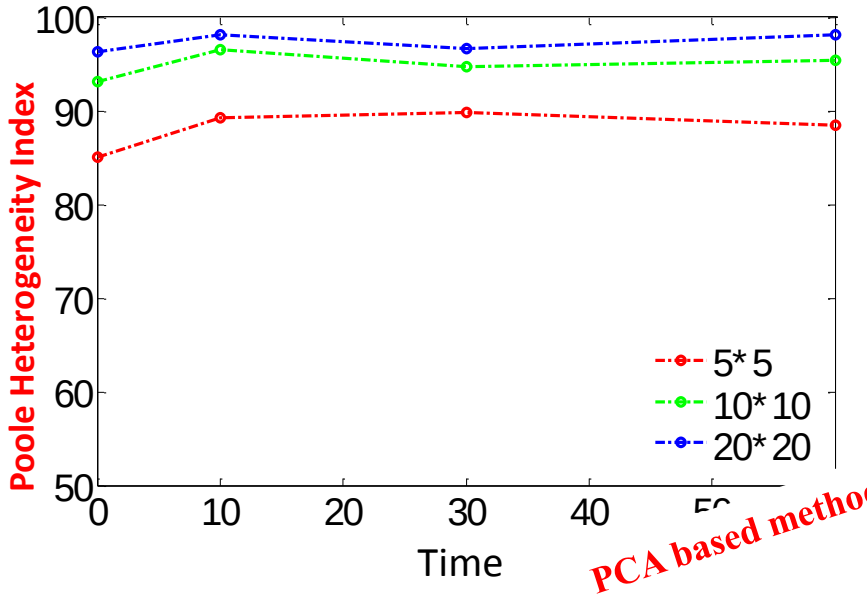
t = 60 min







MCR-ALS based method



PCA based method

10%Soya / 90%Corn

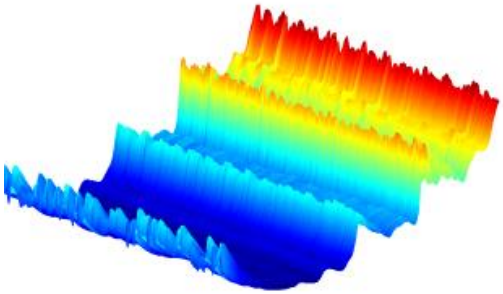
Conclusions

- Distribution maps of concentration or score values obtained at a pixel level help in the study of the distributional heterogeneity of the samples.
- Distributional heterogeneity can be represented by heterogeneity curves using micropixel analysis. These curves can help to follow the blending process.
- Under appropriate macropixel size, the heterogeneity indexes curves can be used to monitor the continuous mixing process to judge blending endpoint.
- The mixing proportion of materials, macropixel size and the particle size of sample will influence the value of the heterogeneity indexes.
- The proposed method based on PCA scores can be used for the analysis of heterogeneity distribution in hyperspectral images without calibration models or binarization processing.

Vibrational Spectroscopy and Chemometrics

Training Session

12 March–16 March 2018



Wallonie recherche CRA-W

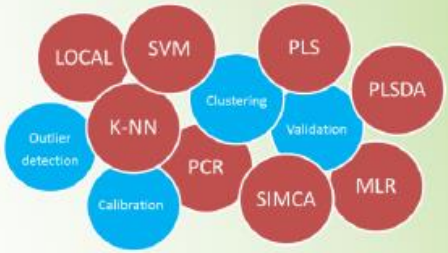
Vibrational Spectroscopy

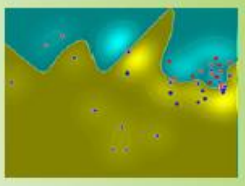
NIR/MIR/RAMAN/NIR microscopy and Imaging

Embedded & on-line NIR/networks/uncertainty

Sampling/Tips and Tricks

Chemometrics applied to vibrational data





Invited speakers

TOM FEARN

PIERRE DARDENNE

Thank you for your attention