

Unconventional machine vision techniques for industrial applications

Study:

Physics Degree – Physics of Matter @Physic department of Milan

PhD – Physics of matter (Molecular Physic) @ Polytechnic University of Marche, Materials engineering department

Activities (from the past up to now)

- Interferometric systems at VIRGO (EGO) gravitational waves detector
- Non destructive inspection and materials characterisation with Neutrons/X-ray diffraction, tomography, small angle scattering
- Optical imaging and laser profilometry for industrial applications
- Spectroscopic methods for materials characterisation
- Hyperspectral methods for materials and pharmaceutical products analysis



Vittorio Calbucci
SEA Vision R&D Engineer

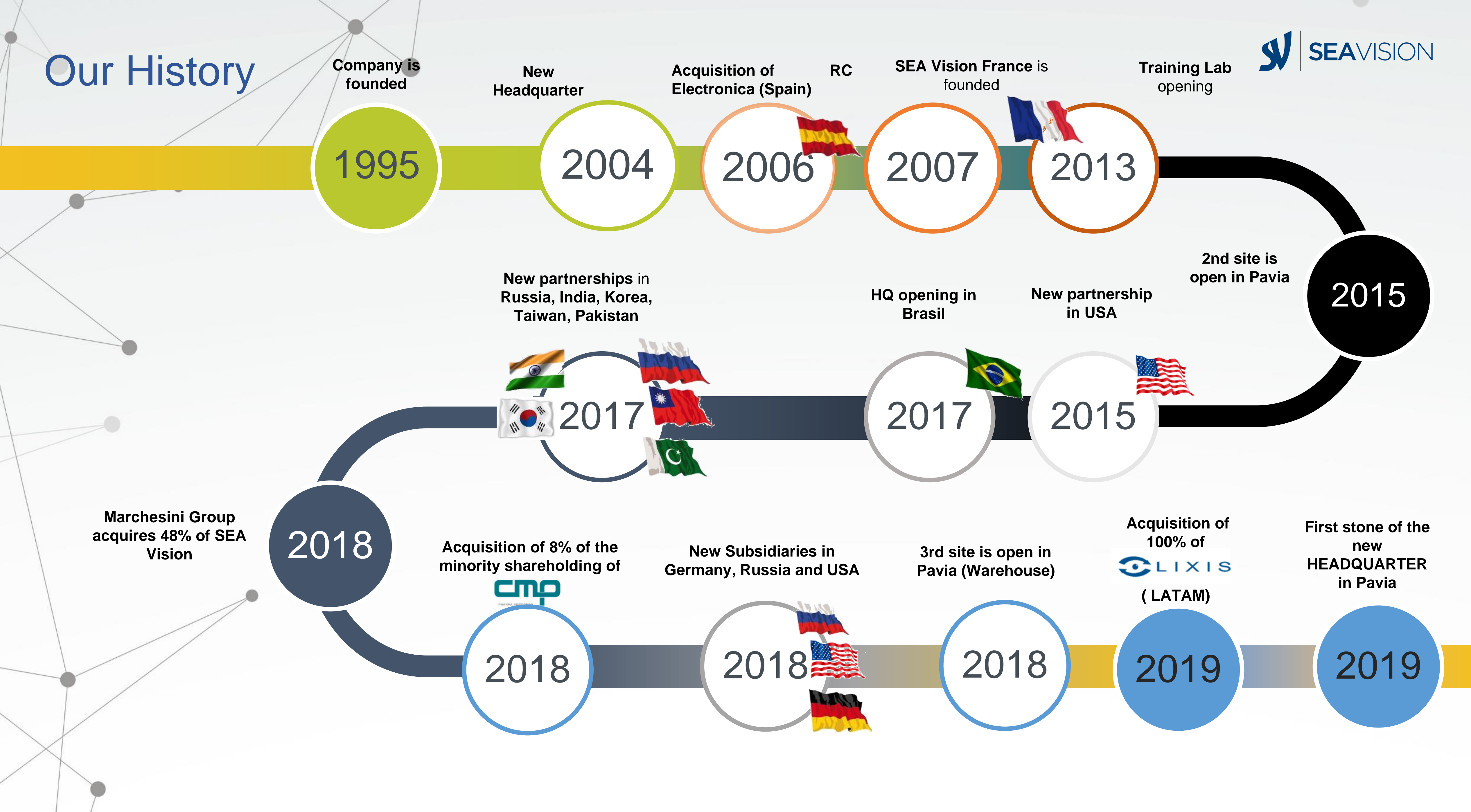
Area of business

Vision Inspection
systems for Pharma
Industry

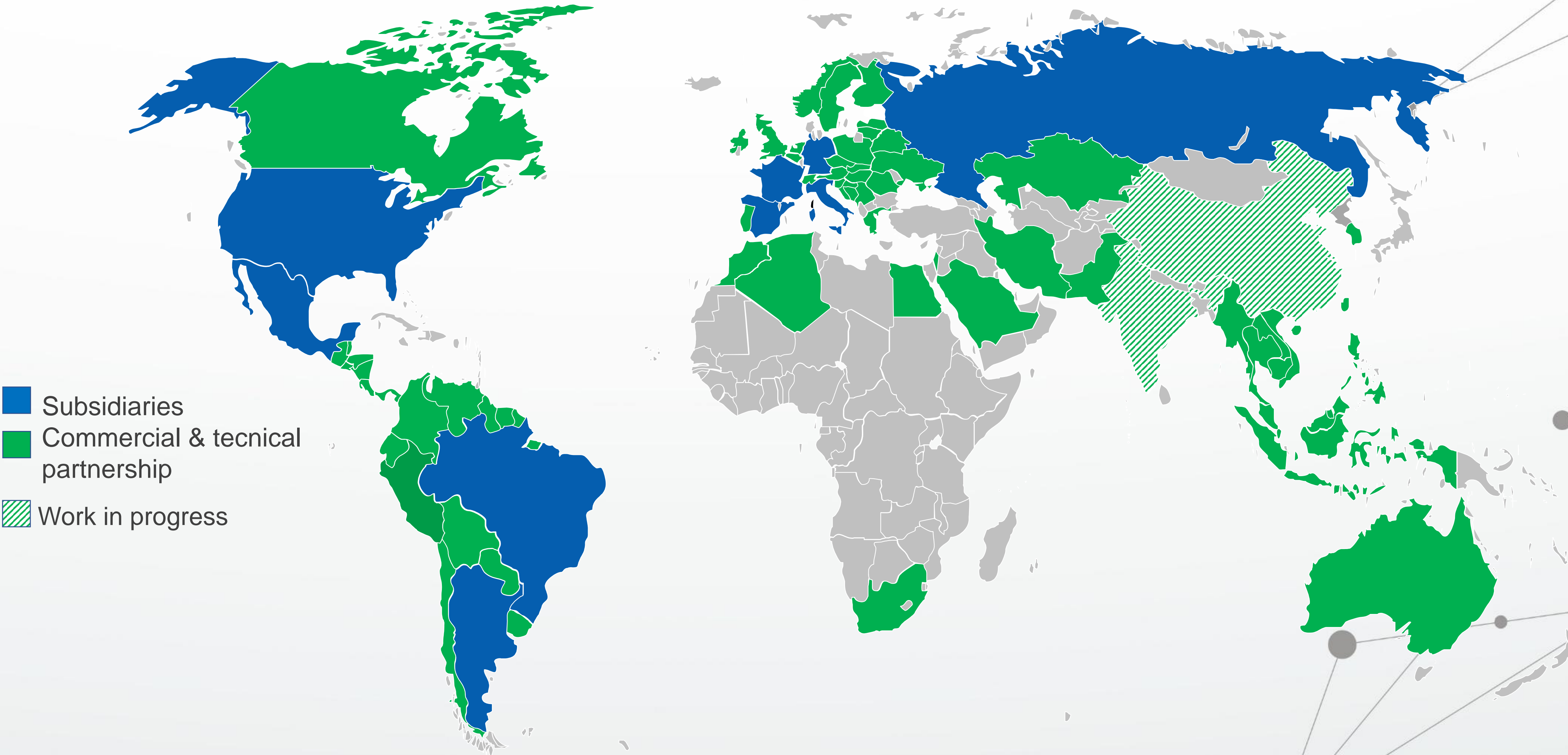
Software for Track &
Trace + Aggregation
of Pharma Products

Business Intelligence
Software Suite

Our History



Today global reach

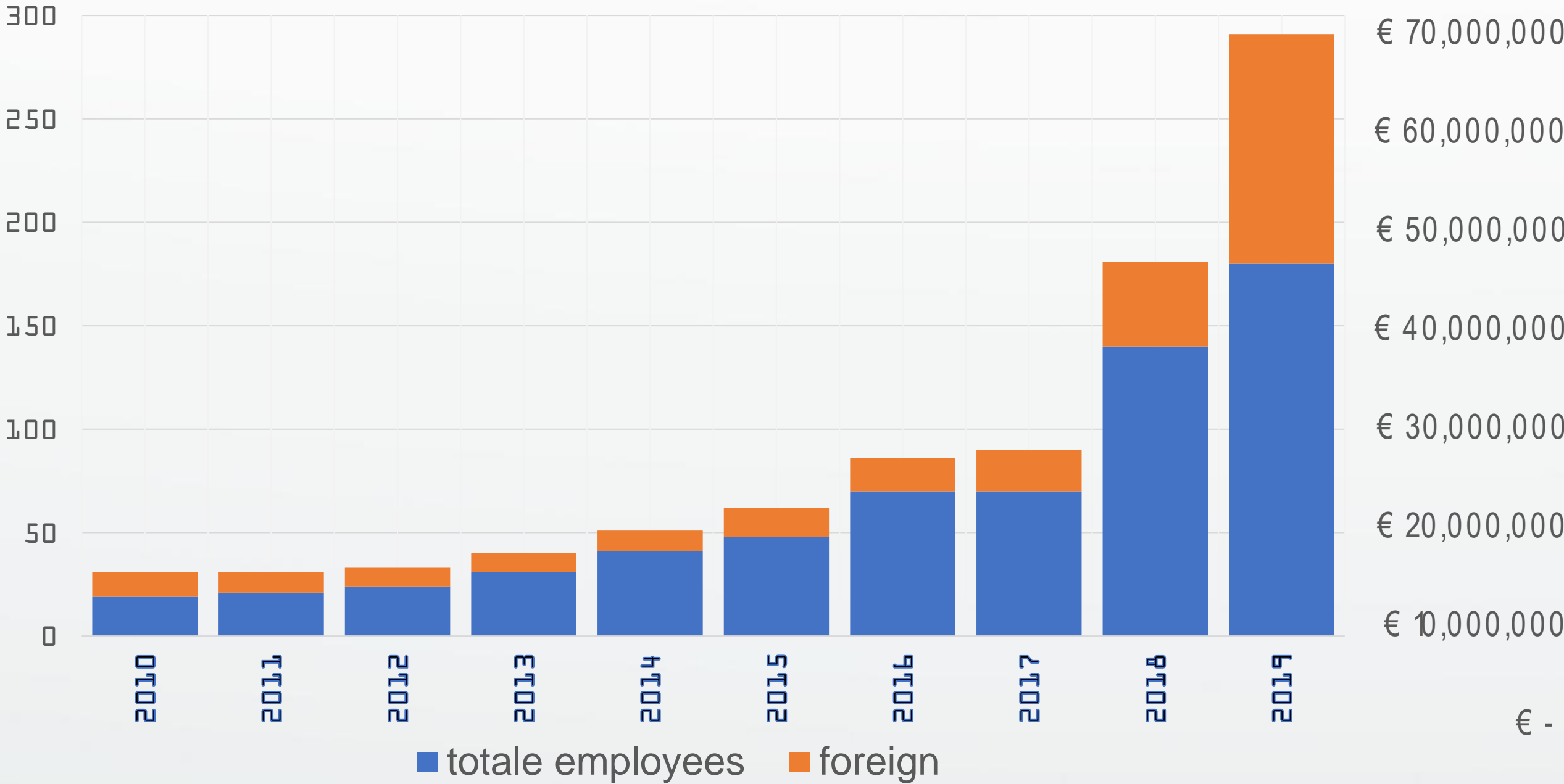


Employees and Sales results

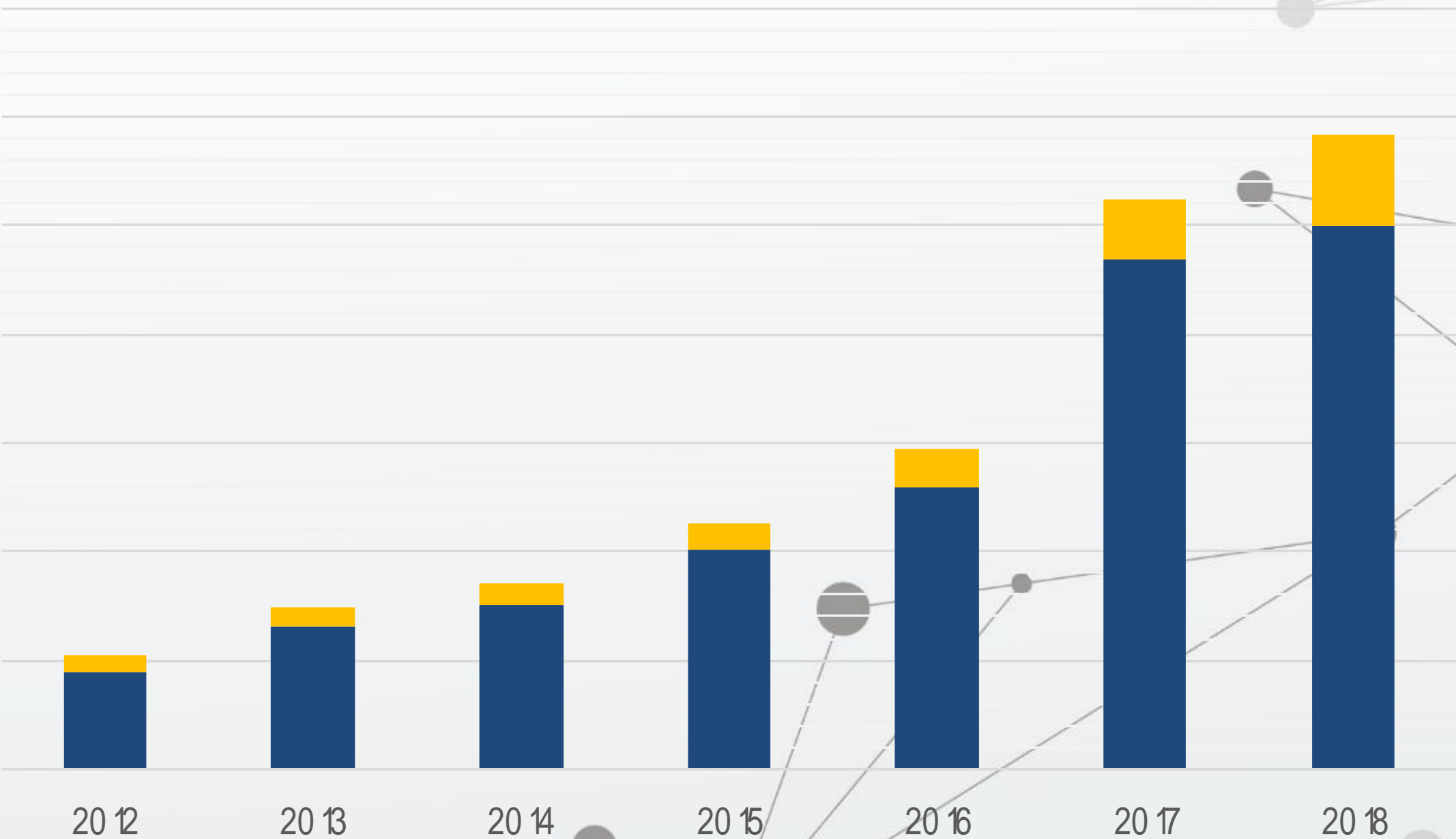
Our staff expertise combined with a proportional staff growth rate ensure customers the highest level of service.



Employees



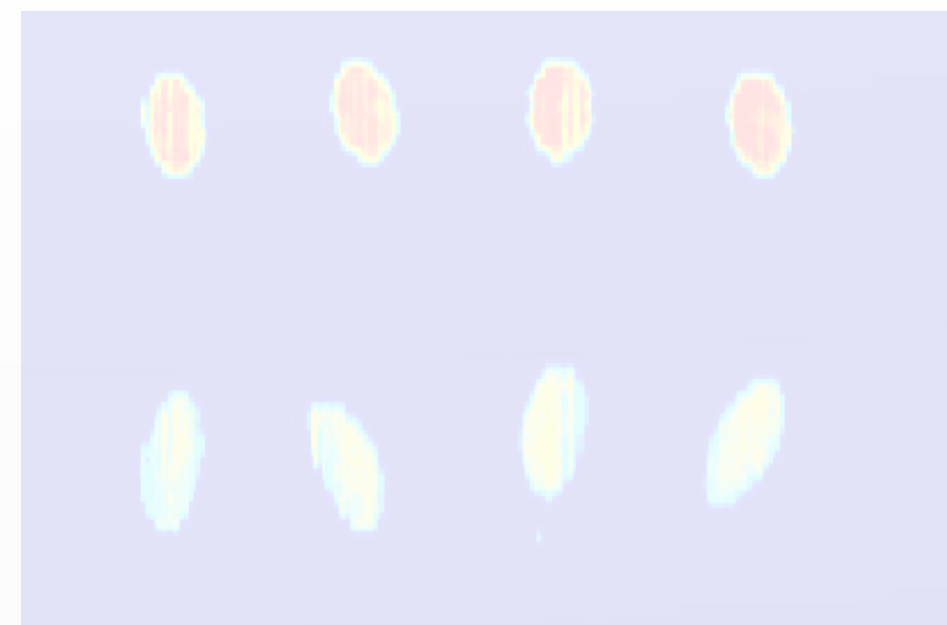
Sales results



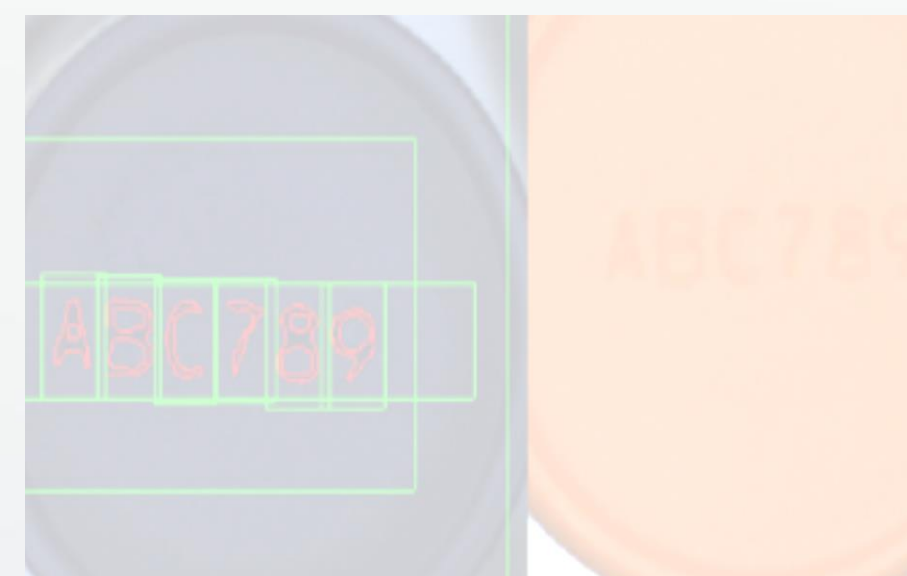
SEA Vision Products



HARLEQUIN
vision software
for the qualitative and
quantitative control of
pharmaceutical products



HARLENIR
vision software
for the chemical
composition inspection
of pharma products



OCV
solutions for the
traceability of the drug
along the distribution chain
and vision qualitative
control

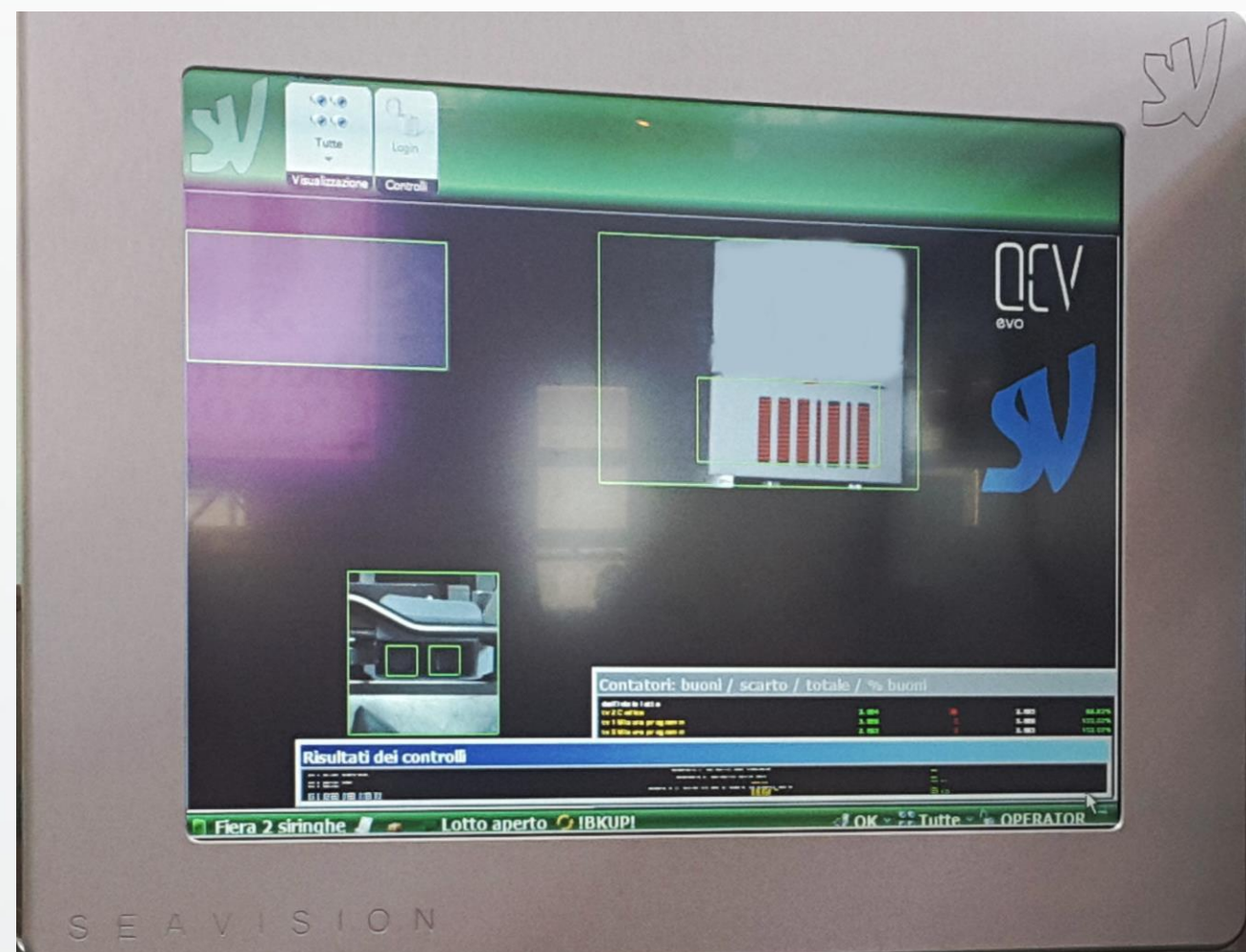


YUDOO
modular suite software for the
management of optical drug
production lines 4.0 including
data collection, data analytics
and business intelligence

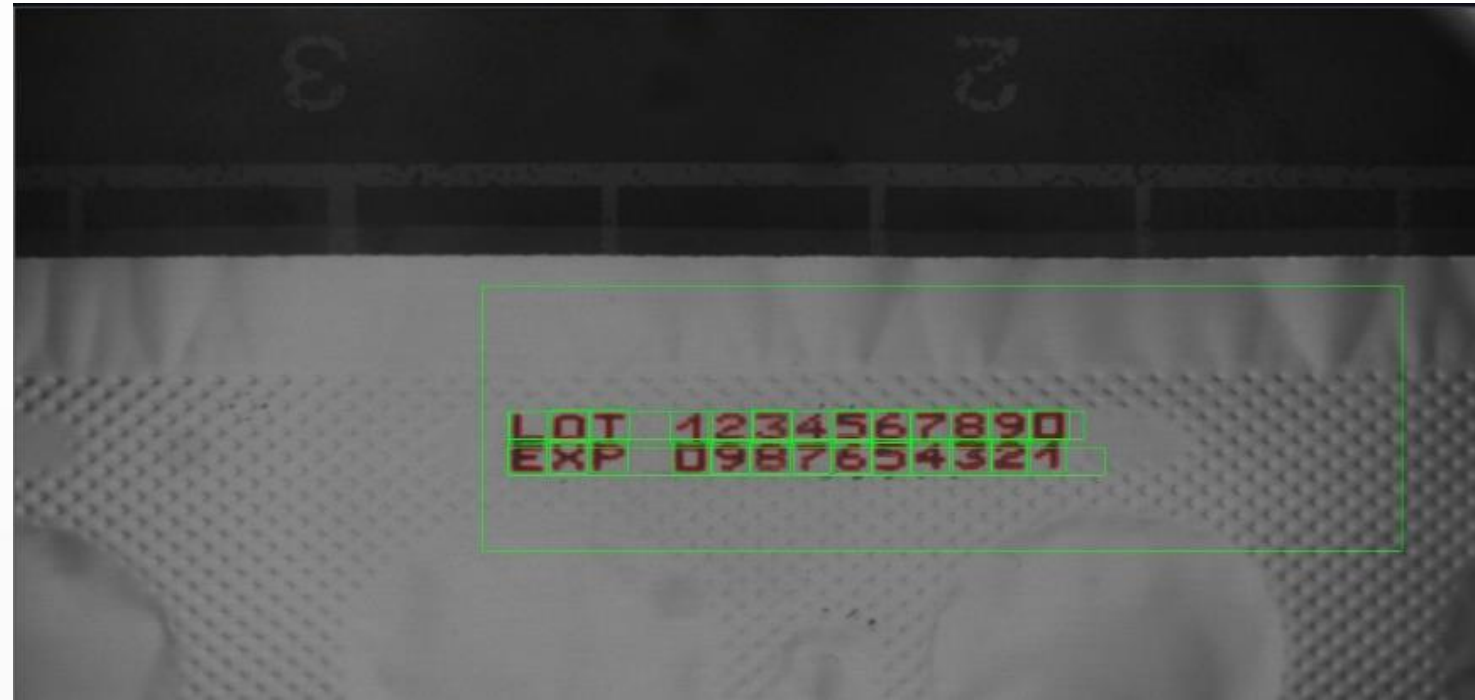
OCV

OCV is our vision system that can be adapted to basically any kind of control requested in the primary and secondary packaging process.

On of the most powerful tools of the OCV are **serialization / aggregation** and the **programmable measure**.



OCV - Serialization and Aggregation



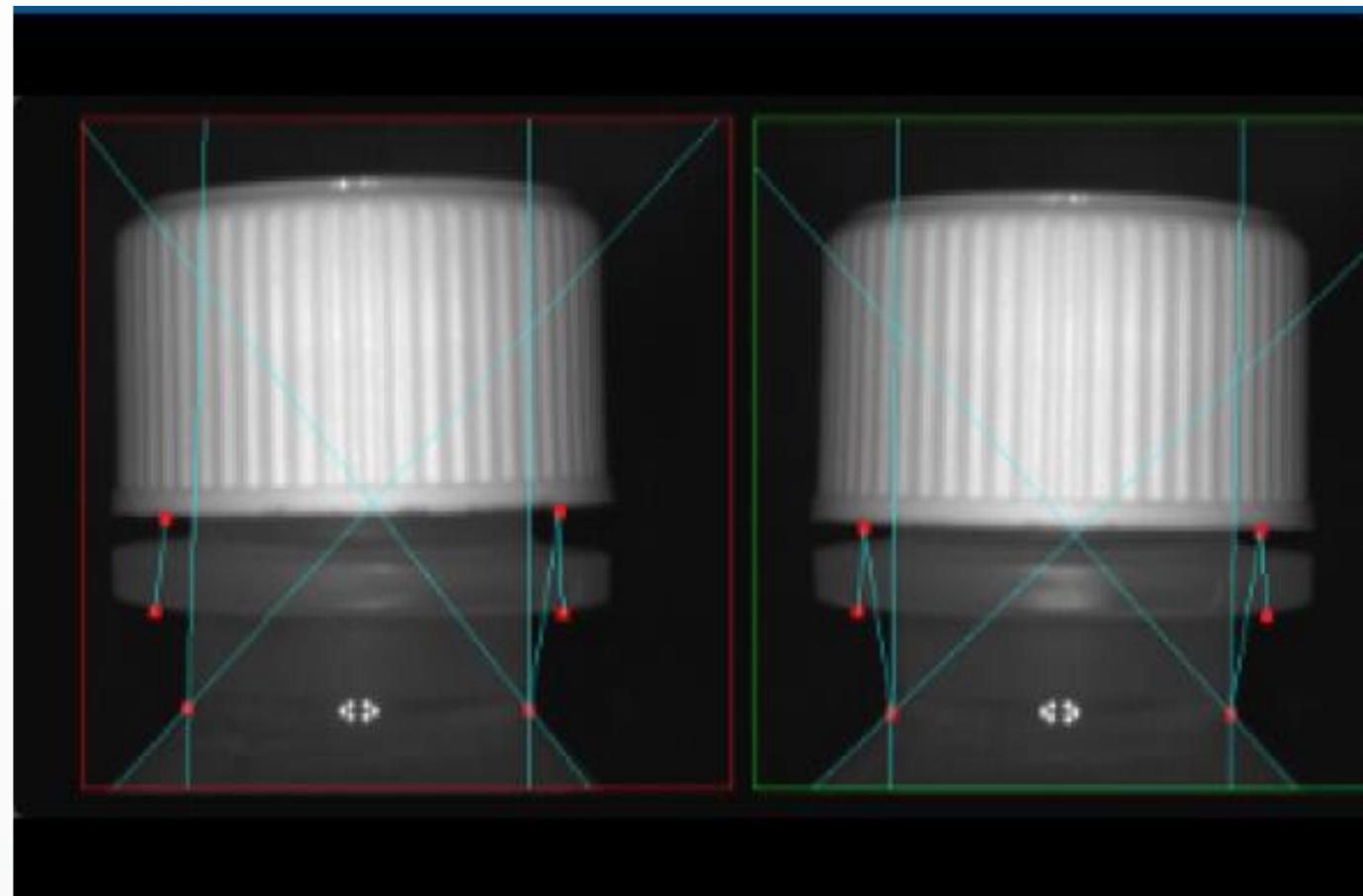
OCV is the platform that we use for **serialization and aggregation application**.

In addition can operate:

- ▶ Real time printer management
- ▶ Real time operations
- ▶ Remote Batch connector (Start,Stop,Hold,etc...)
- ▶ In Batch Rework operation
- ▶ Adaptable configuration for manufacturing process

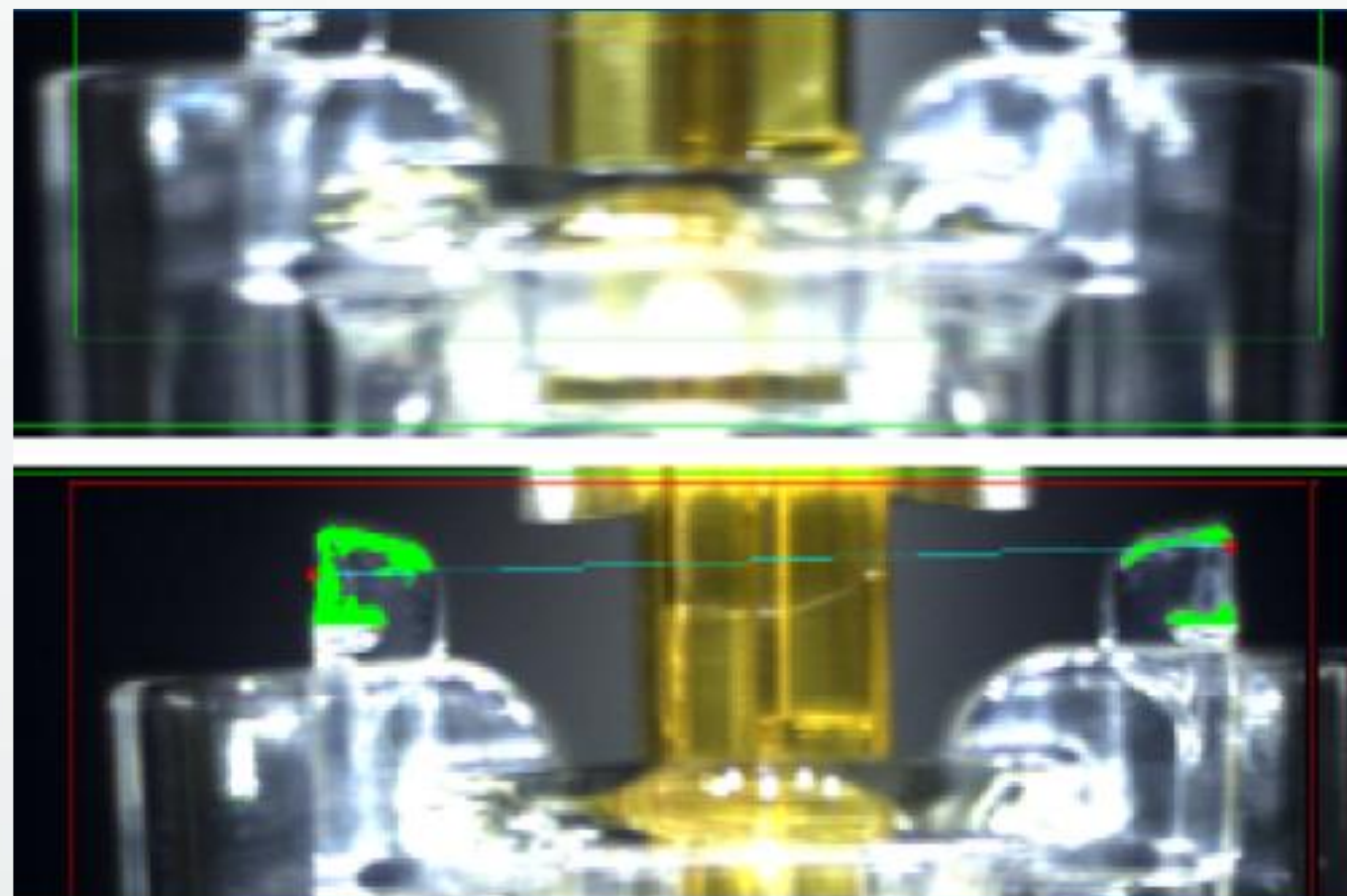


OCV - Programmable Measures



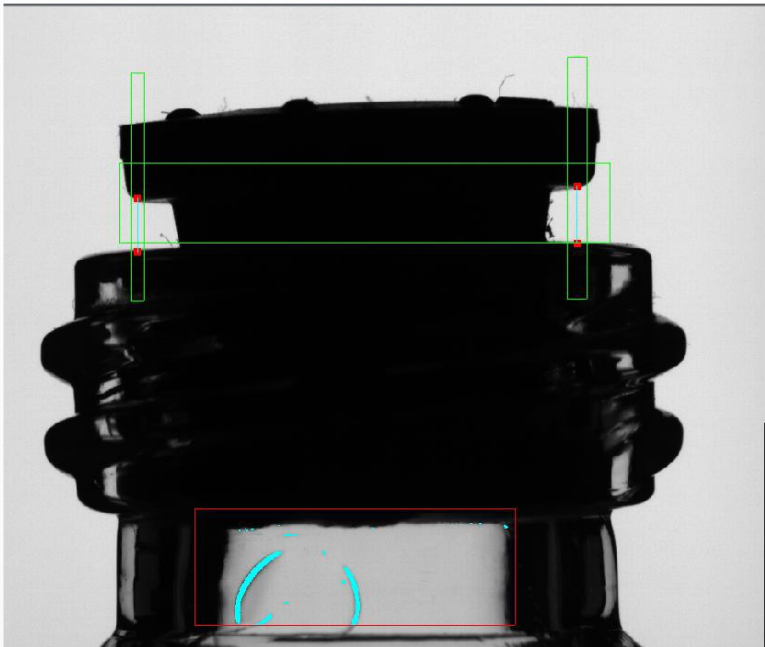
Programmable Measures are a library of simple image processing tools (edge detection, blob detection, extraction of pixels, distance calculation...), allowing the operator to create a customized application for image analysis with specific acceptance conditions.

This tool is very powerful because allow us to create for a standard library of algorithm a step-by-step control that may have multiple check build inside.



OCV - Integrity Checks

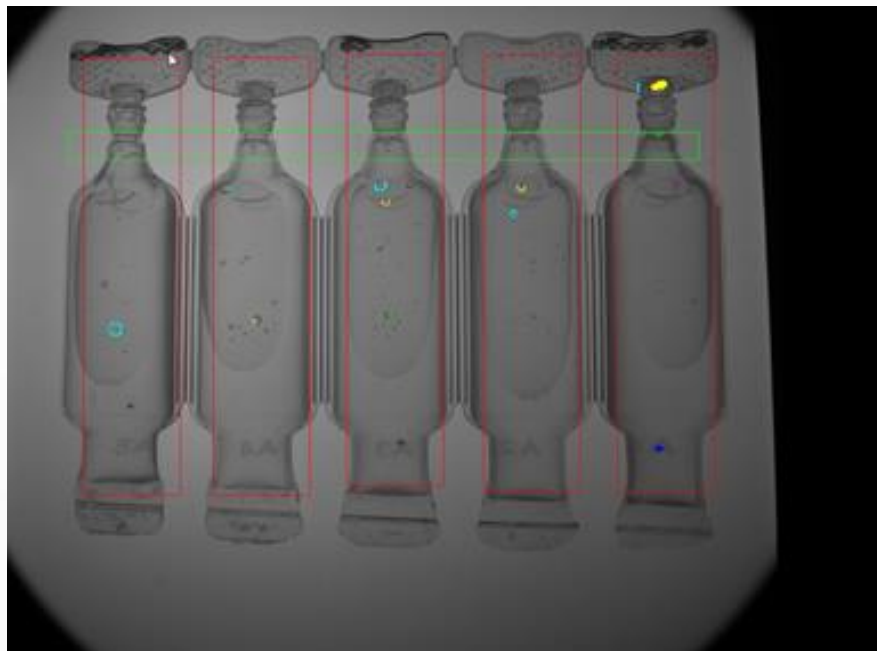
OCV was developed back in the days for code reading and OCV/OCR controls.



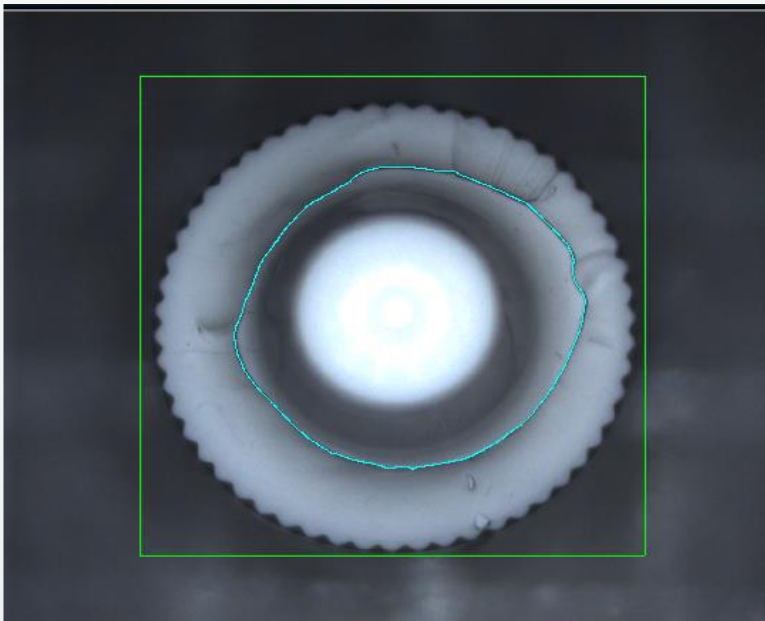
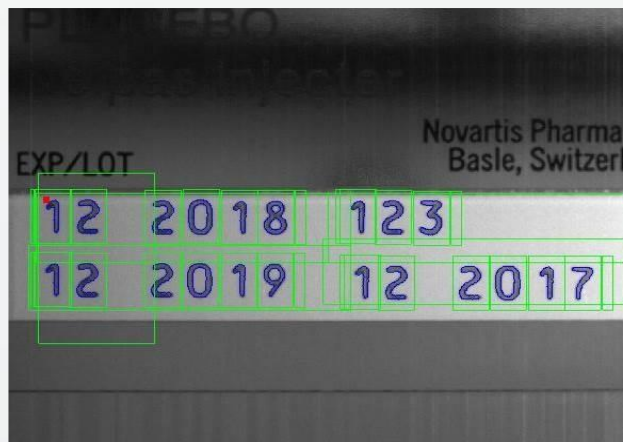
Cap Position and glass scratch



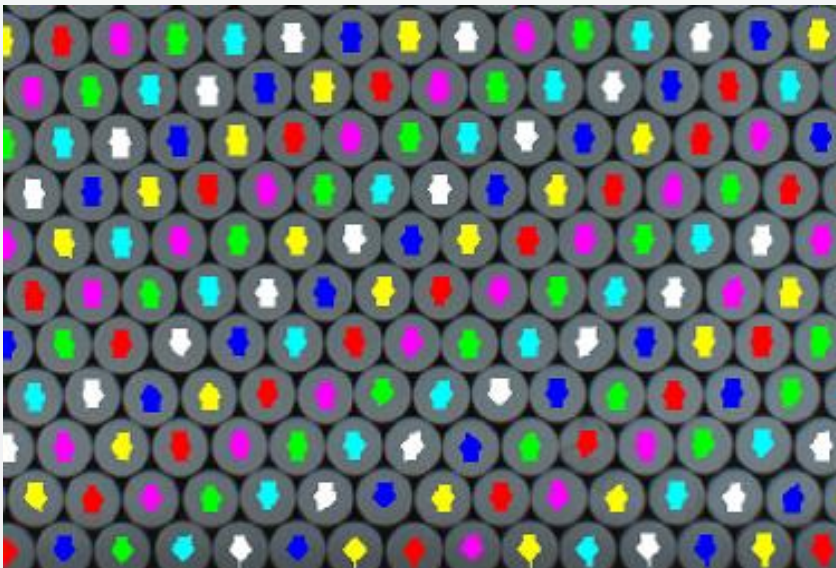
Liquid presence, label presence and ampoules ring check



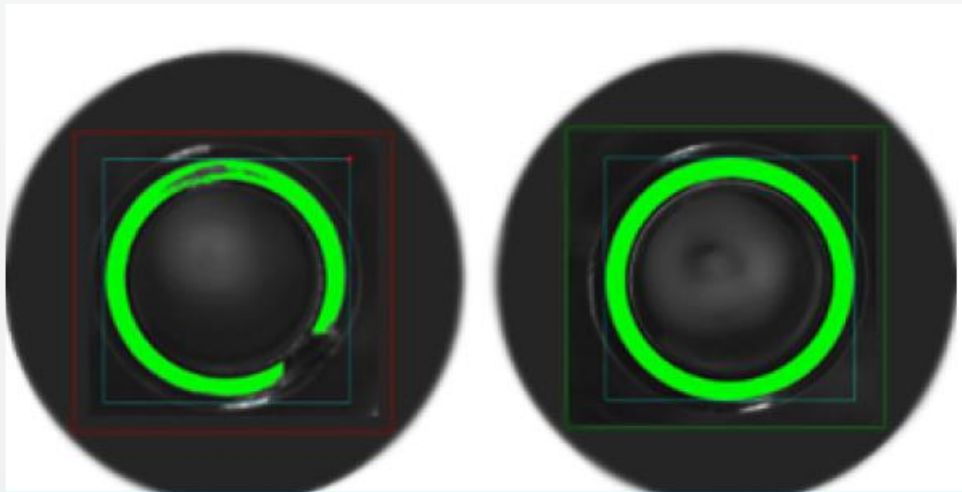
Impurities on plastic



Sleeve Presence



Product quantity check



Bottle Neck Integrity

OCV / OCR

Harlequin

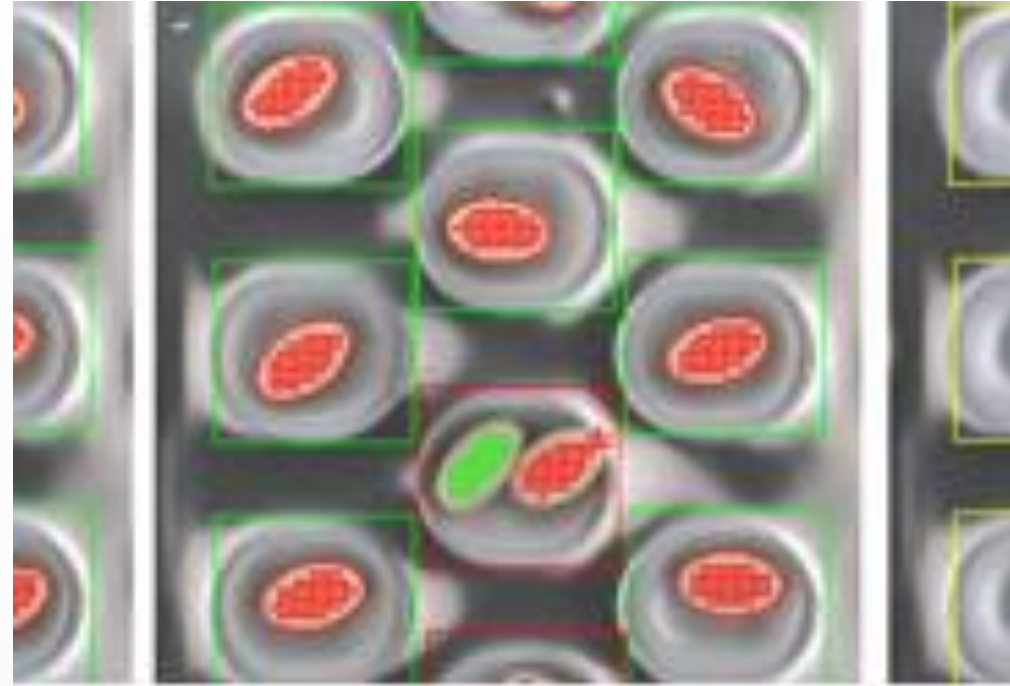


Harlequin is the vision system for the inspection of oral solids forms and pharmaceutical kits on blistering and thermoforming machines

- ▶ Components presence/integrity in white PVC, transparent and paper-made tray
- ▶ Mainly vials, syringes, ampoules
- ▶ Barcodes, 2D codes and online-printed variable data



Harlequin - Components presence/integrity



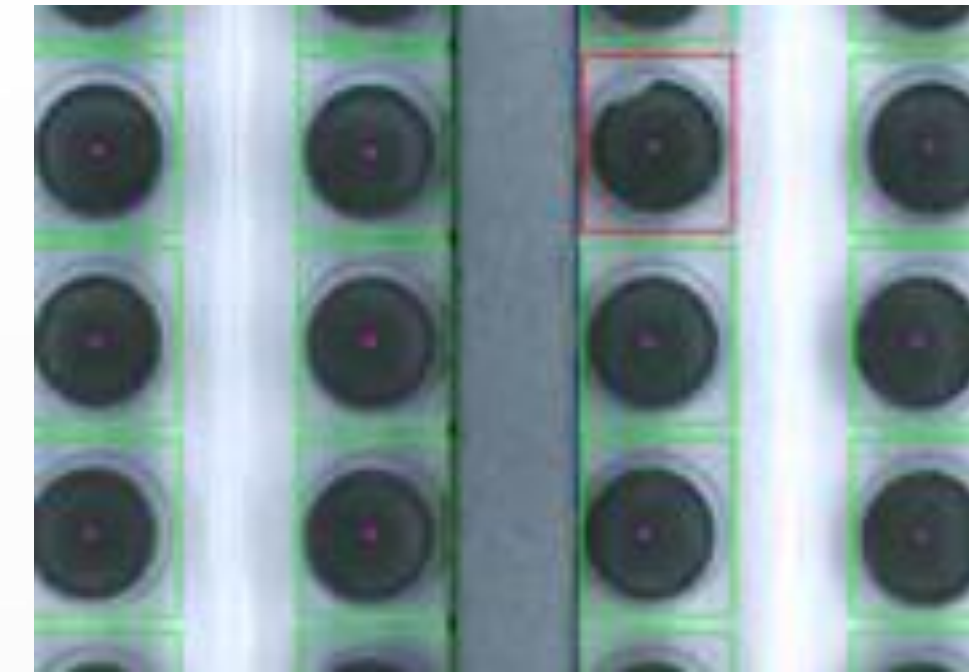
Tablets and capsules inspection on ALU-ALU:

- Presence, Color, Integrity
- Multi-product on the same cavity

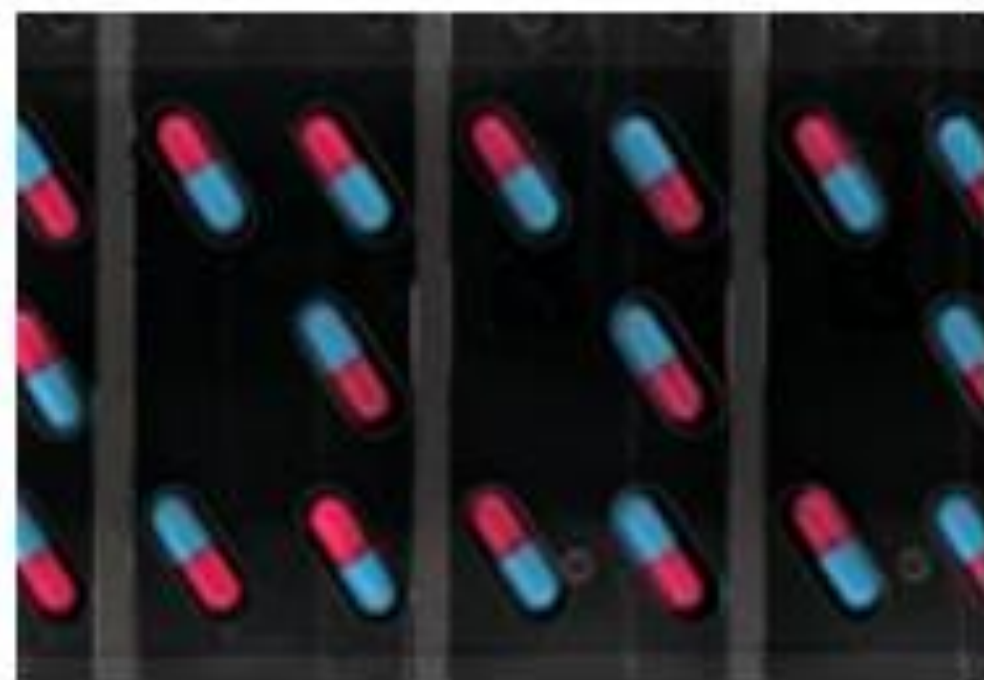


White Tablets on White Blister:

- Presence of defects: Cracks, Dents, Black Dots
- Chromatic inspection



Tablets Inspection on transparent PVC:
Presence, Color, defects



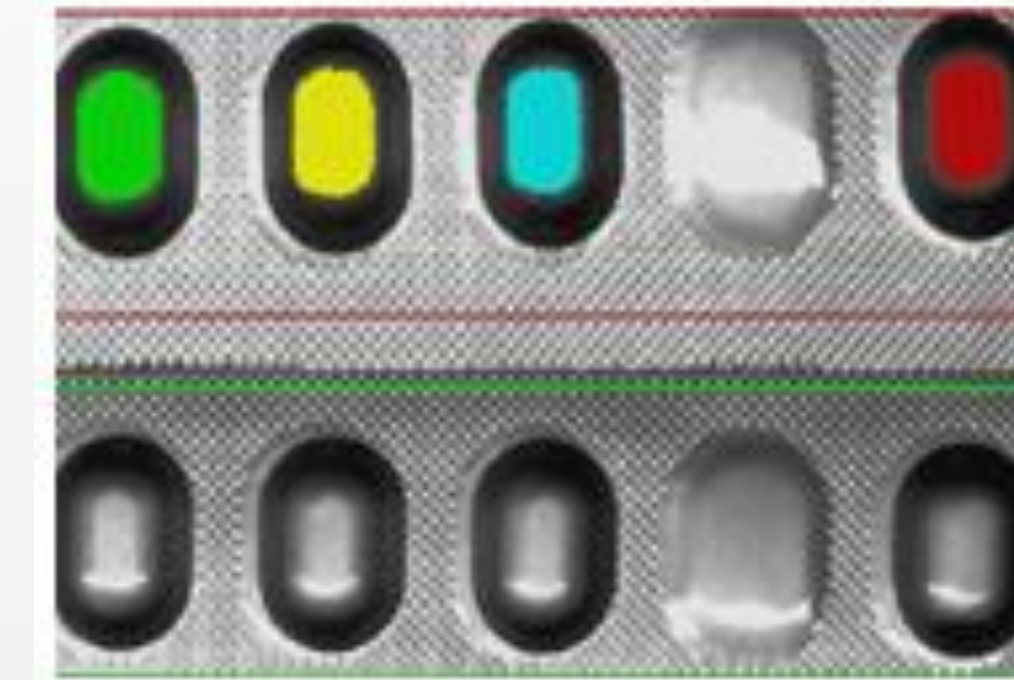
Capsules Inspection on PVC

- Presence, Color, Integrity, Dimensions
- Double Chromatic Check for color inspection



Capsules in Blue/Transparent Blister

- Presence, Color
- Double products in the same cavity



Control in the cavity of the shape and tablet position

Harlequin - Packaging integrity



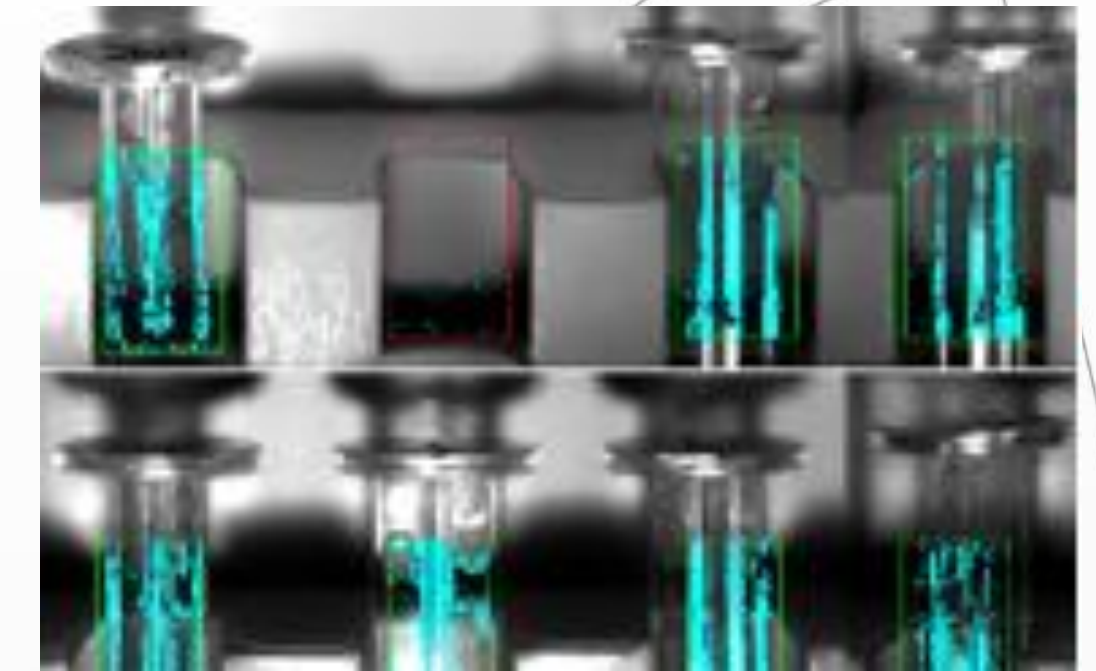
Presence of impurity and defect on the blister surface



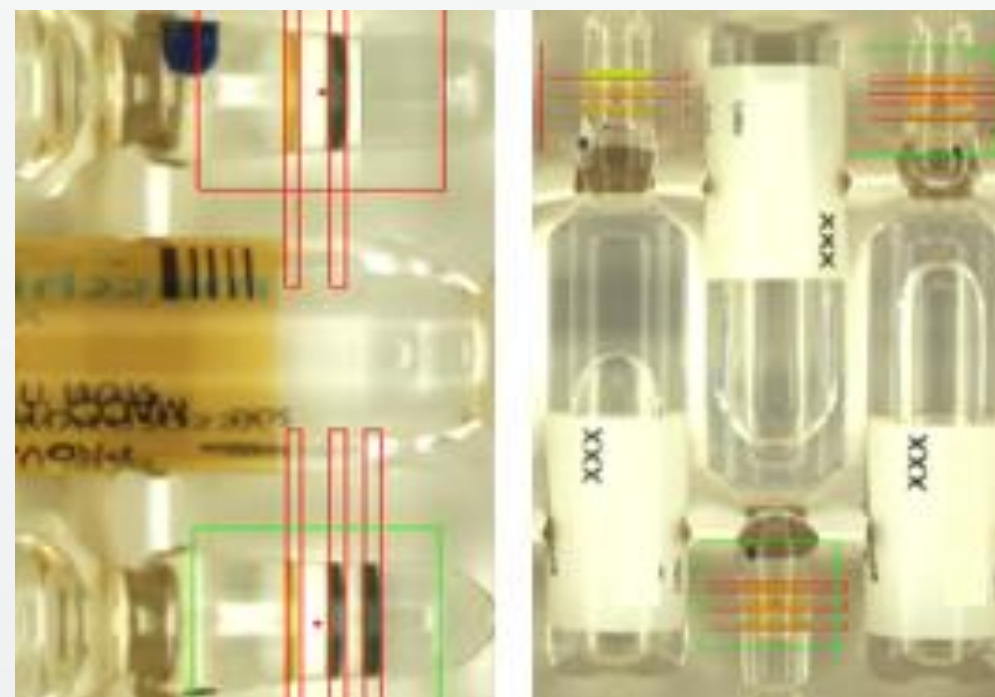
Control of components in tray



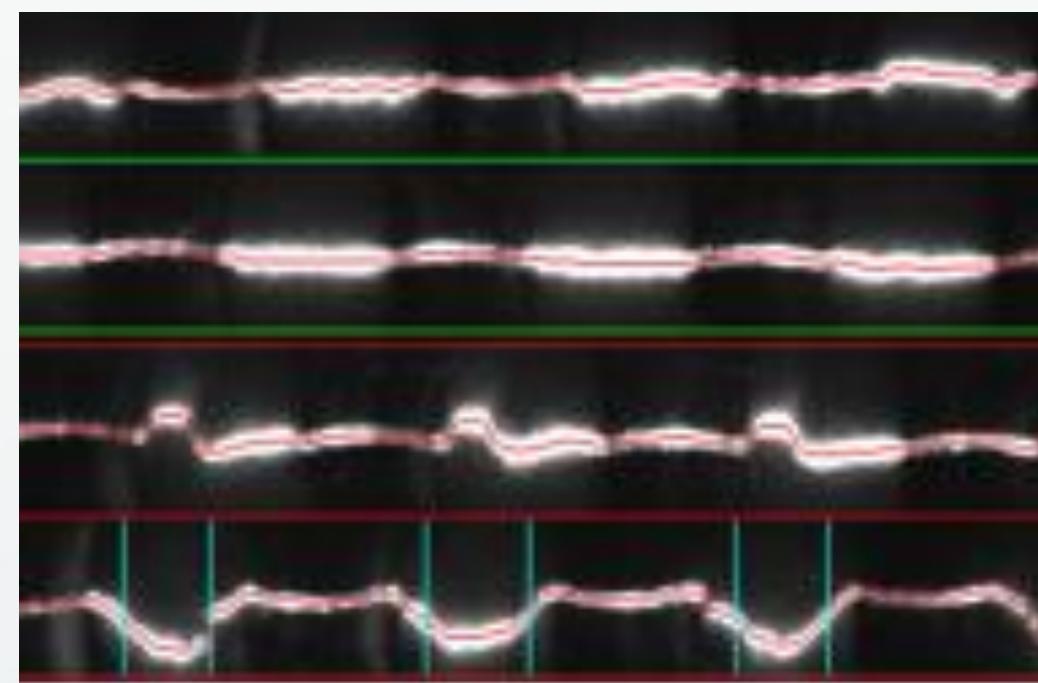
Control of tray formation



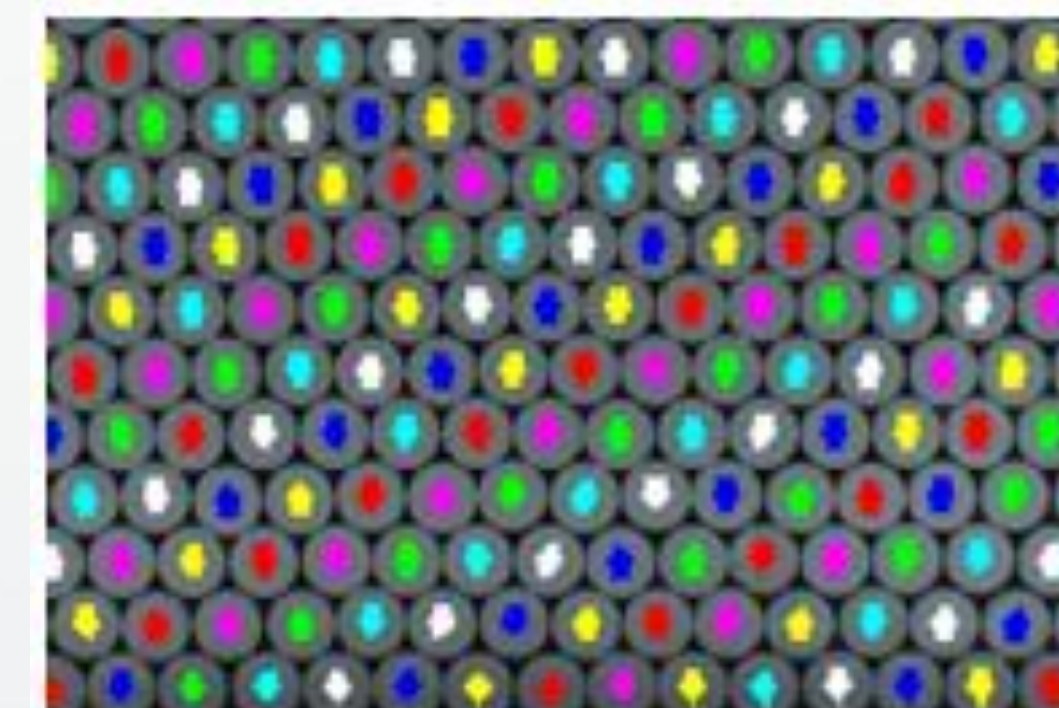
Syringes inspection: Integrity, completeness



Control of Color rings in vials



Powder level inside the vials: 3D inspection



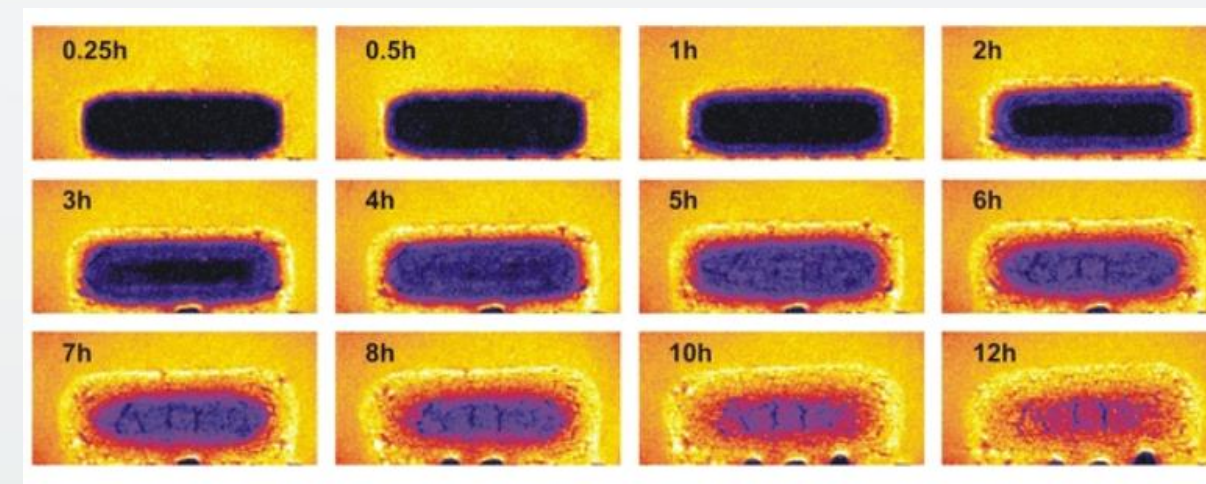
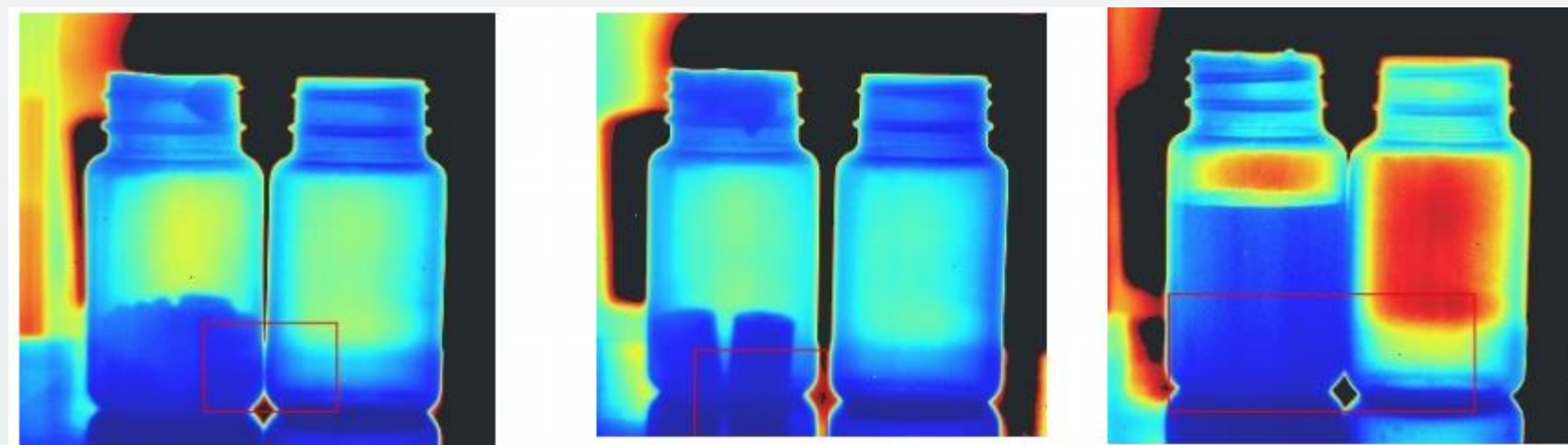
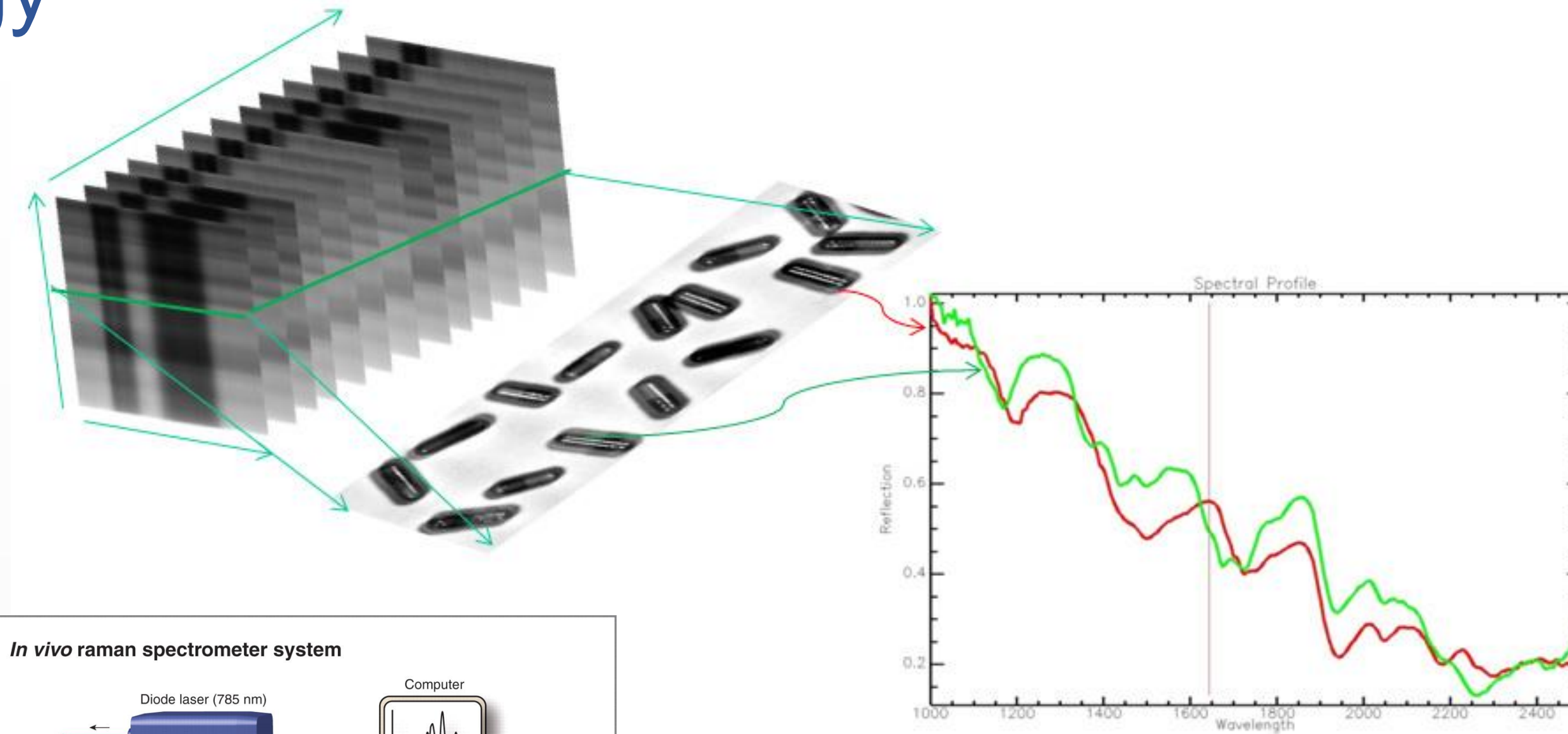
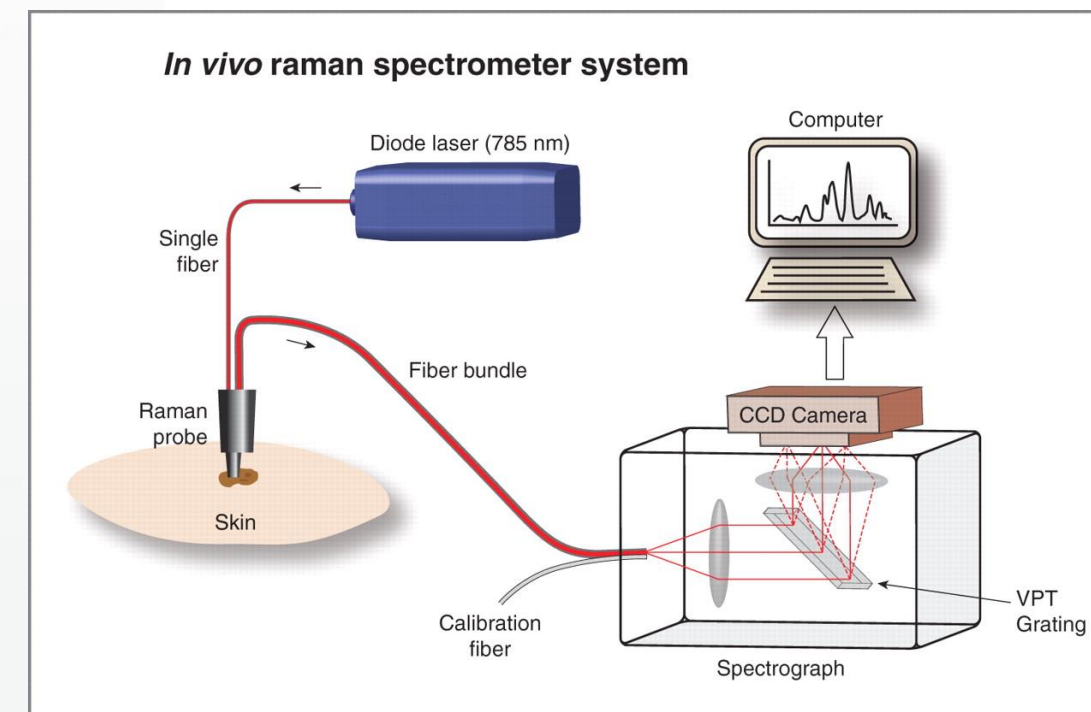
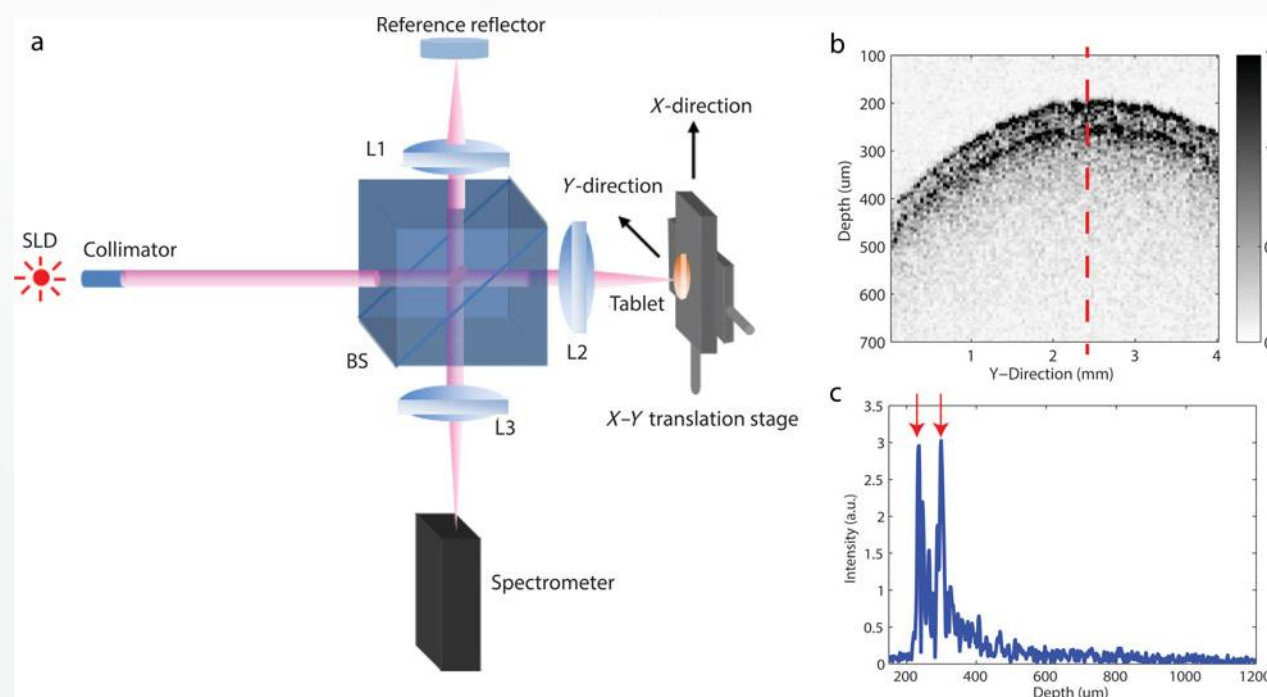
Counts vials in a tray



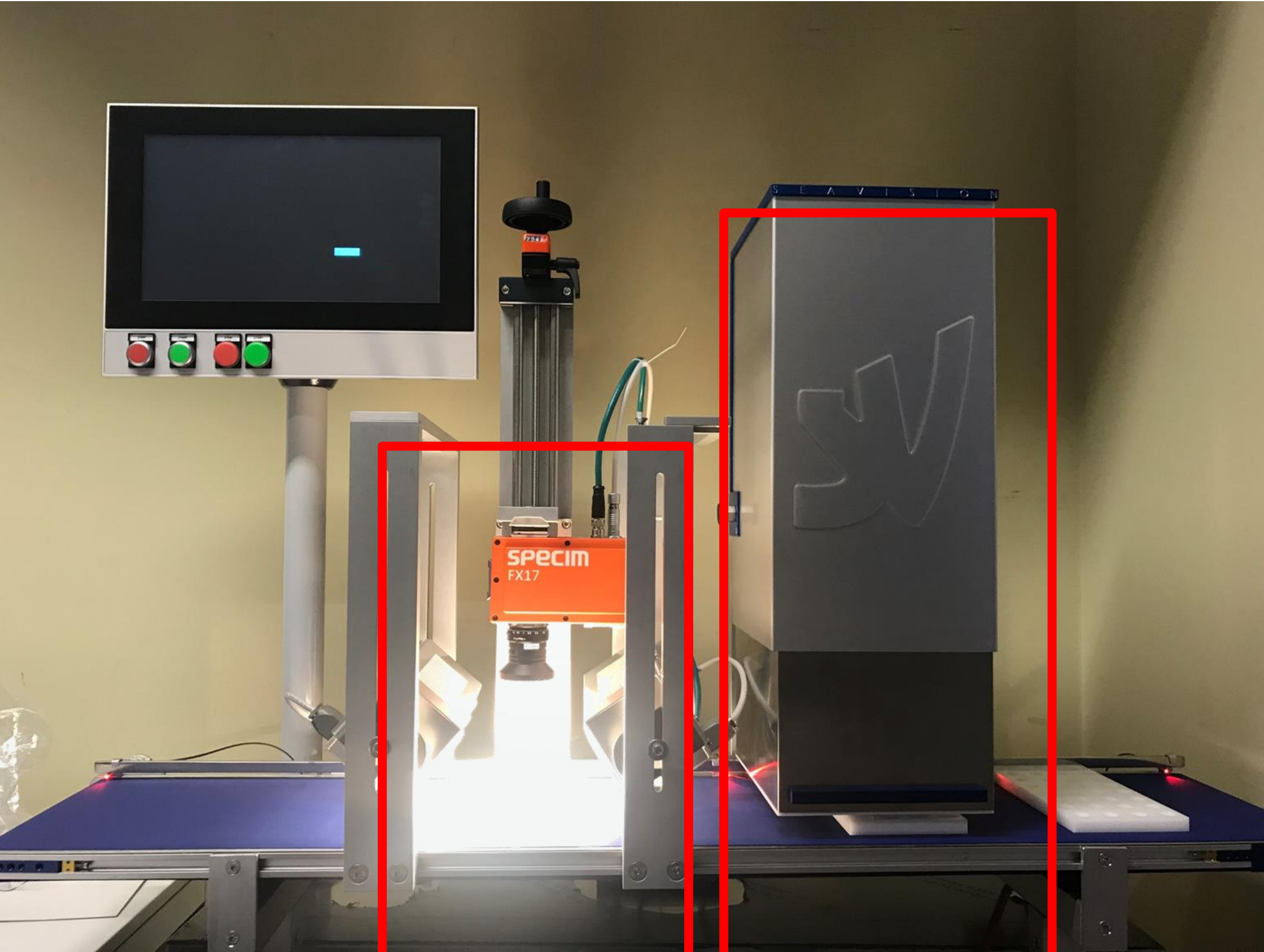
Control of forming cartons for inserting components

Non-Destructive technology

- Hyperspectral Imaging
- Optical Coherence tomography
- Thermography
- Optical Spectroscopy
- Terahertz Imaging
- Nuclear Magnetic Resonance



HarleNIR - Chemical imaging



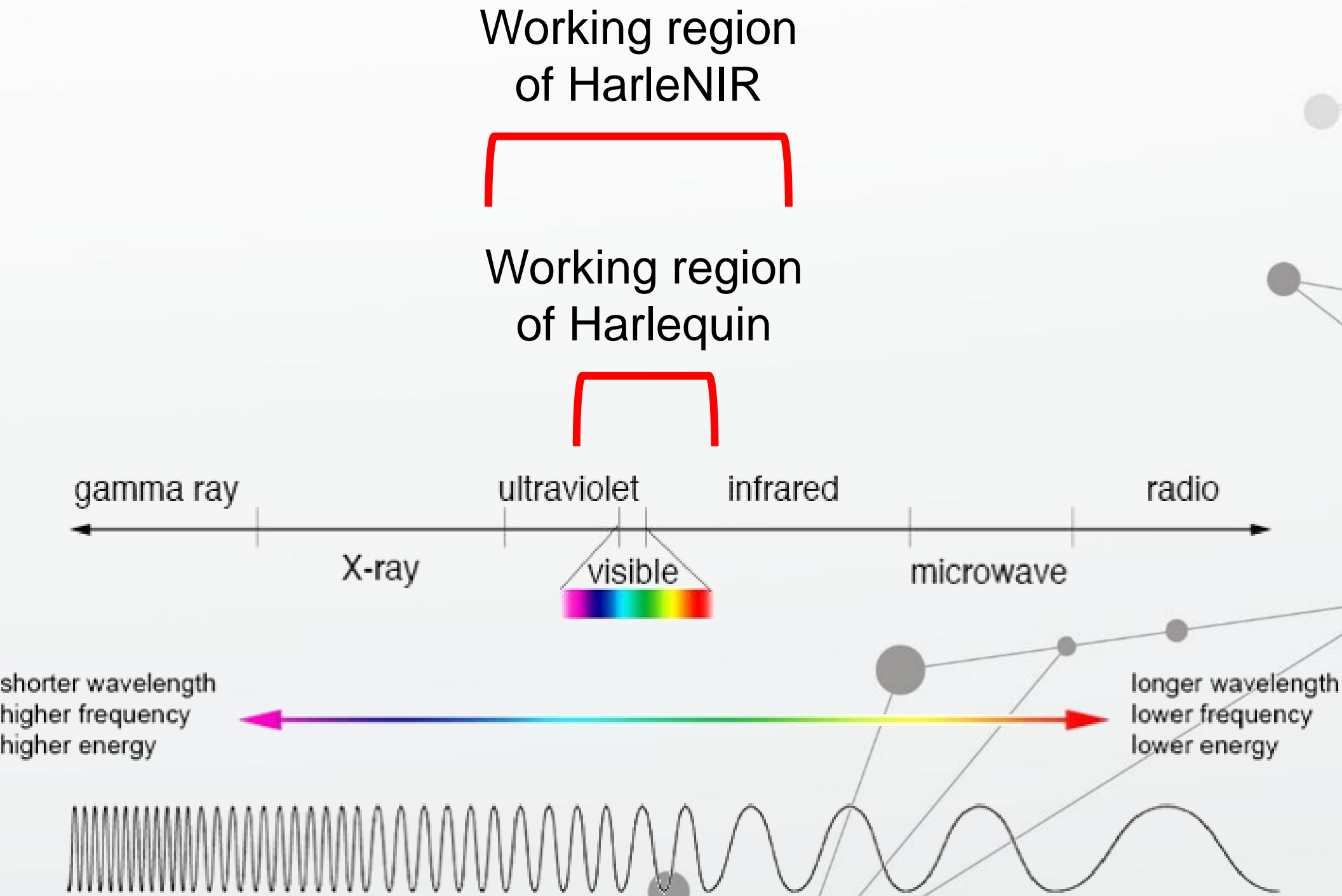
Hyperspectral
camera system

B&W or RGB
camera system
Harlequin

Customized light source depending on the application

With the introduction of the hyperspectral camera as inspection system for the pharmaceutical products Harlequin is becoming HarleNIR.

HarleNIR working range 300 – 1700nm



HarleNIR - Possible applications on a pharmaceutical products

	PHARMACEUTICAL PRODUCTS		
	TABLETS	CAPSULES	POWDERS
VIBRATING PLATE			
Mix-up avoidance	●	●	
Foreign object identification	●	●	
Presence of cracks	●	●	
Absence of coating		●	
Overlapping defects		●	
Identification of empty blister	●		
Moisture content determination	●	●	
BLISTERING MACHINE			
Mix-up avoidance	●	●	
Foreign object identification	●	●	
Presence of cracks	●	●	
Absence of coating		●	
Overlapping defects		●	
Identification of empty blister	●		
Measure of the active principle distribution	●		
Moisture content determination	●	●	
GRANULATOR			
Moisture content determination			●
Homogeneity of blend			●

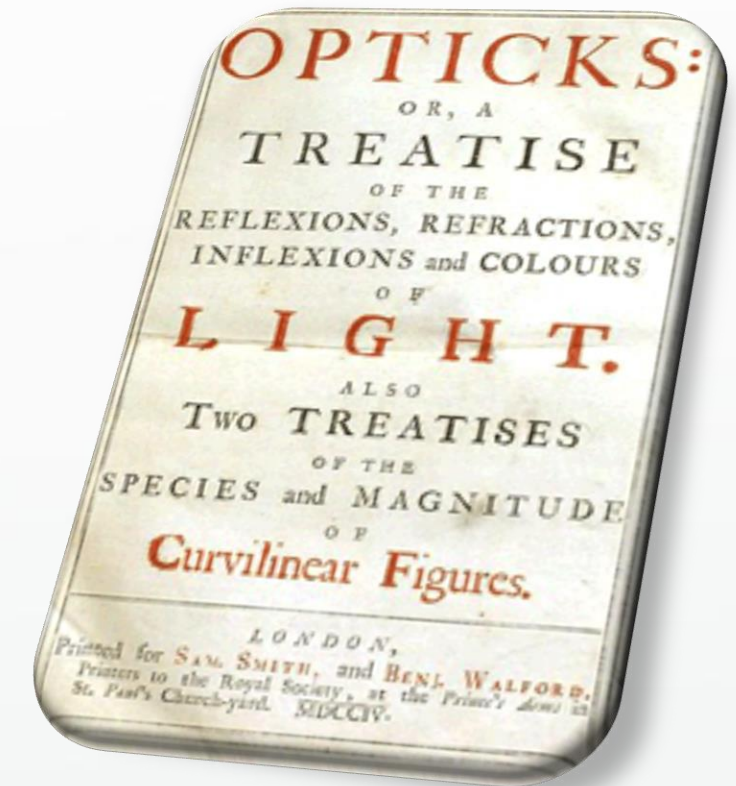
Origin of the spectroscopy



In the year 1704 **Sir Isaac Newton** build the first Spectrometer described on it's book.

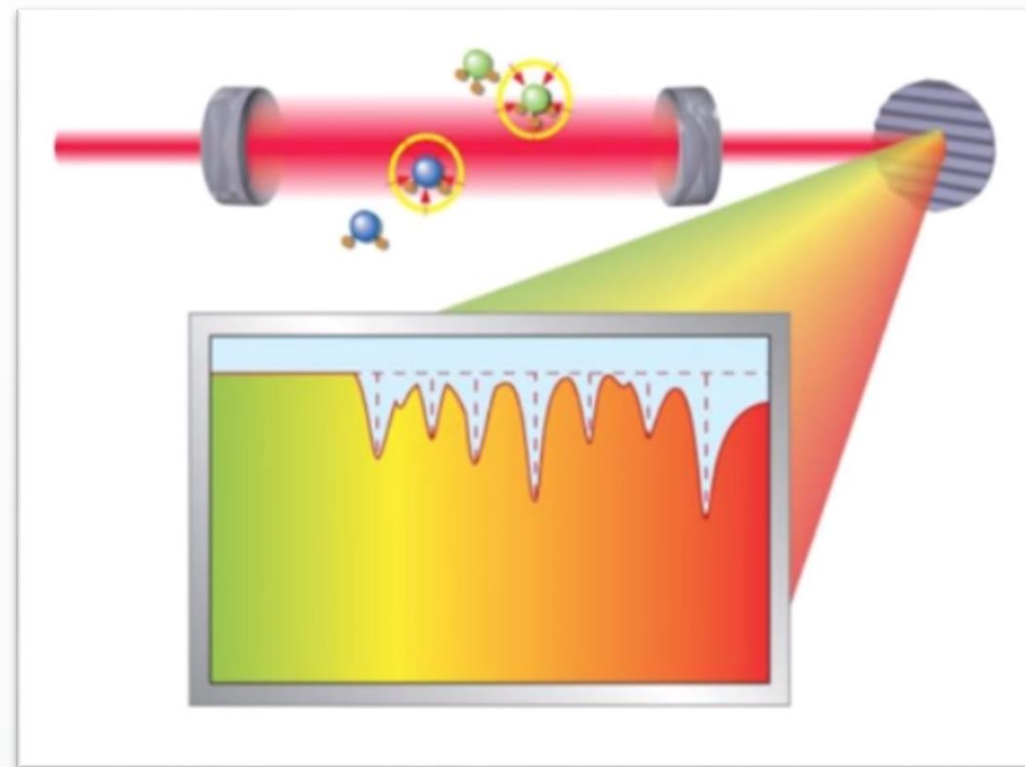


In the year 1800, **Sir William Herschel** discovered the existence of infrared radiation.



Where and what we are looking for?

Spectroscopy is the study of light interacting with matter.



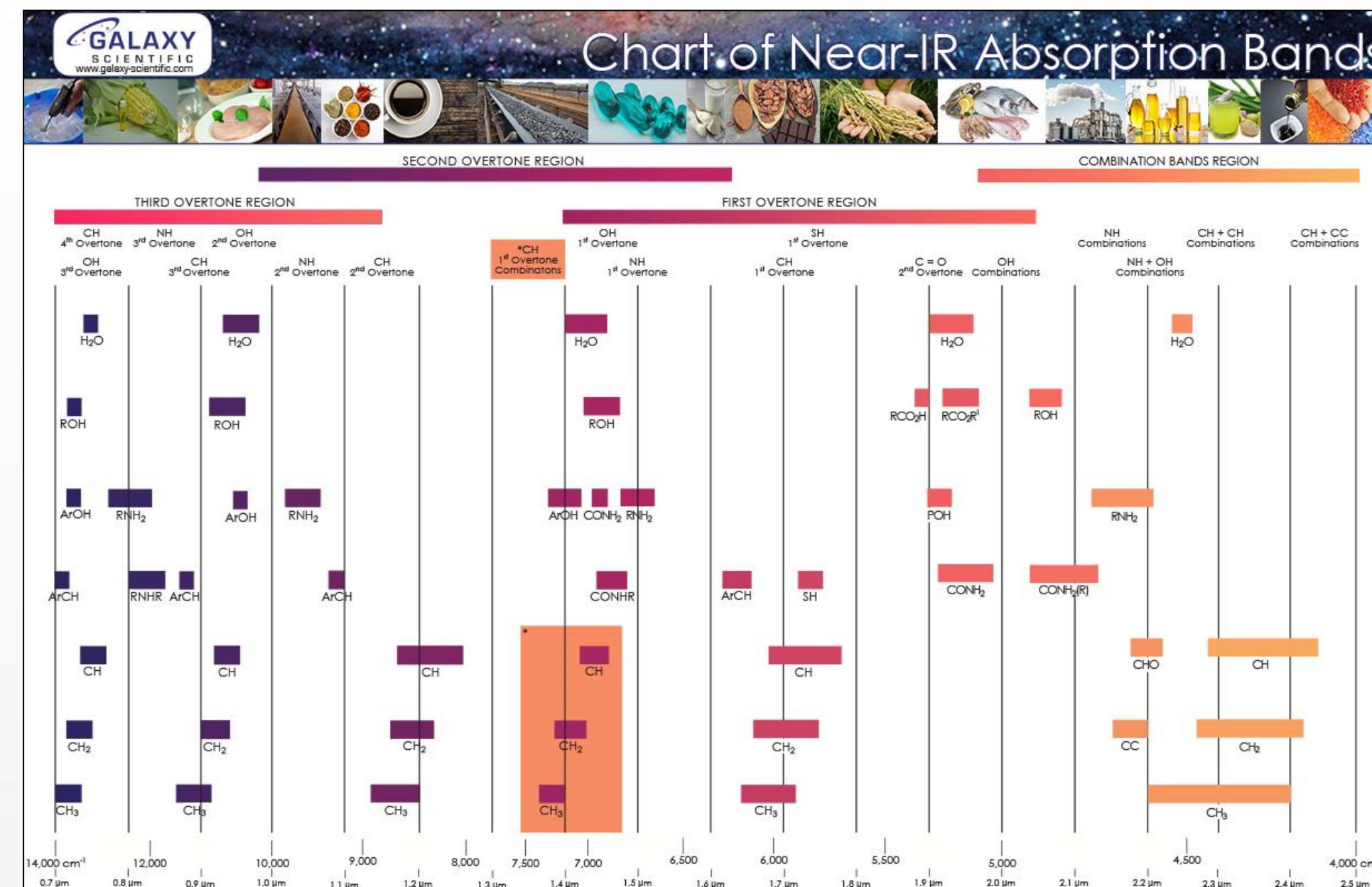
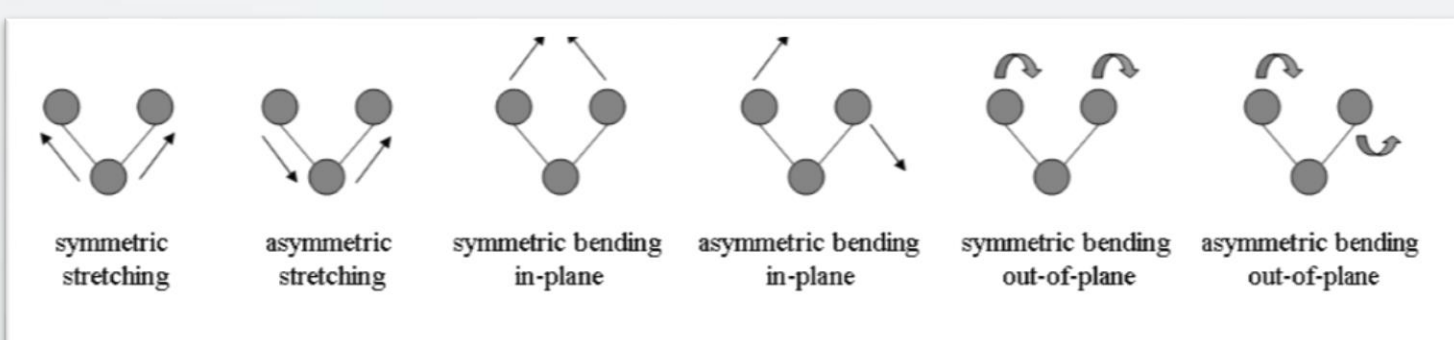
Dipole Moment

$\mu = \alpha d$

Relationship between IR intensity and dipole moment

$I_{IR} \propto \left(\frac{d\mu}{dQ} \right)^2$

Q is the vibrational coordinate

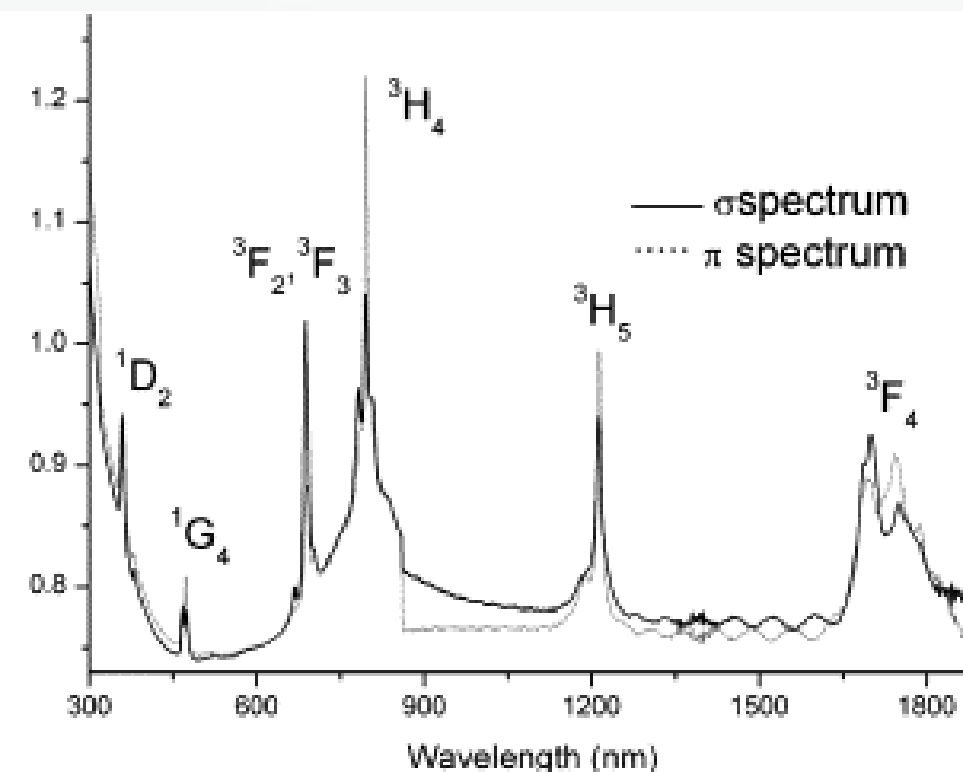
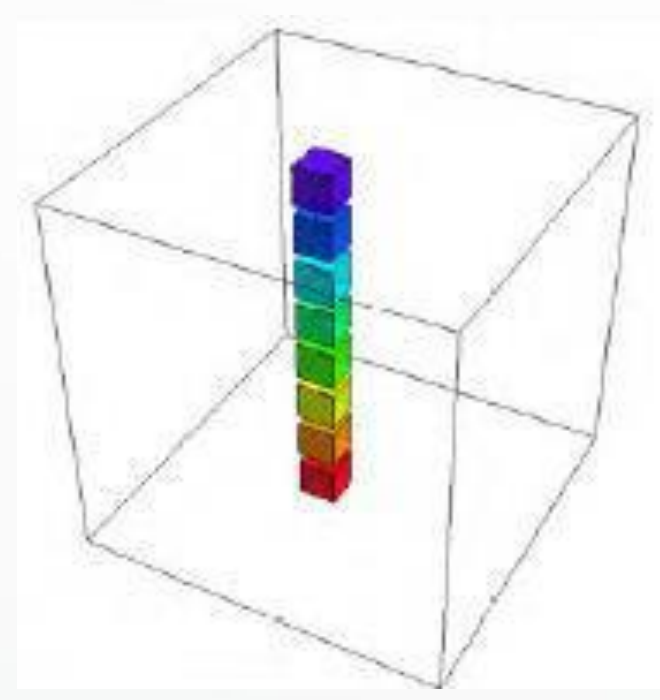


NIR has become the first choice in many areas of application

Some of the most common functional groups, e.g., C-H, O-H and N-H are measured with NIR.

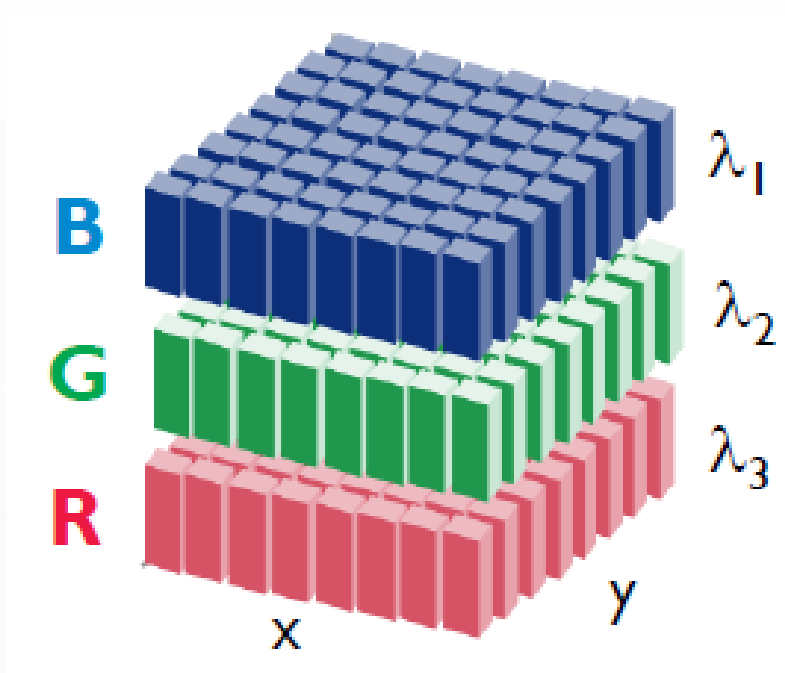
Spectral imaging open new dimensions

SPECTROSCOPY



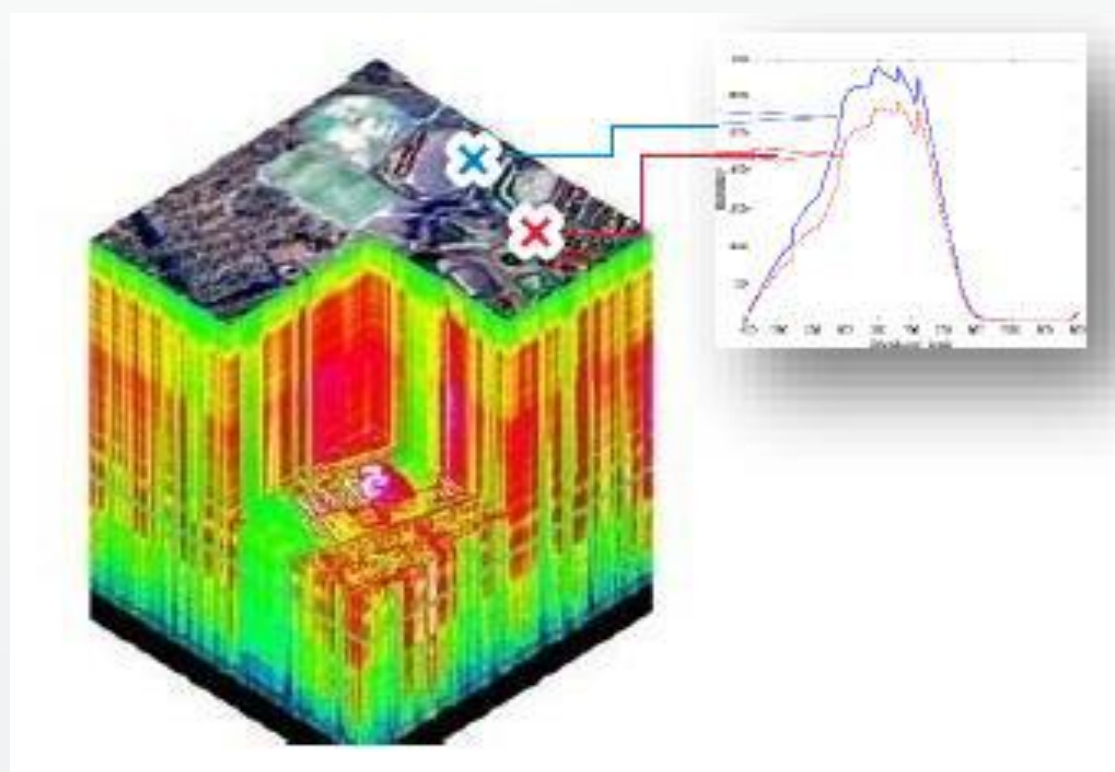
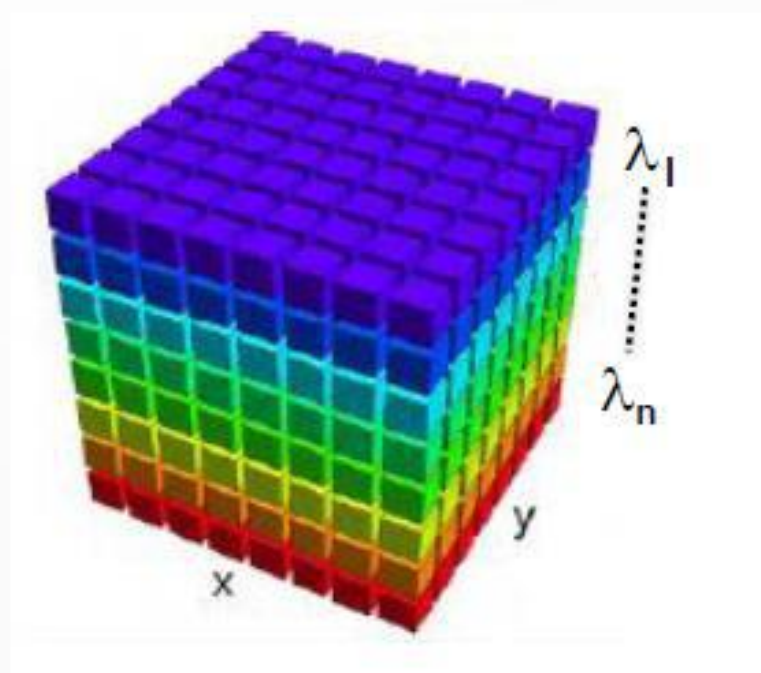
Accurate spectral analysis of one spatial pixel only

COLOR IMAGING



Seeing RGB colors of one image only

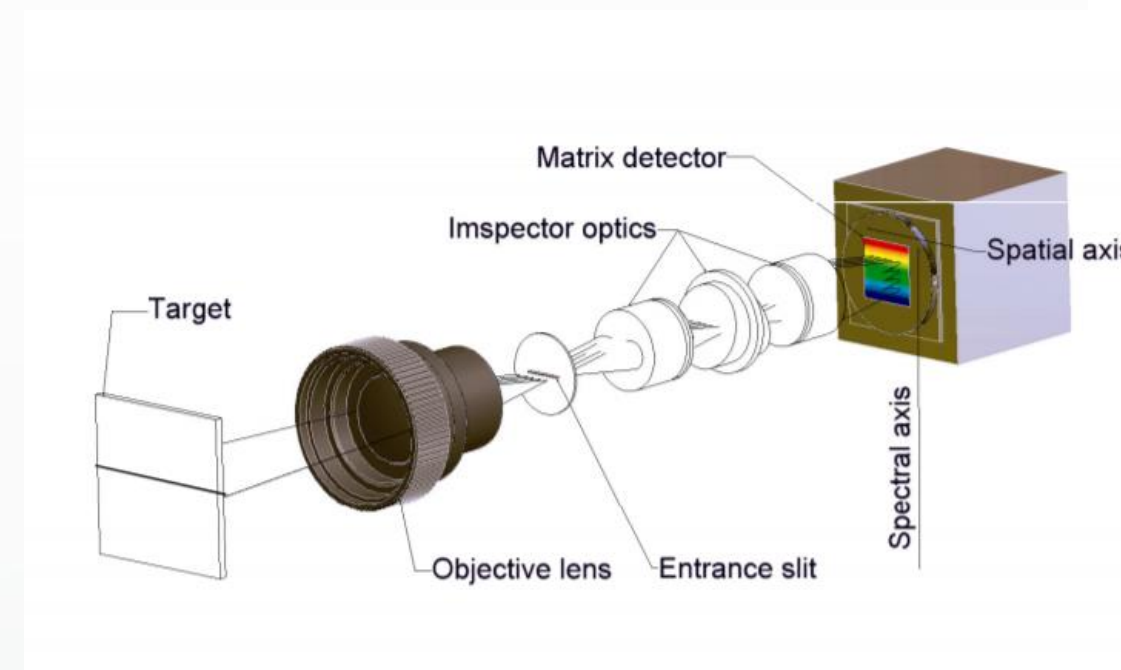
HYPERSPPECTRAL IMAGING



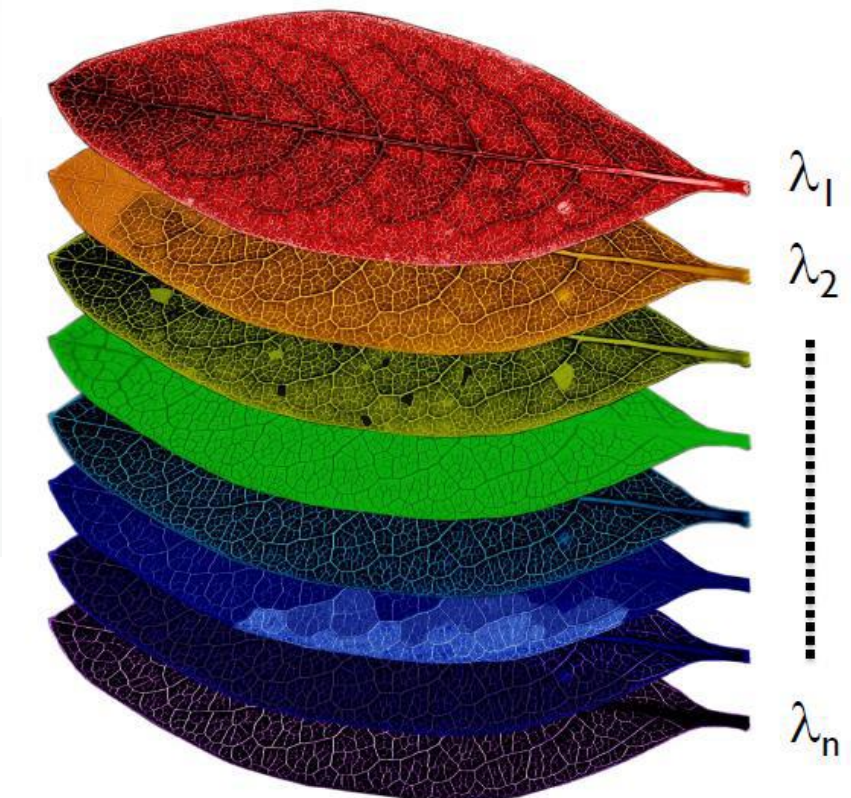
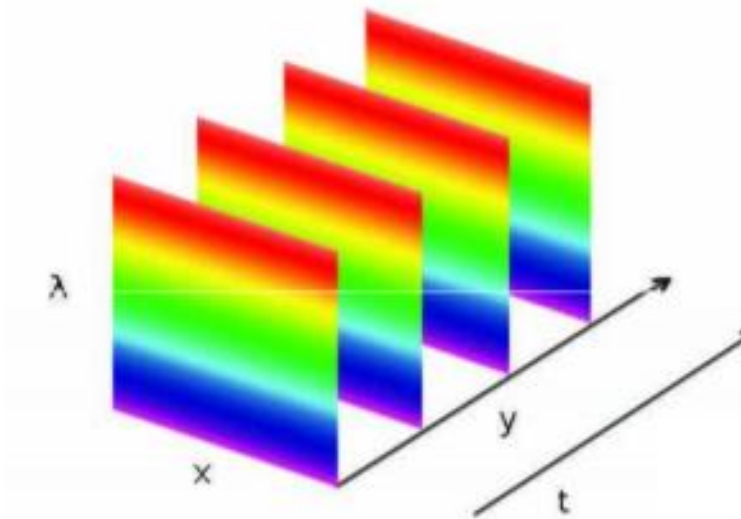
Spectral signature images revealing objects chemical composition

Hyperspectral Imaging

Hyperspectral vision system: the natural subsequent step on the evolution of the vision system starting from the black/white cameras and passing from the RGB and the multispectral cameras.

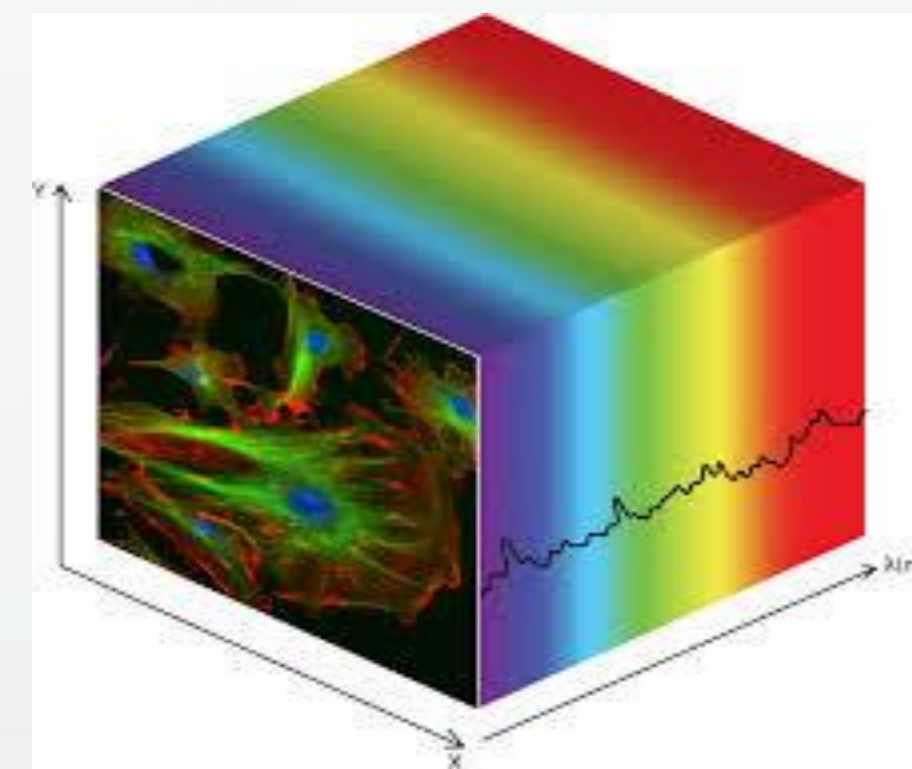


Pushbroom

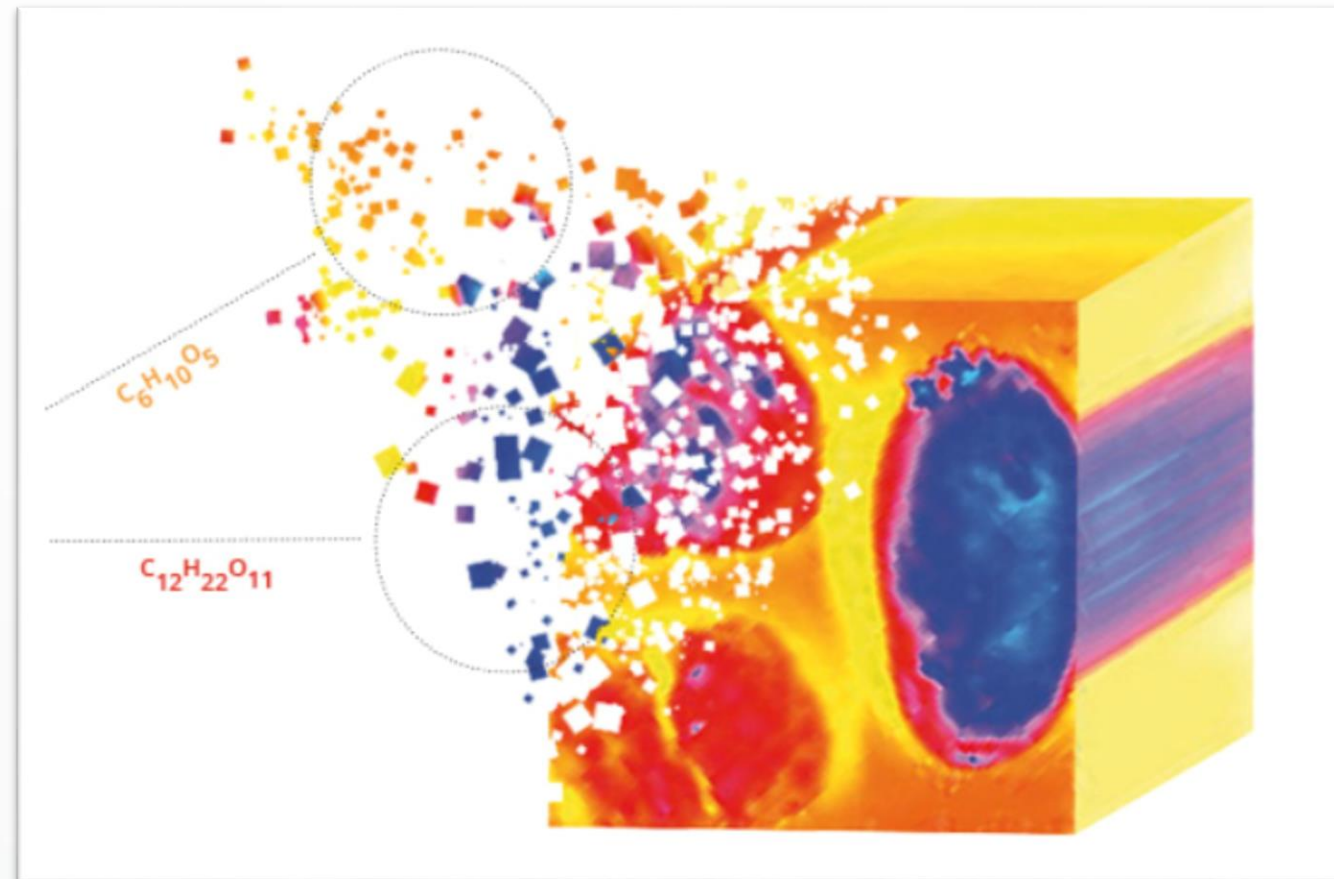


Hyperspectral System works in several spectral range:

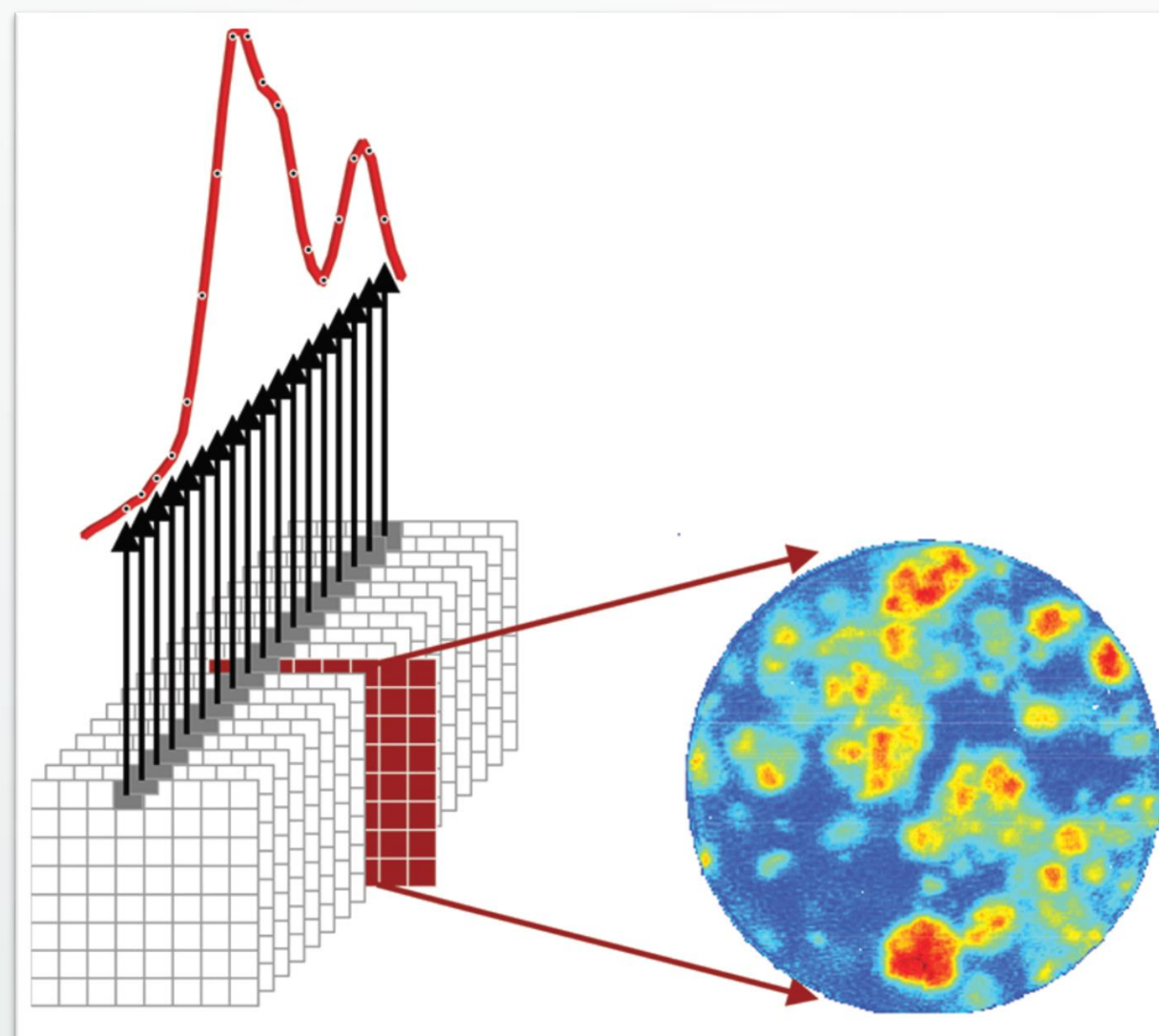
- | | |
|---|---------------|
| 1 – Visible Spectra range: | 400 – 700nm |
| 2 – Visible – Near InfraRed Spectral Range: | 400 – 1000 nm |
| 3 – Near InfraRed Spectral Range: | 900 – 1700 nm |
| 4 – SWIR Spectral Range: | 1700 – 2500nm |



Chemical imaging - General definition



Chemical imaging technique, is the combination of spectroscopy and digital imaging. A spectral image contains many spectra, one for each individual point on the sample's surface. The image contains valuable information about the spatial distribution of the materials within the sample.

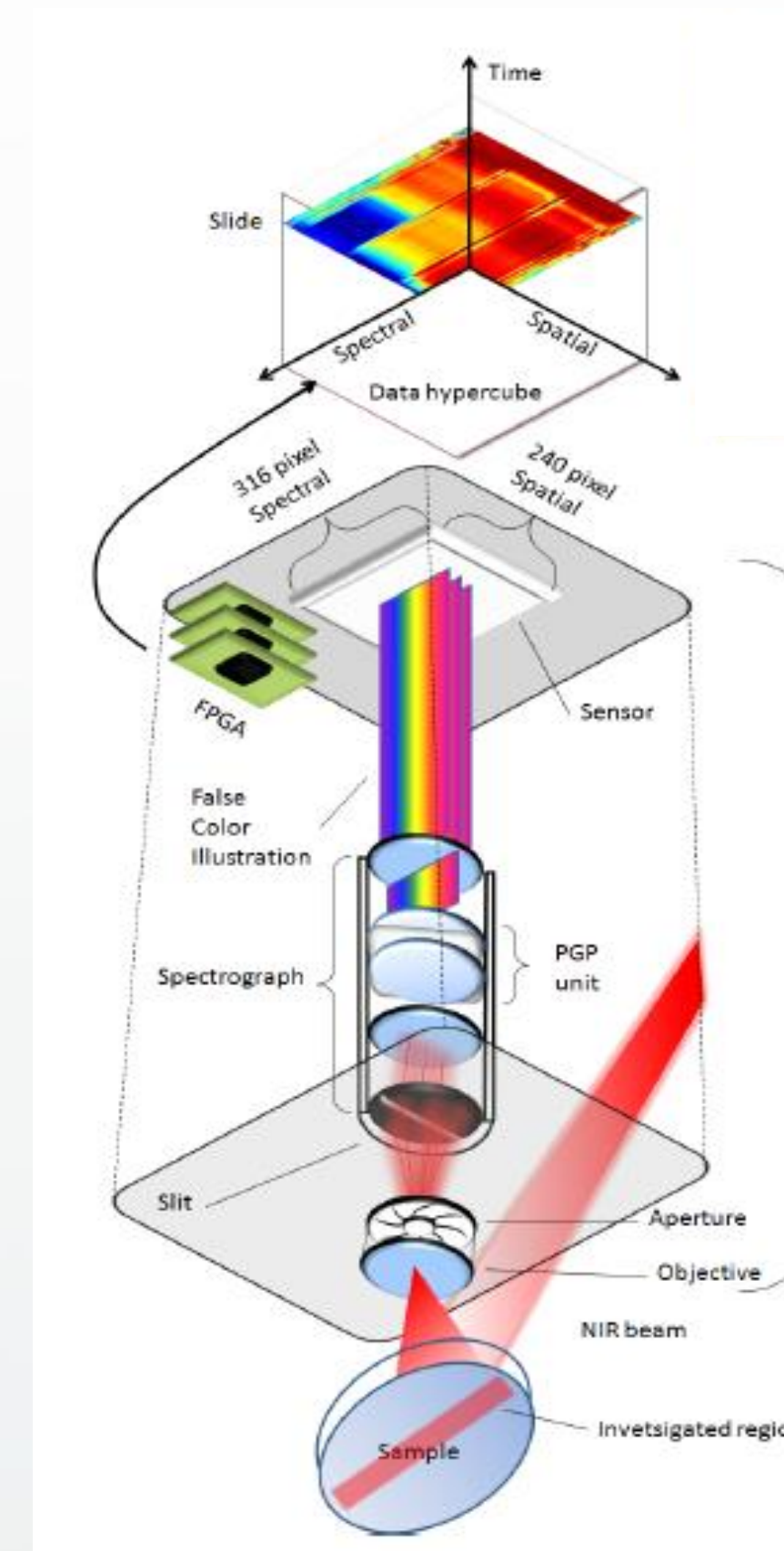
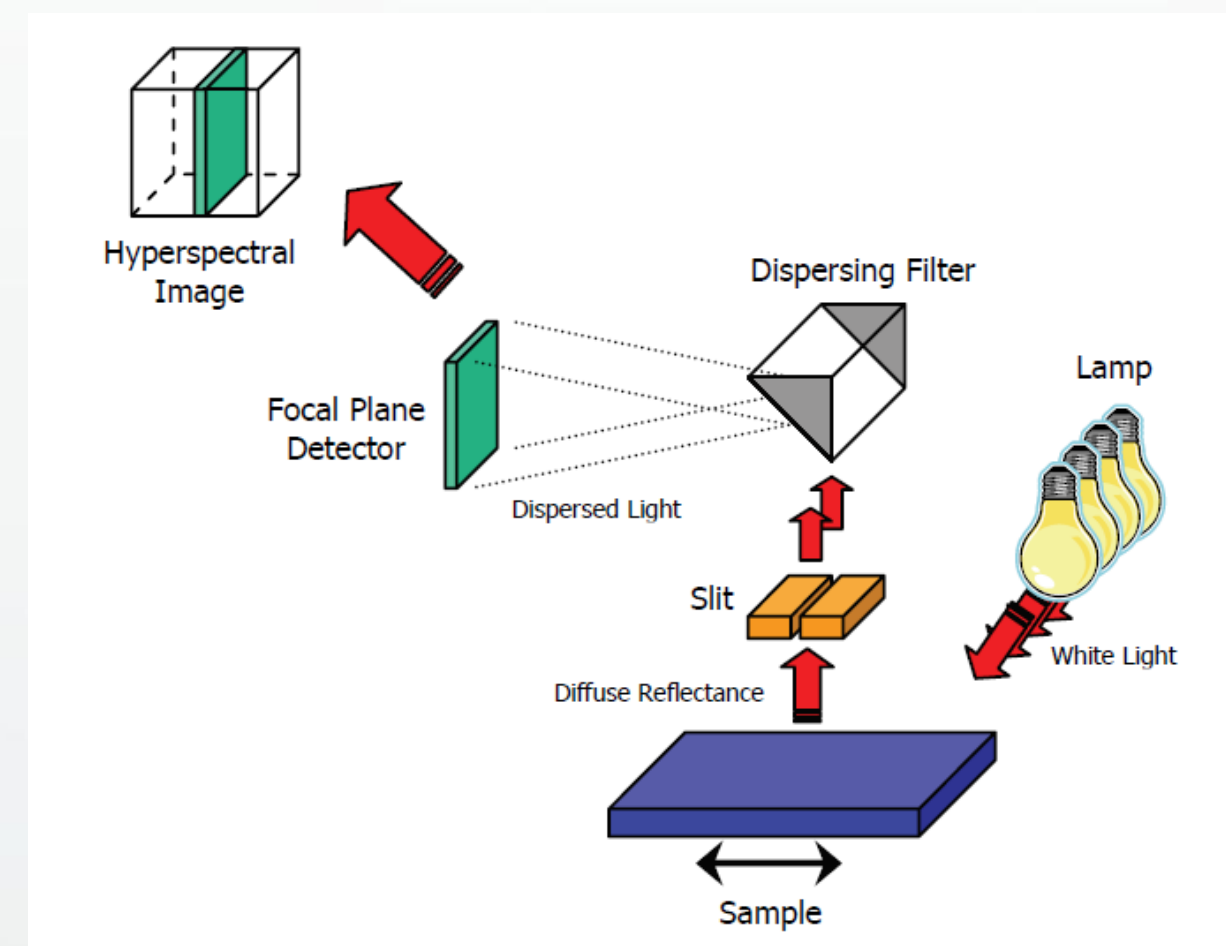
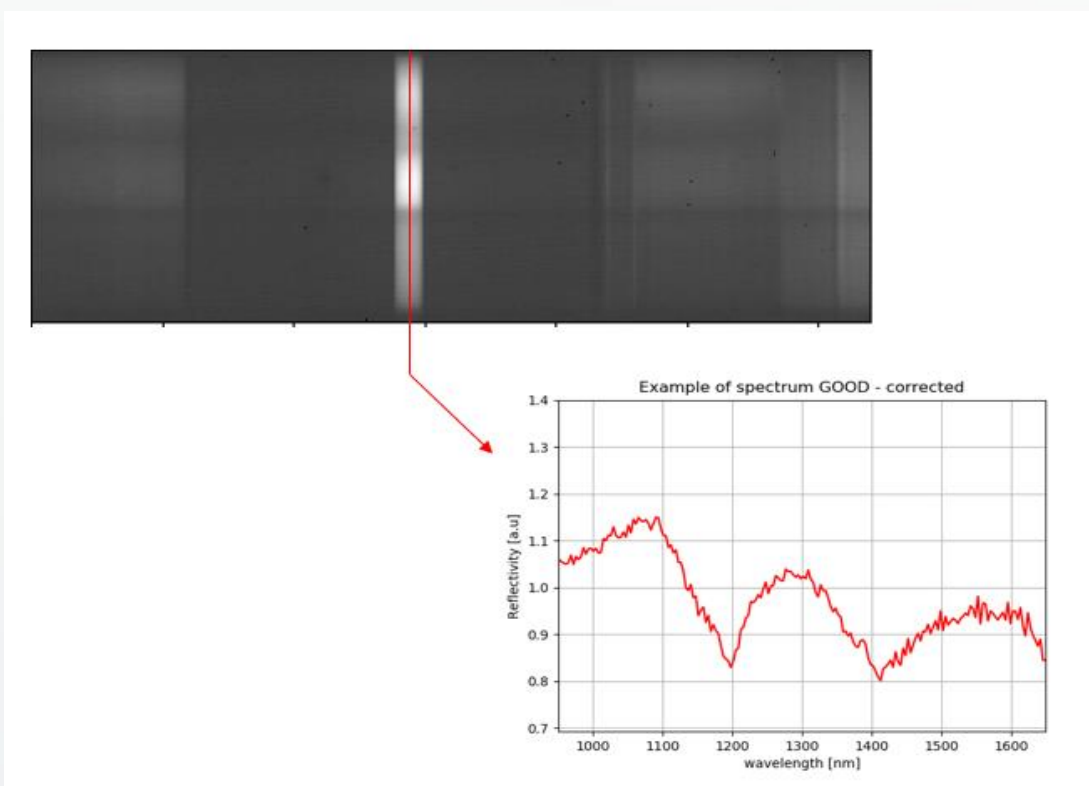
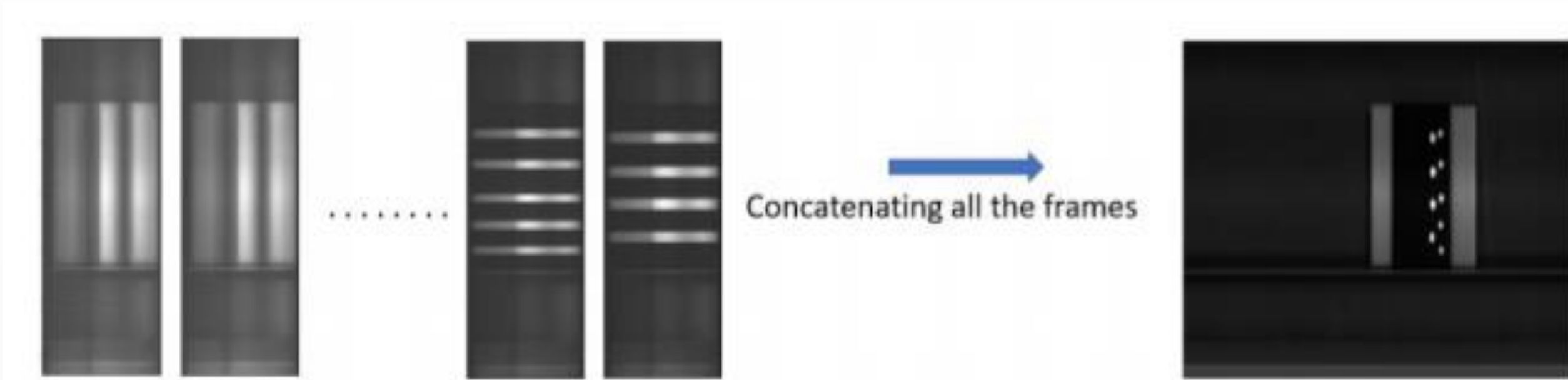


The analyst may choose to take as many data spectrum measured at a particular chemical component in spatial location at time. This is useful for chemical identification and quantification.

The goal of hyperspectral imaging is to obtain the spectrum for each pixel in the image of a scene with the purpose of finding objects, identifying materials, or detecting processes.

How the data are obtained? - Pushbroom imaging

Starting from the analysis of the spectra will be possible to extract the chemical information regarding the observed objects.



Concept of frames

Analytical methods - how the data are treated?

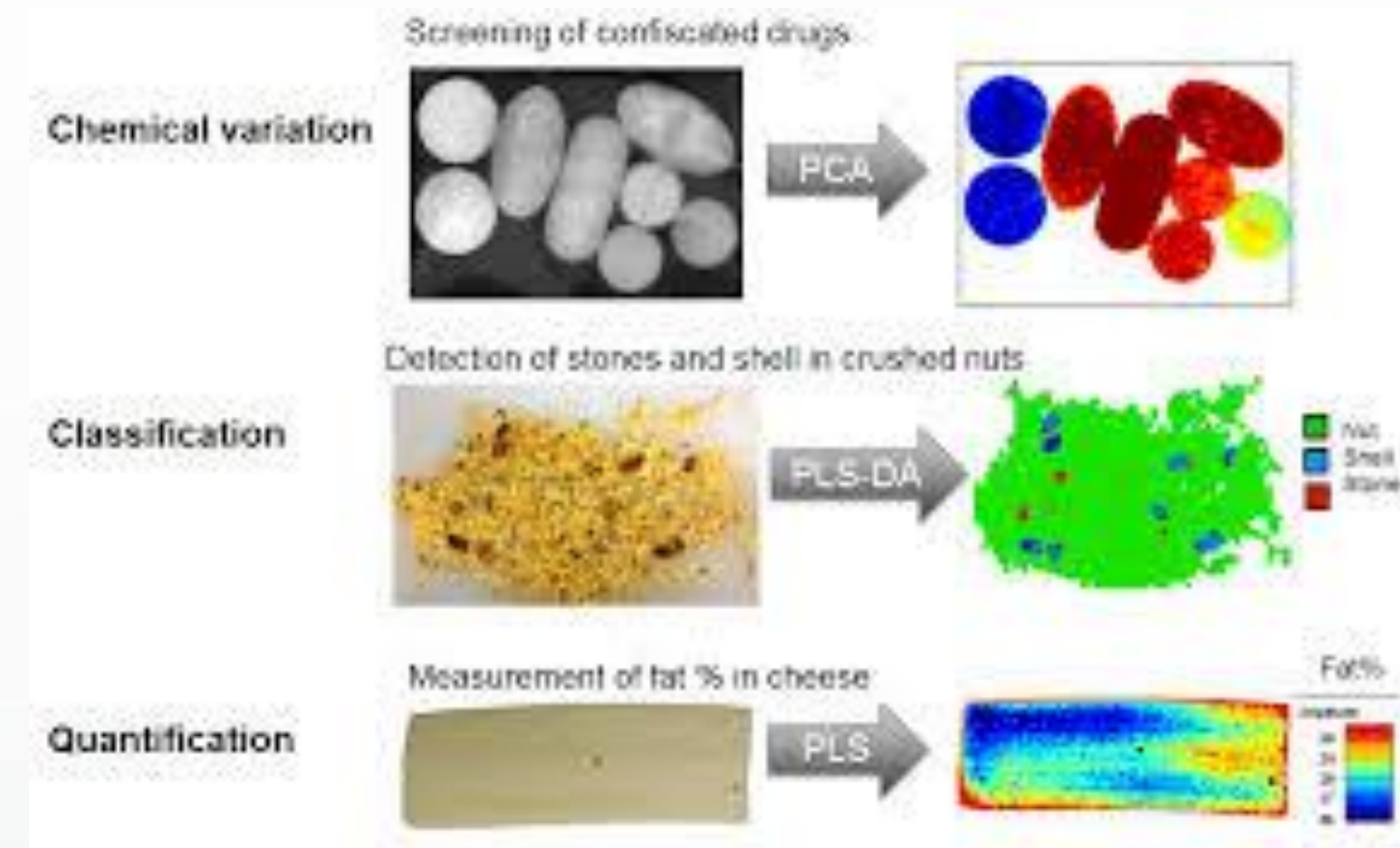
Non - Supervisioned methods → QUALITATIVE ANALYSIS

ANLYTICAL METHODS:

Pre-processing of the data: Normalisation, Derivative, Smoothing

Processing:

- Correlation function,
- Inner Product
- PCA



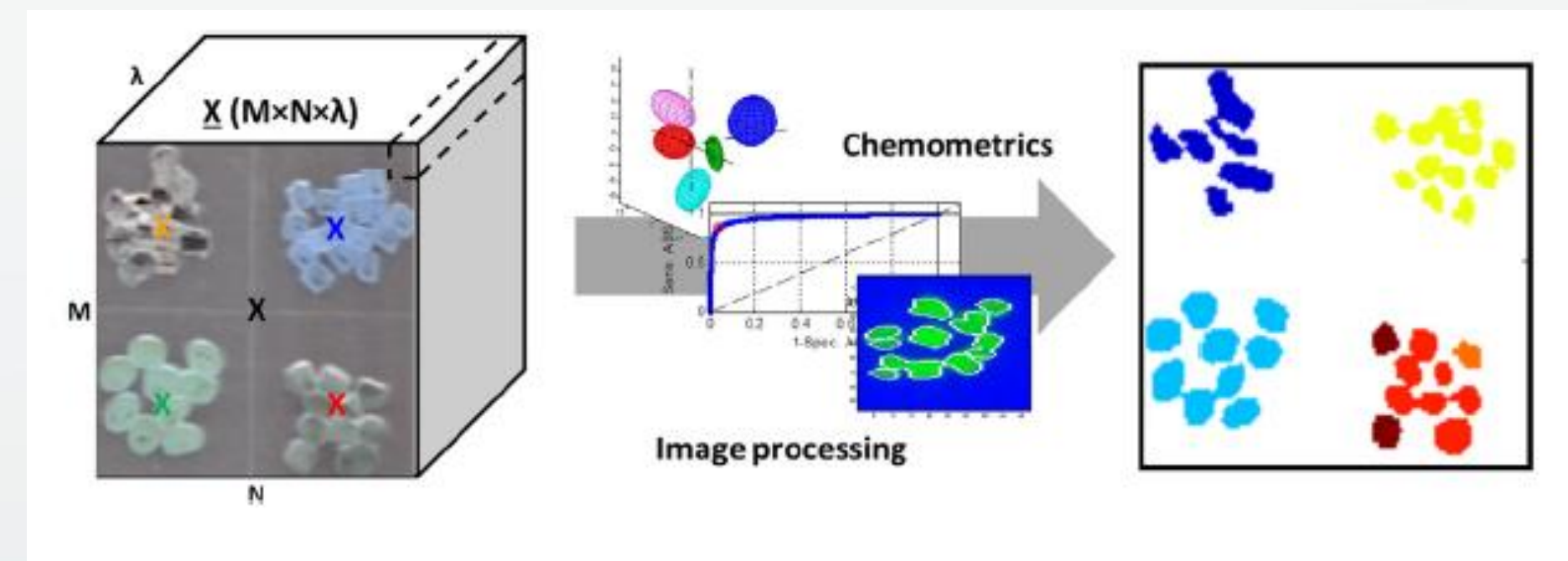
Supervised methods → QUANTITATIVE ANALYSIS

ANLYTICAL METHODS:

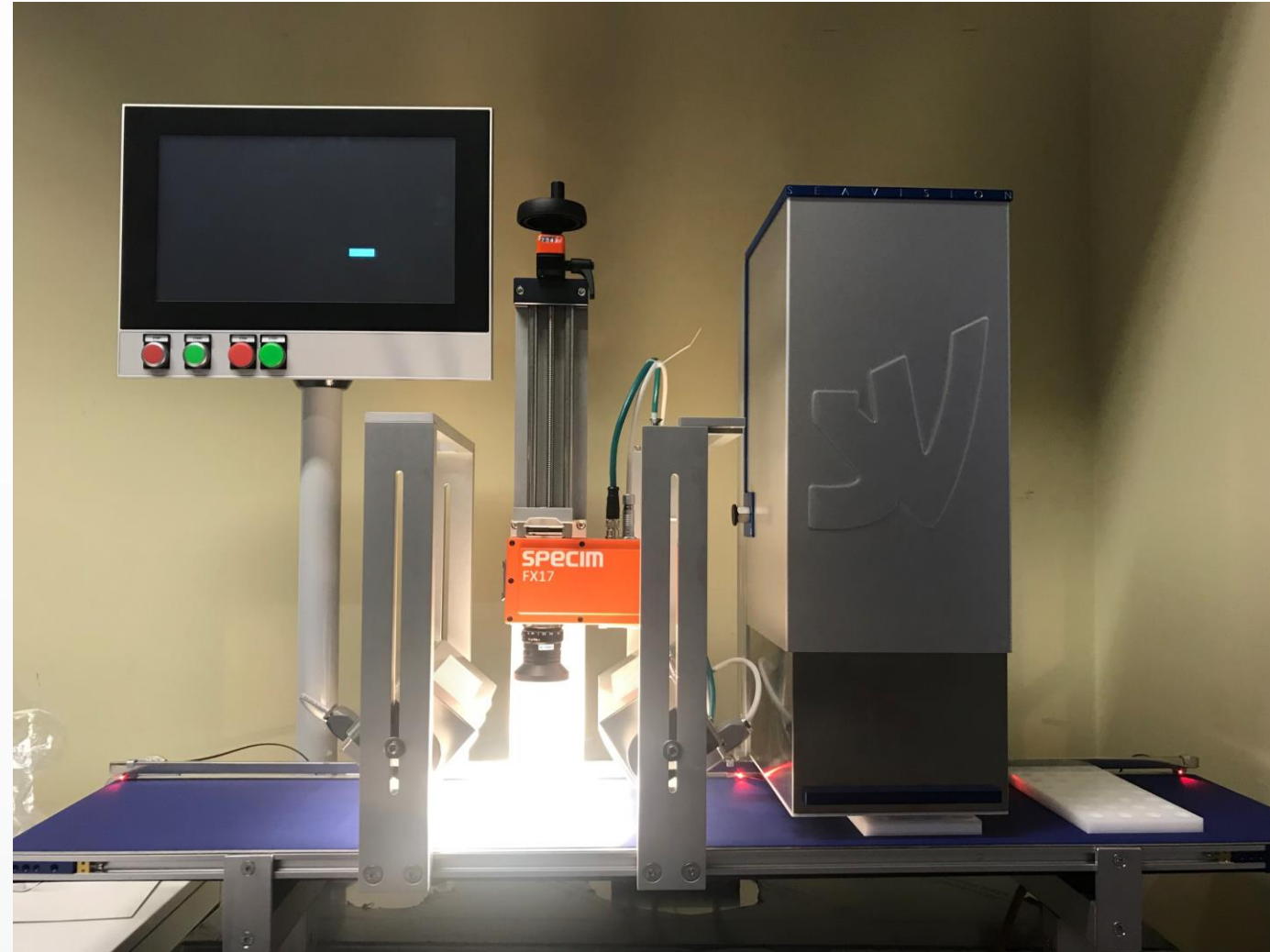
Pre-processing of the data: Normalisation, Derivative, Smoothing

Processing:

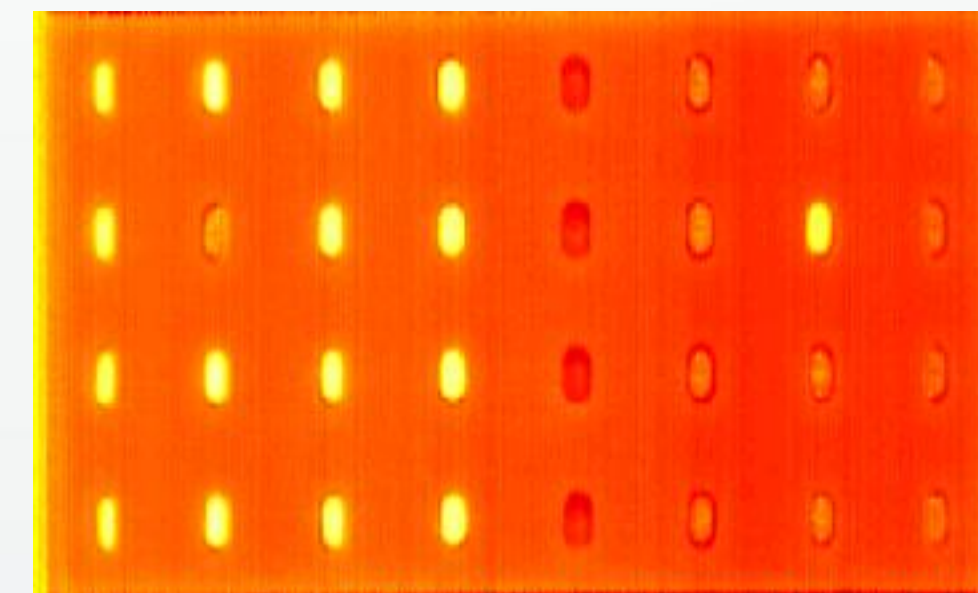
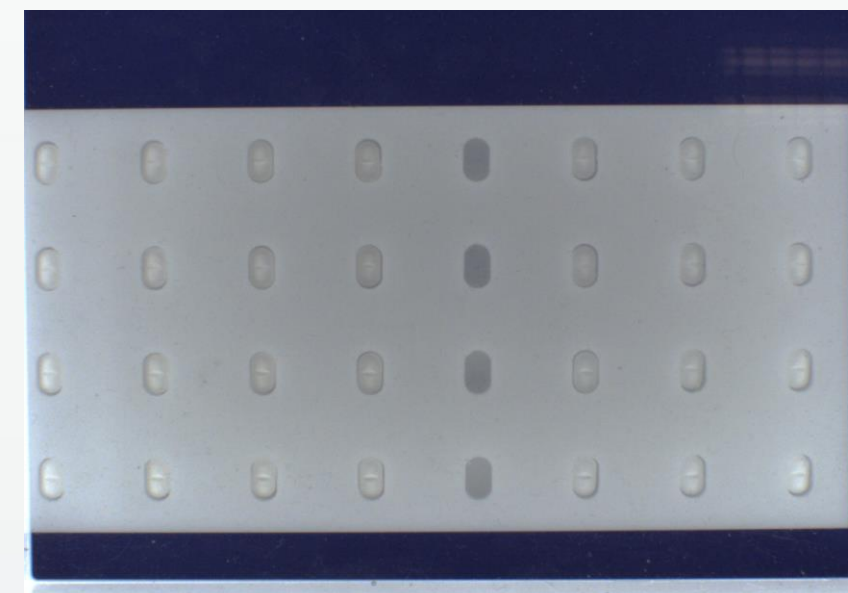
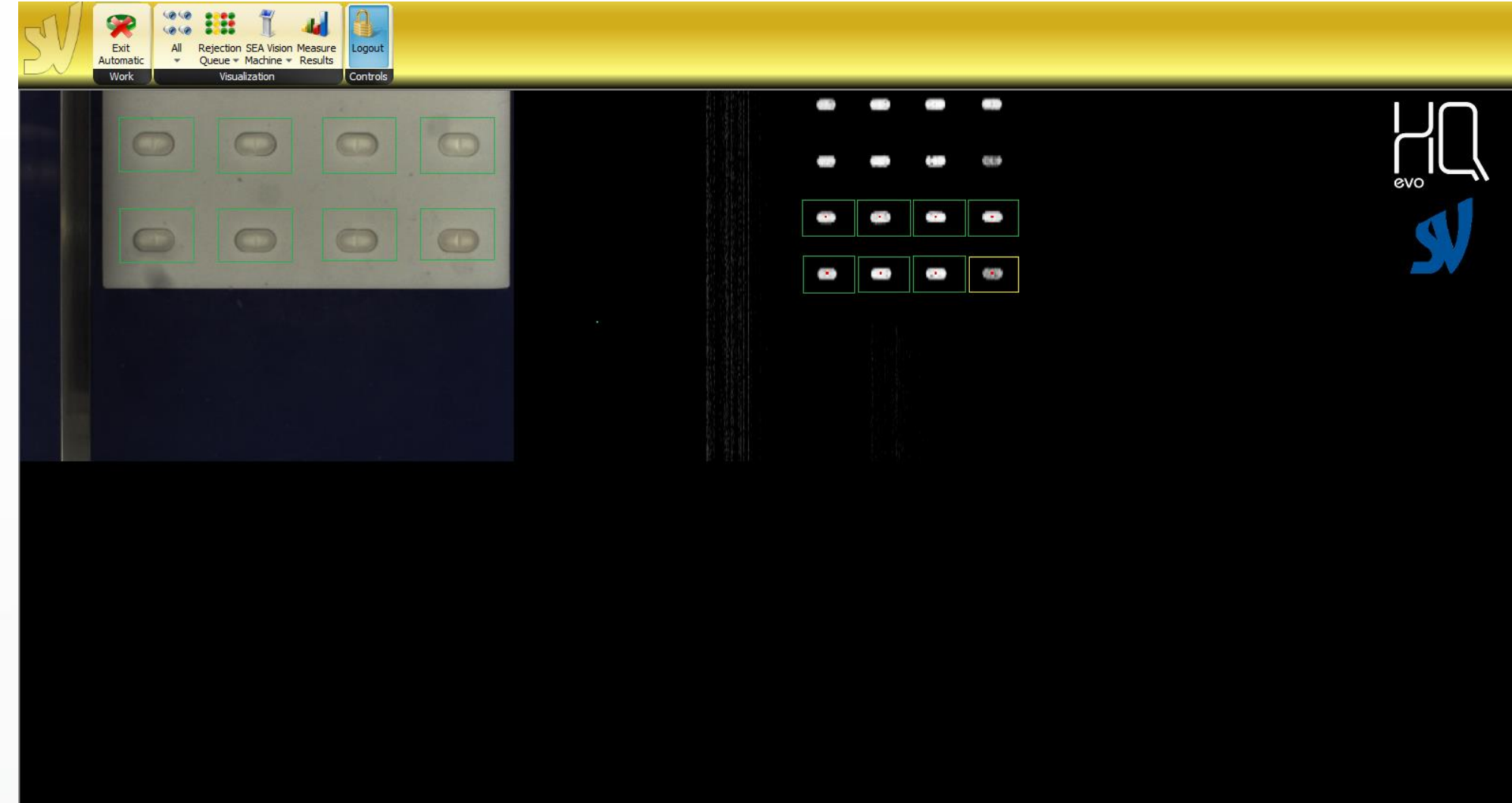
- Multivariate Analysis: PCA, PLS – DA (linear regression)
- Clusterization: K-means



HarleNIR R&D applications - Feasibility studies



The tablets on the right column are all equal. The other tablets are different for the dosage and the distribution of principal compound. From a standard RGB camera all the tablets appears the same.

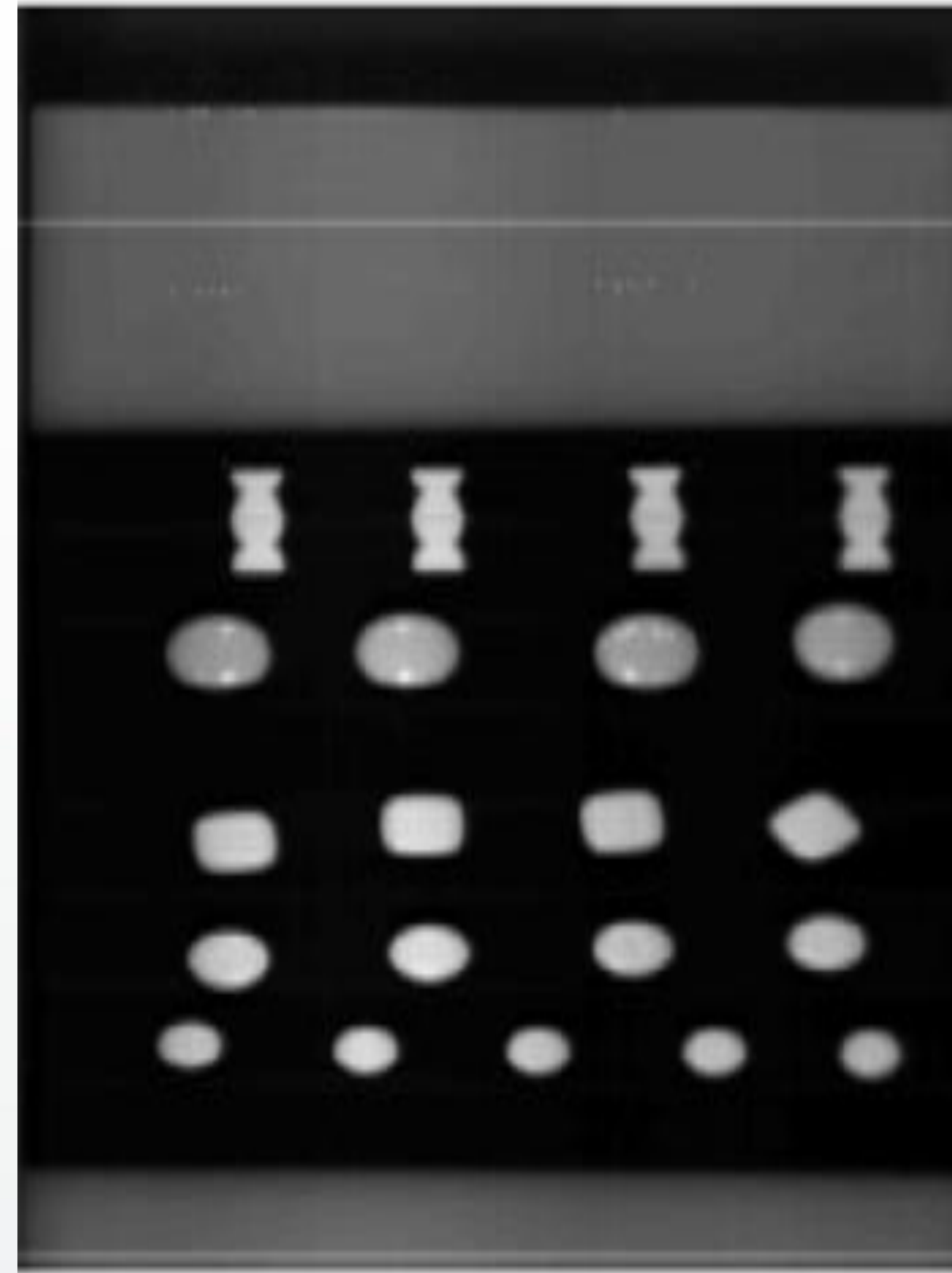


Mix-Up detection

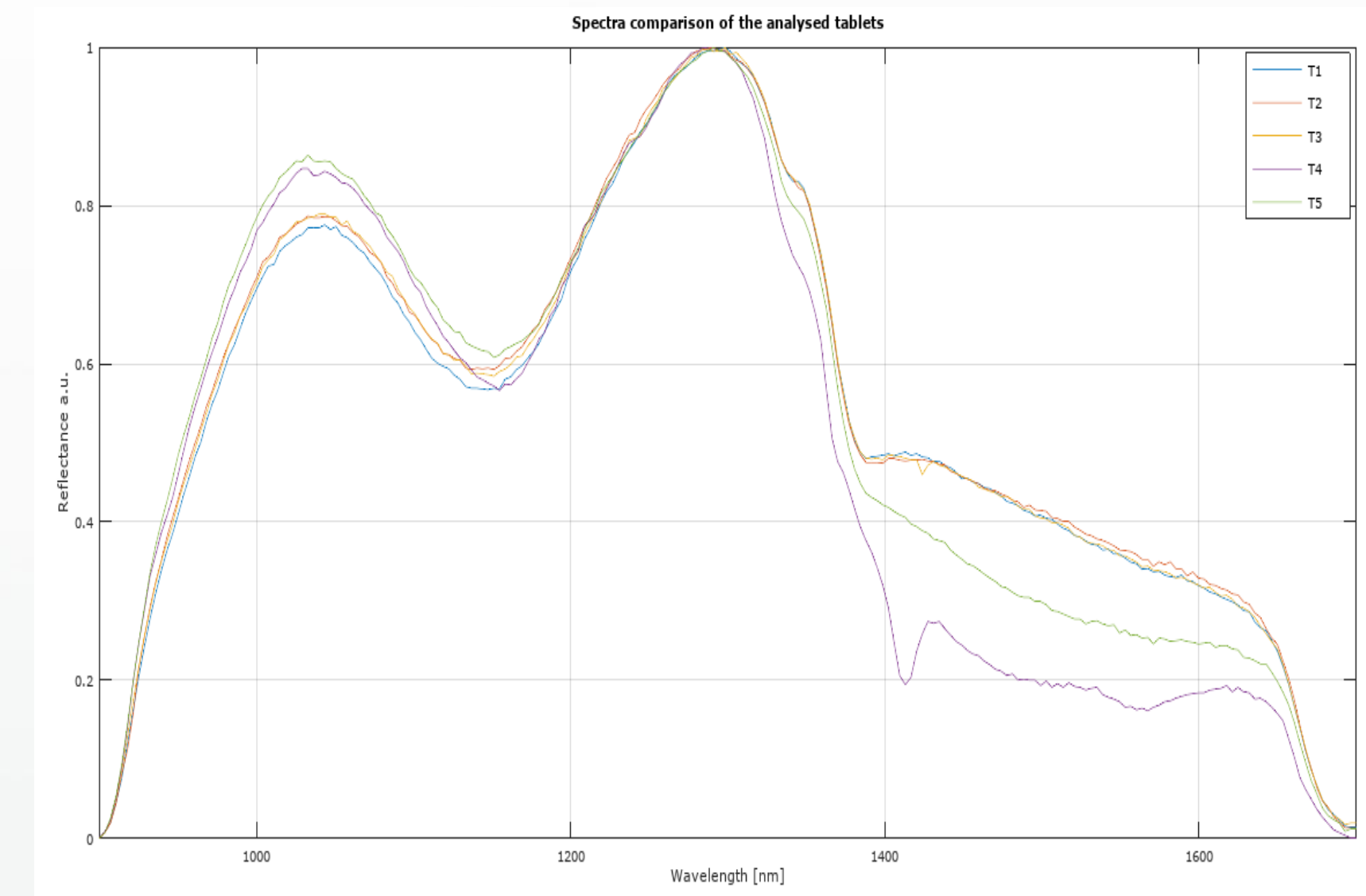
HarleNIR - Example of identification



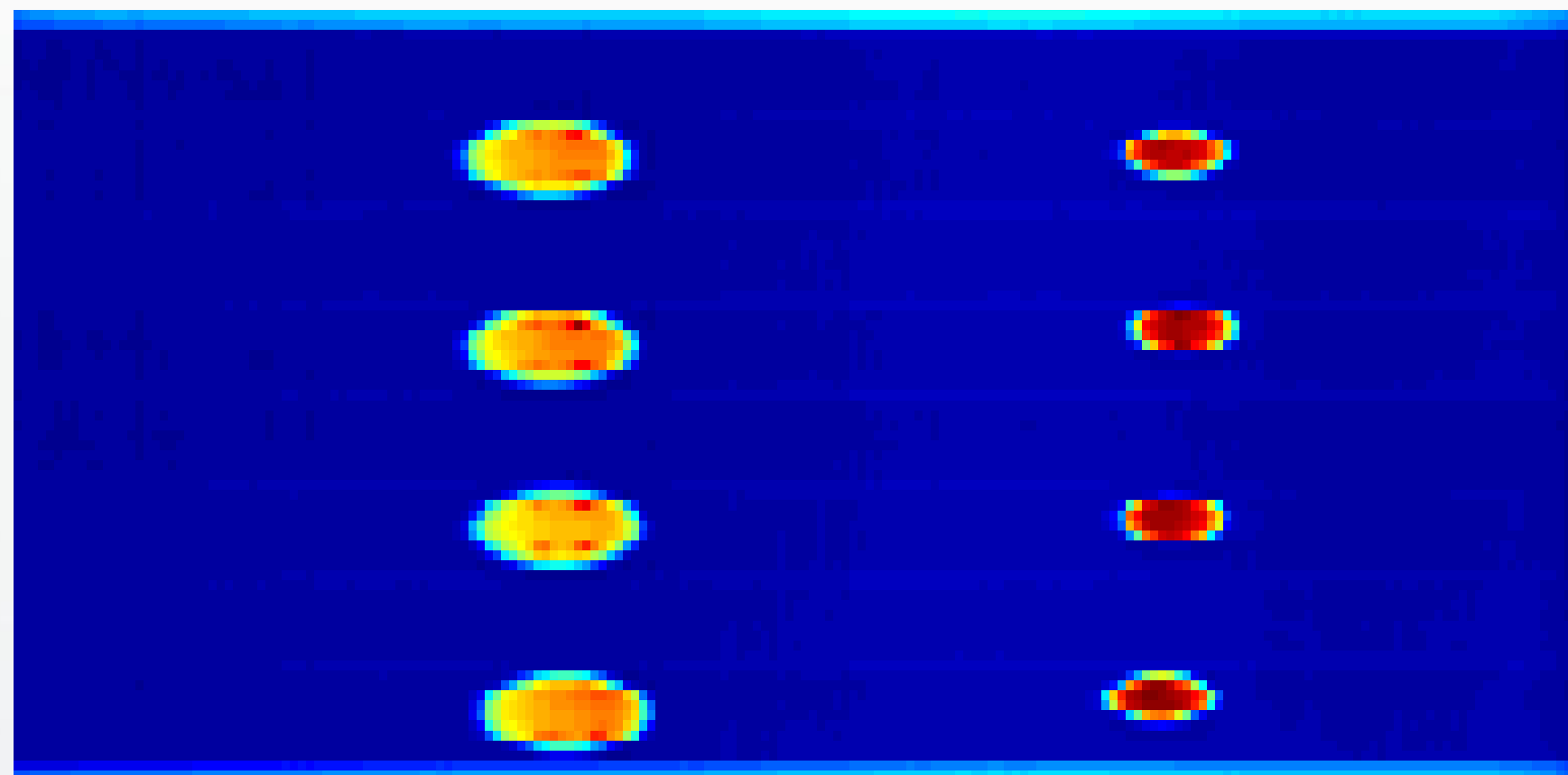
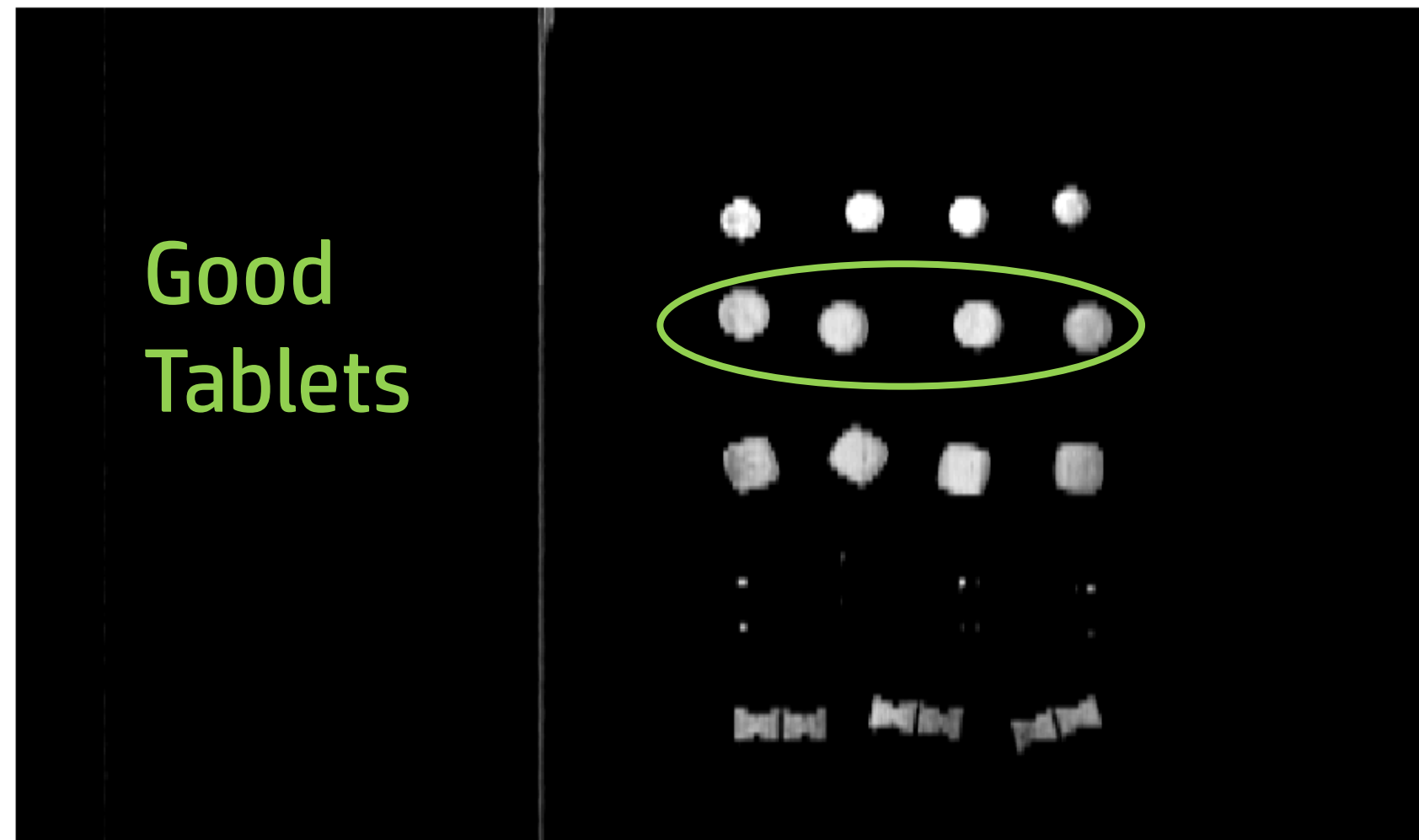
RGB image



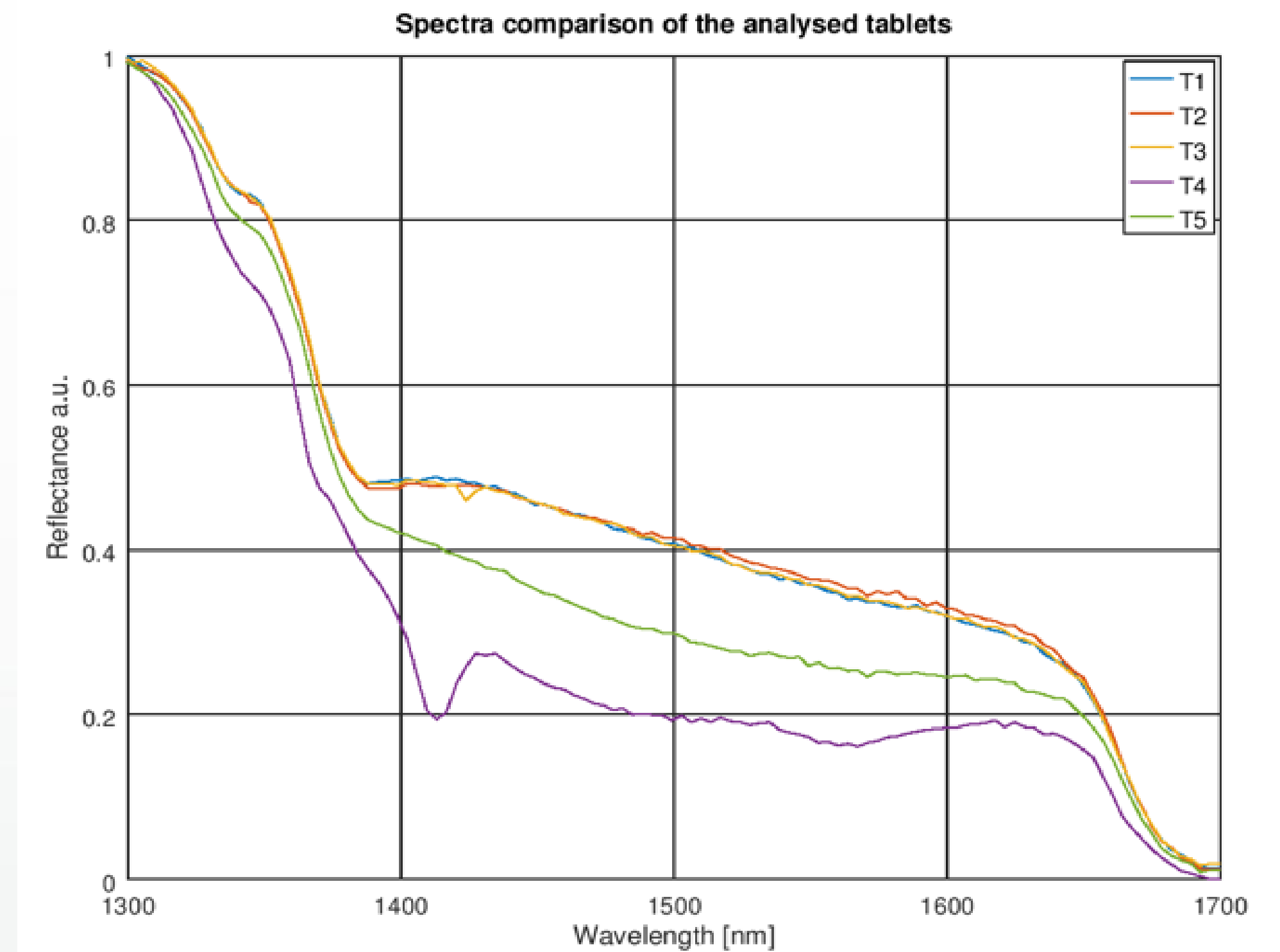
Hyperspectral image



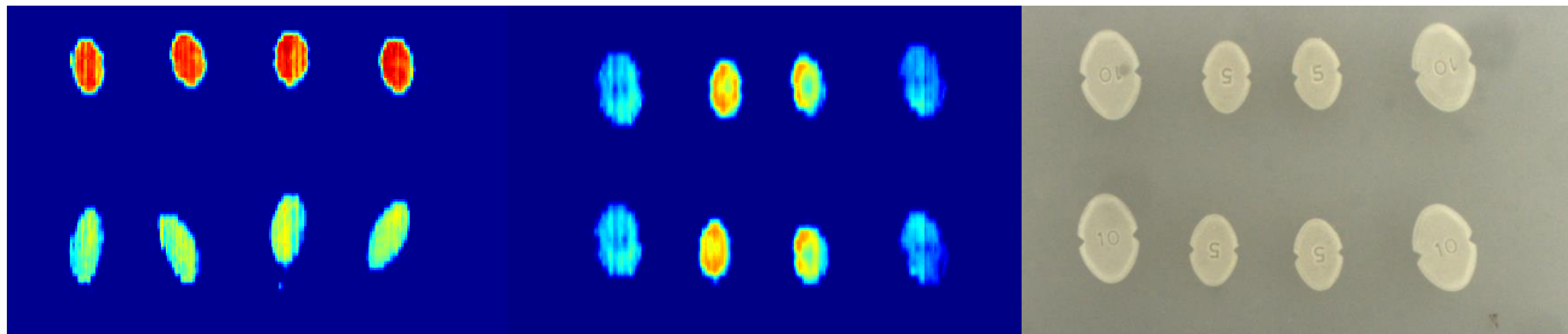
Data extraction



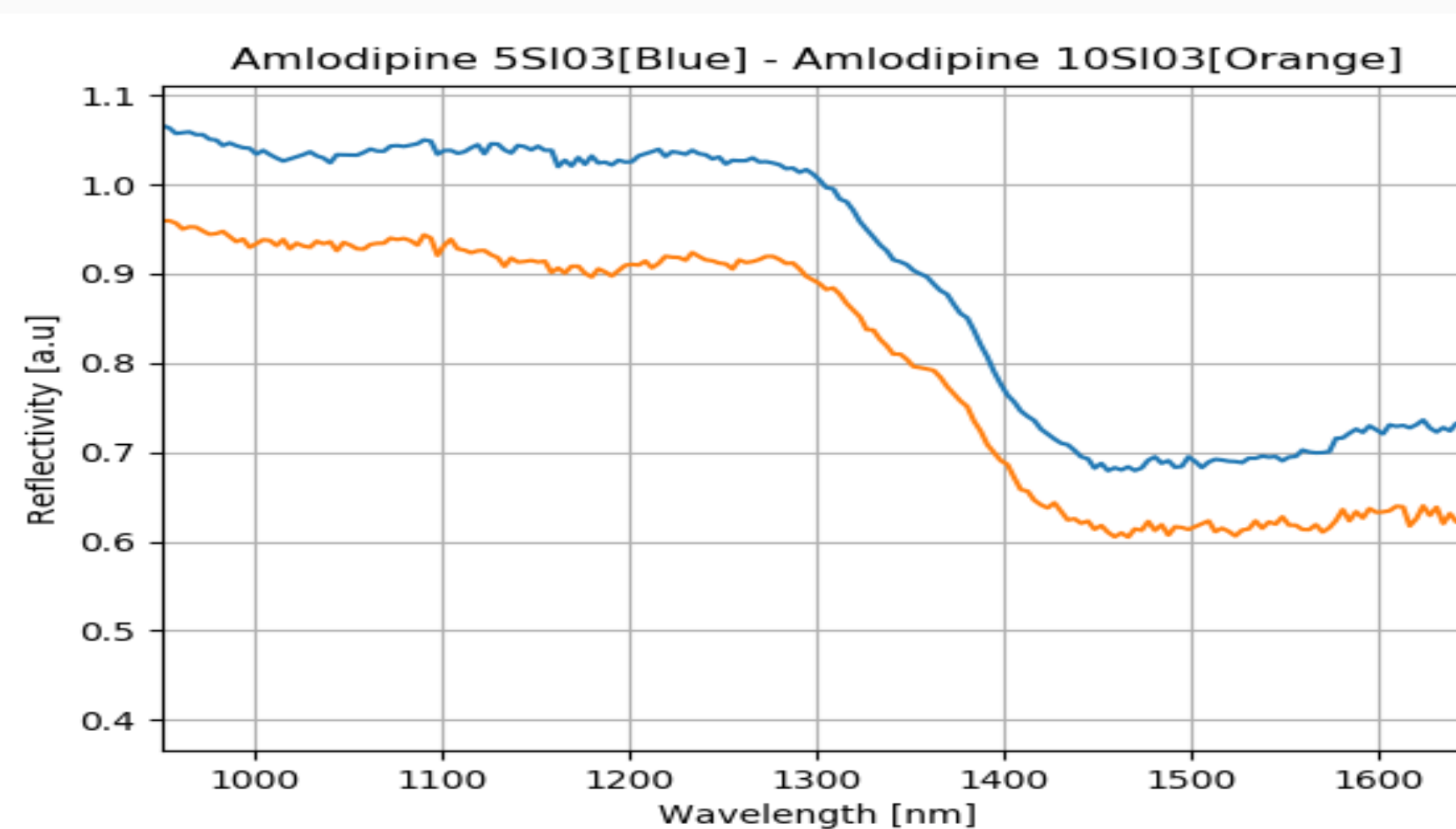
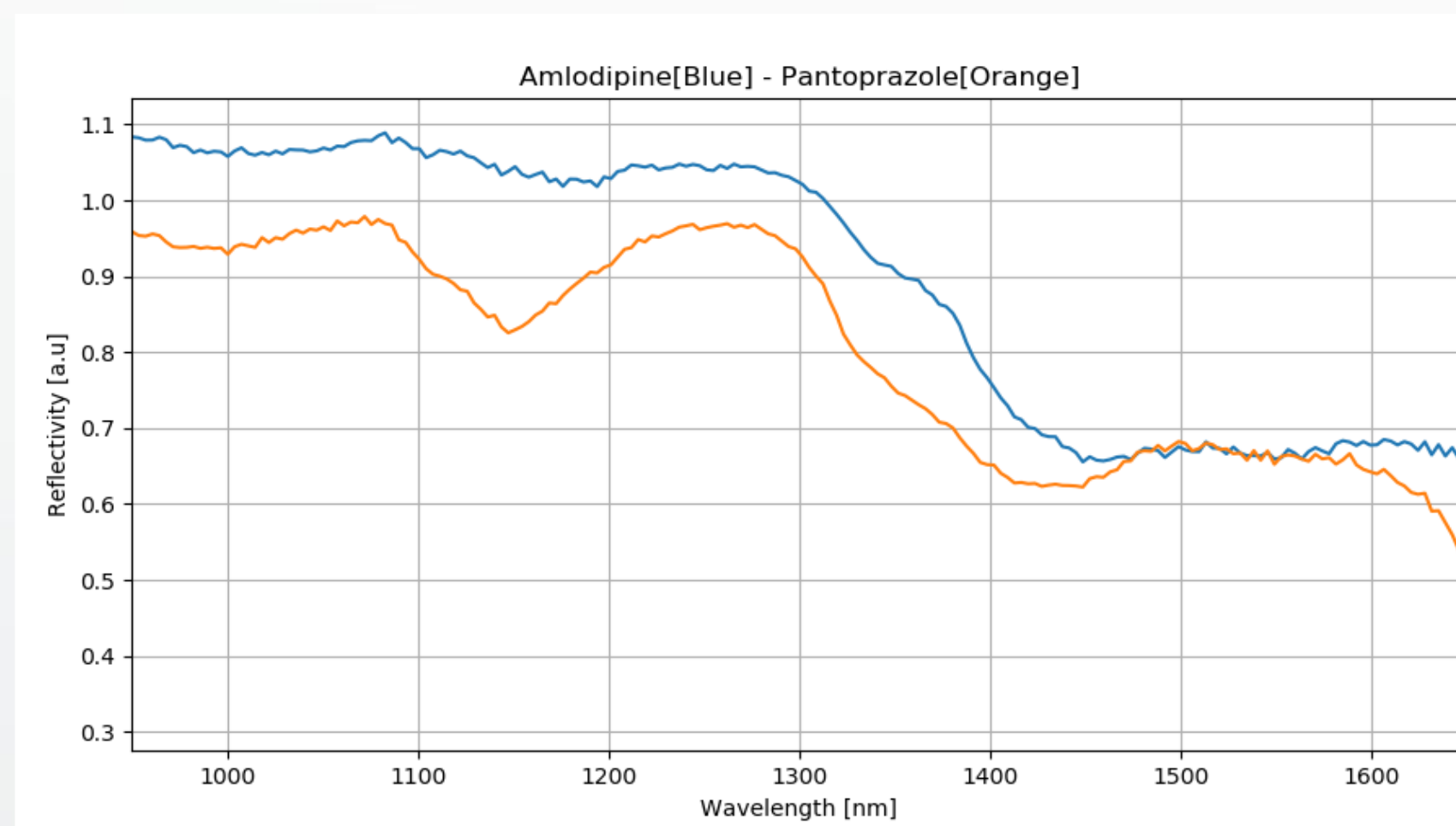
False color image of tablets with different API



Spectral range extraction



Tablets with different dosage



Tablets with different API

HarleNIR - PAT tool for pharmaceutical product inspection



Customized light source
Linear Halogen bulb

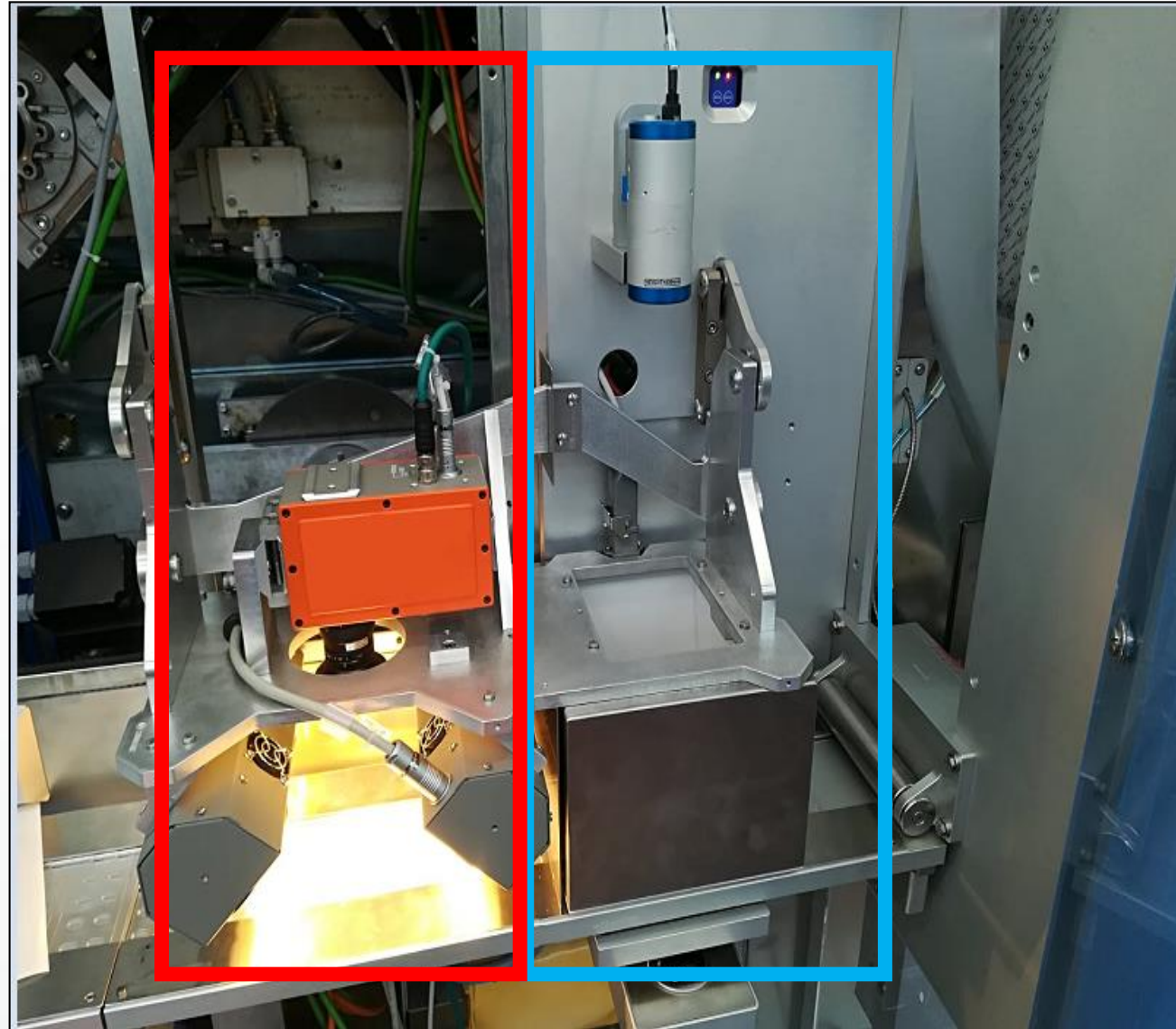
Process analytical technology (PAT) has been defined by the United States Food and Drug Administration (FDA) as a mechanism to design, analyse, and control pharmaceutical manufacturing processes through the measurement of Critical Process Parameters (CPP) which affect **Critical Quality Attributes** (CQA)

Critical Quality Attributes (CQA):

- API content uniformity
- Tablets moisture
- API mix-up avoidance
- Tablet coating uniformity

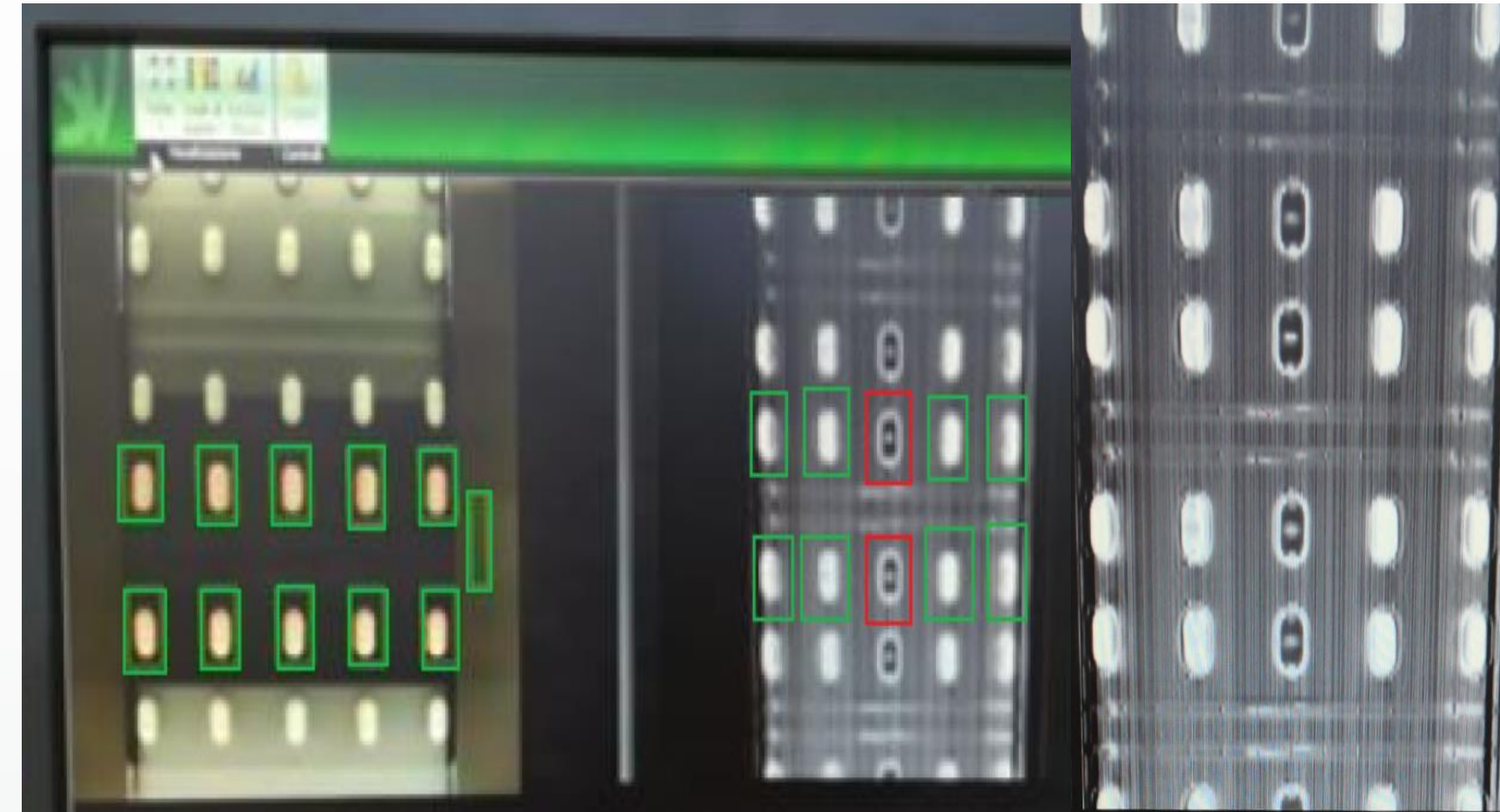
Use of the hyperspectral camera for the API content uniformity → On line products release!

HarleNIR - In line application & Machine integration



Machine speed → 300 blisters/min

Acquisition rate → From 520 (full band) to 15000 frame/s

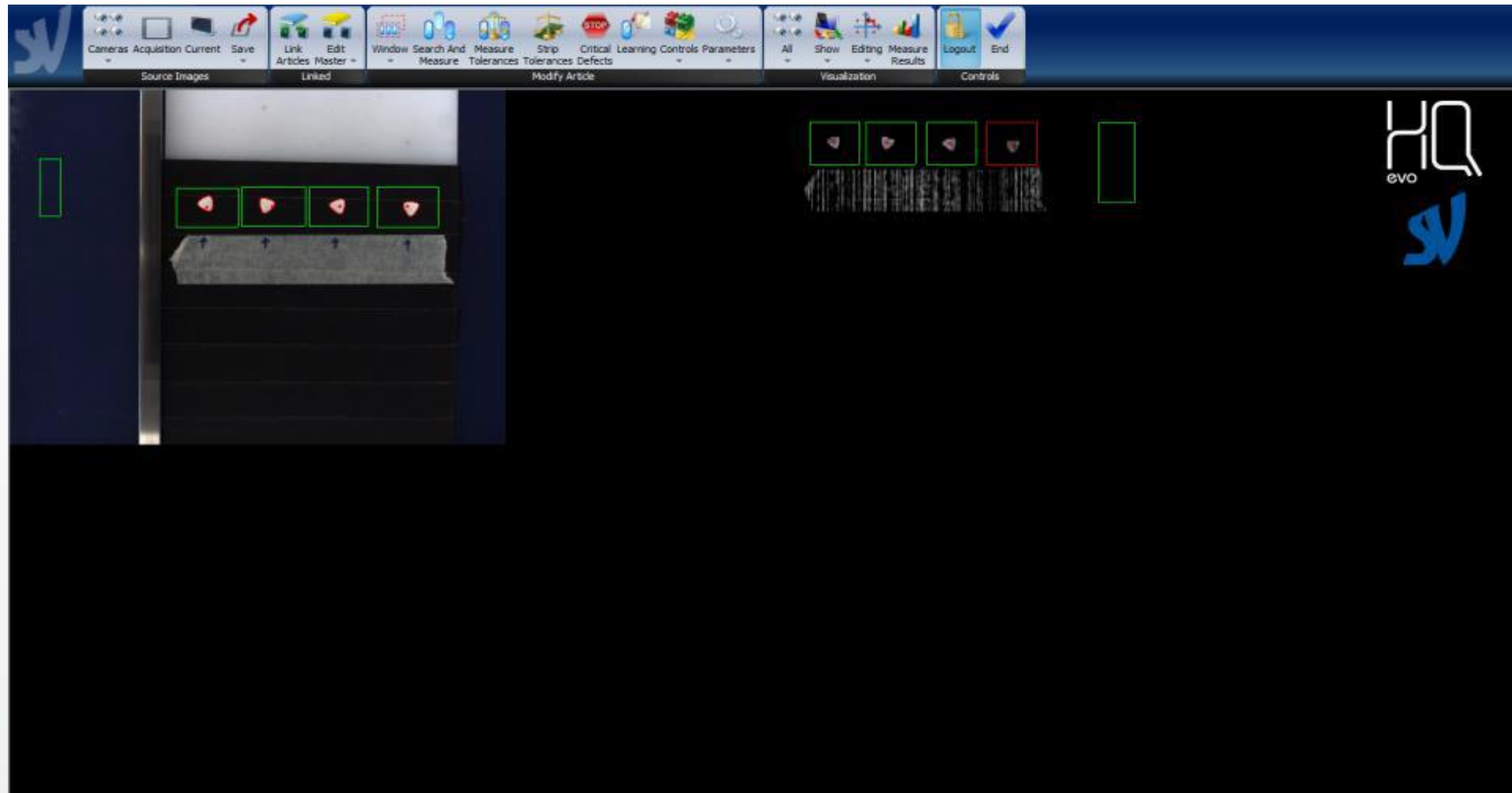


The tablets with different chemical composition are well visible



Produced tablets on the blister machine

HarleNIR - Example of identification



Distinction of product with different dosages

Telecamere Acquisizione Attuale Salva
Assoda Modifica Articoli Master
Finestre Ricerca e Misura Tolleranze Misura Tolleranze Nastro Difetti Critici Apprendimento Controlli Parametri
TV1 Visualizza Modifica Risultati Misure Logout Fine

Immagini Sorgente

Modifica Articolo

Visualizzazione

Controlli

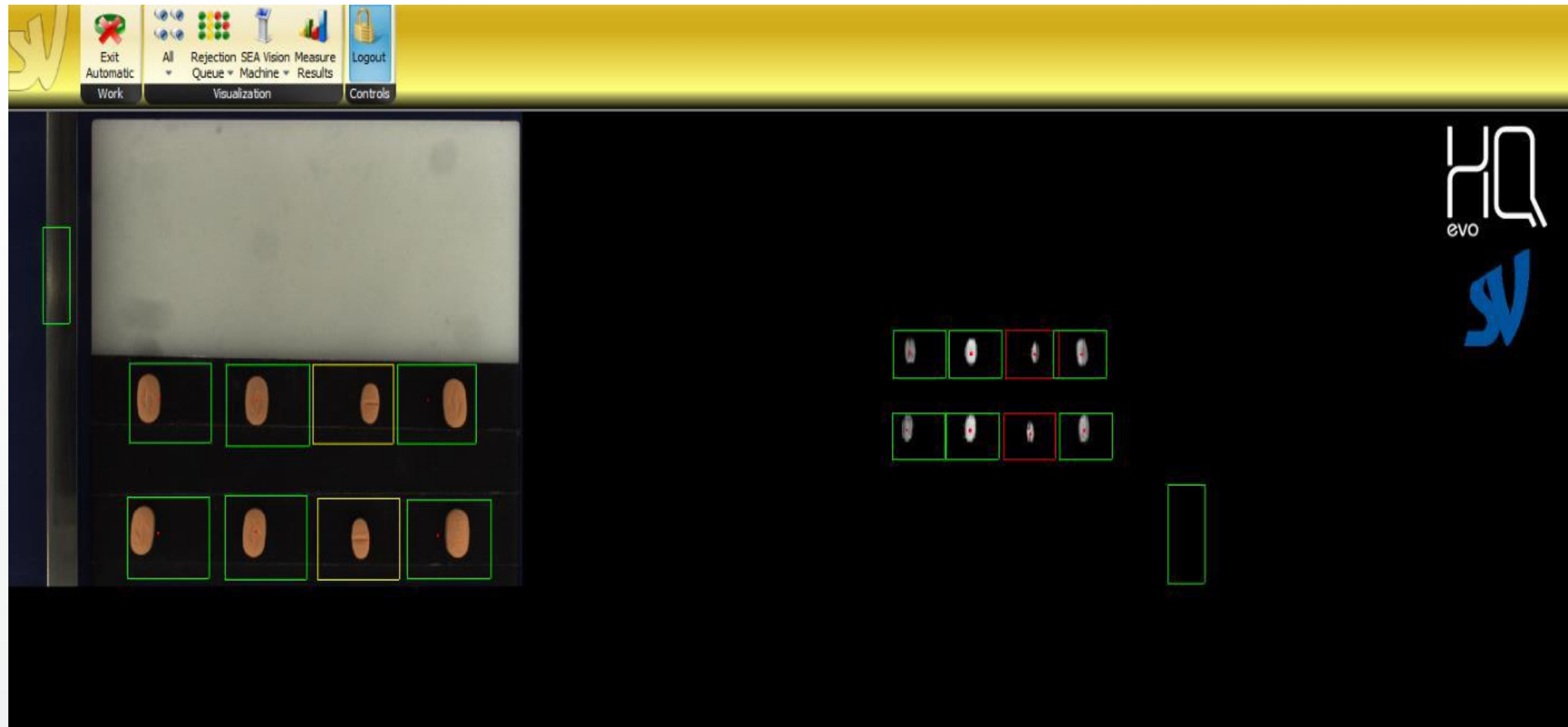
Risultati delle misure

☒ Alveoli buoni
 ☒ Alveoli vuoti
 ☒ Alveoli con difetti
 ☒ Finestre sul nastro

	Area	F.1	F.2	F.3	F.4	Ang.	L.R.	D.R.	L.V.	D.V.	L.B.	D.B.	T.1	S.1	I.1	T.2	S.2	I.2
1-1-2	+0			+0	+0		+0	+0	+0	+0	+0	+0	+0	+0	+0			
1-1-3	+0			+0	+0		+0	+0	+0	+0	+0	+0	+0	+0	+0			
1-1-4	+0			+0	+0		+0	+0	+0	+0	+0	+0	+0	+0	+0			
1-1-5	Alveolo vuoto																	
1-1-6	Alveolo vuoto																	
1-1-7	Alveolo vuoto																	
1-1-8	Alveolo vuoto																	

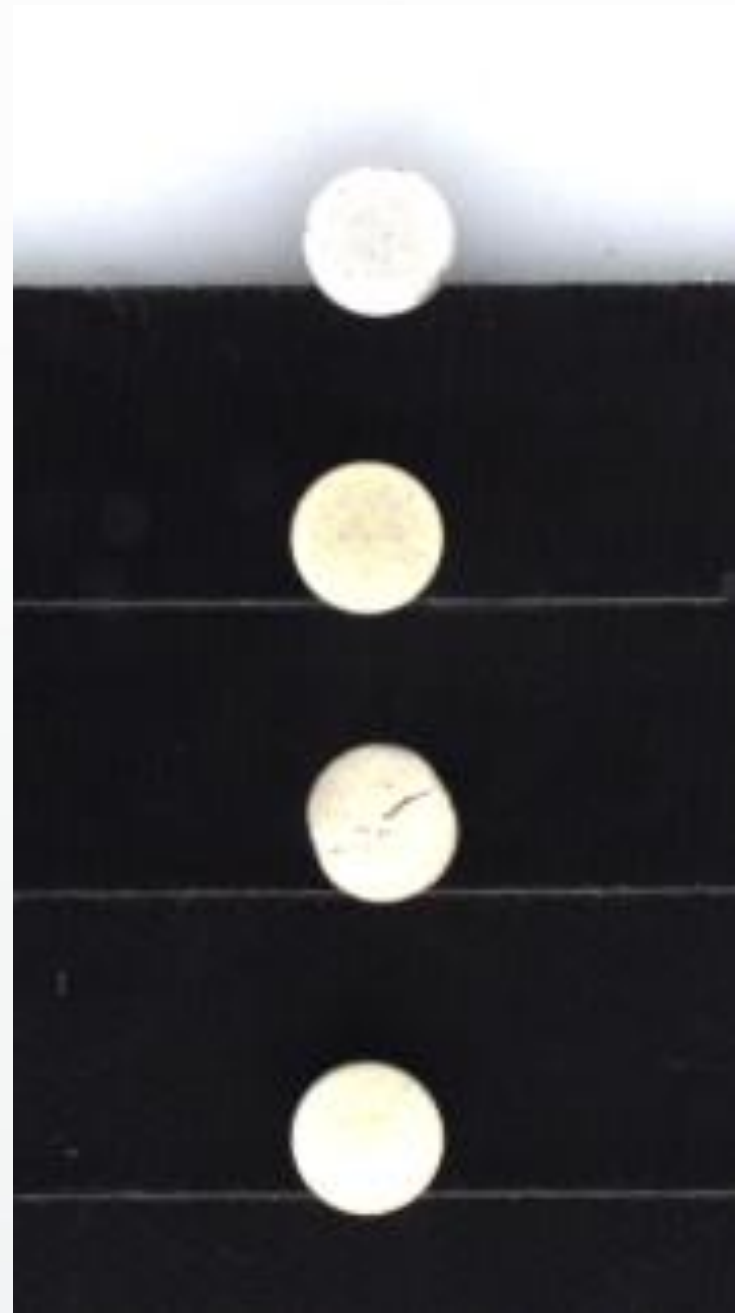


Distinction of product with different dosages

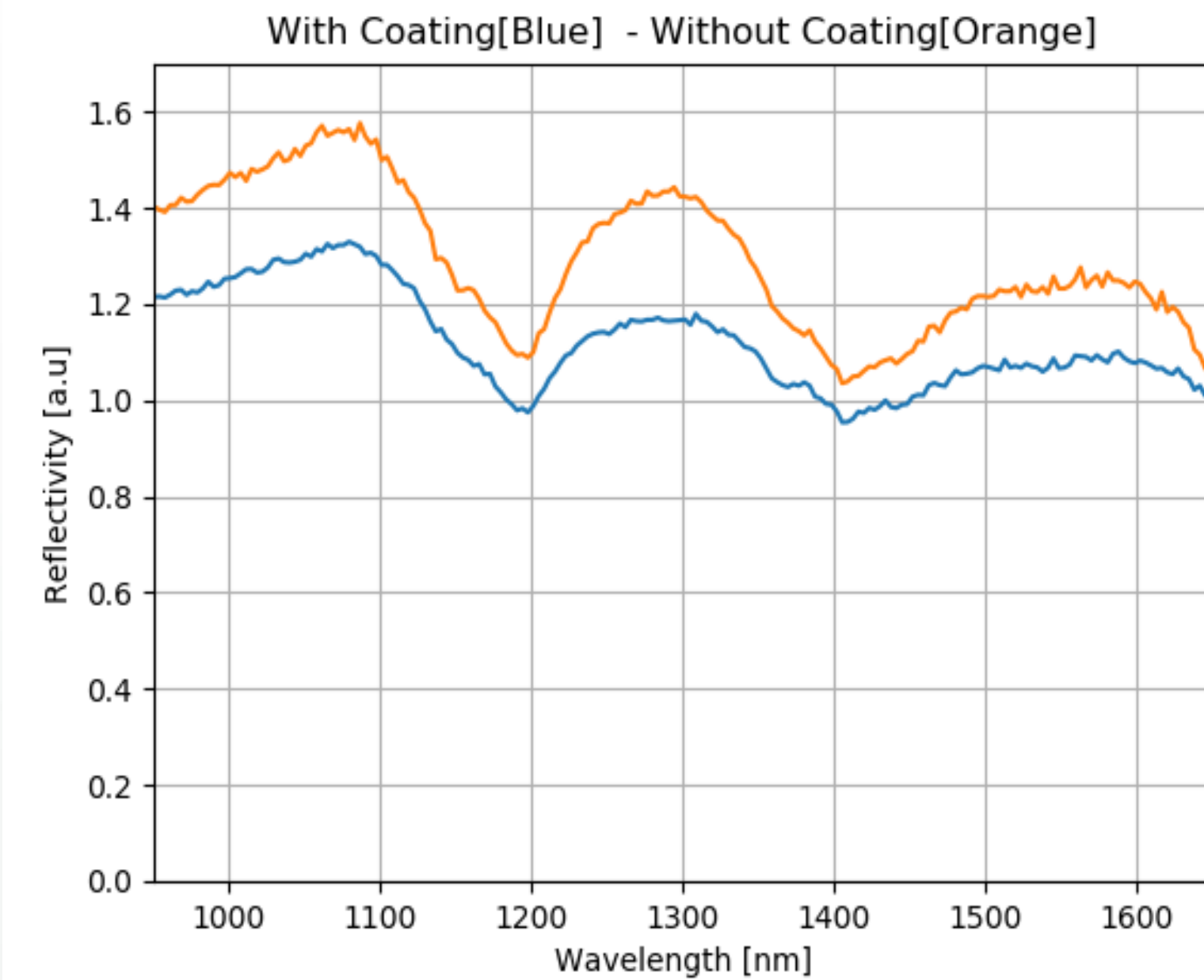
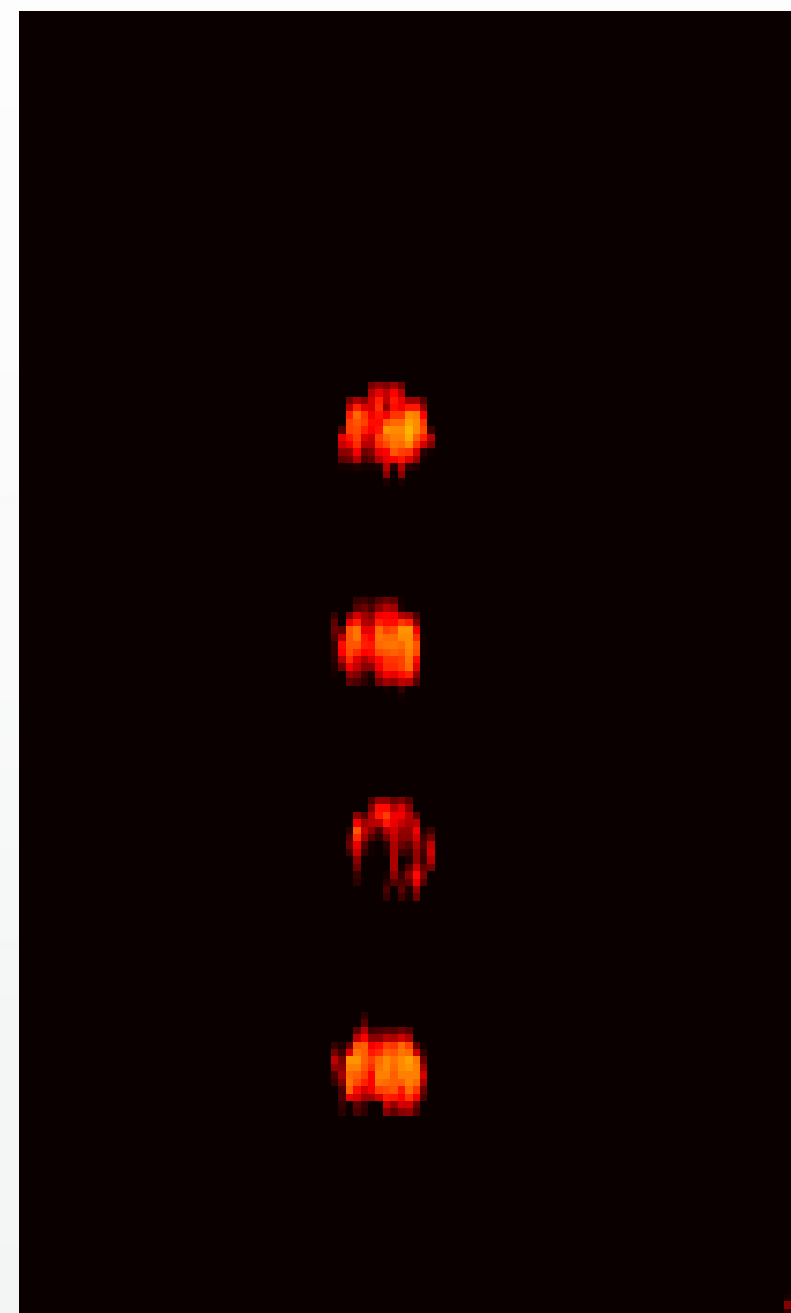


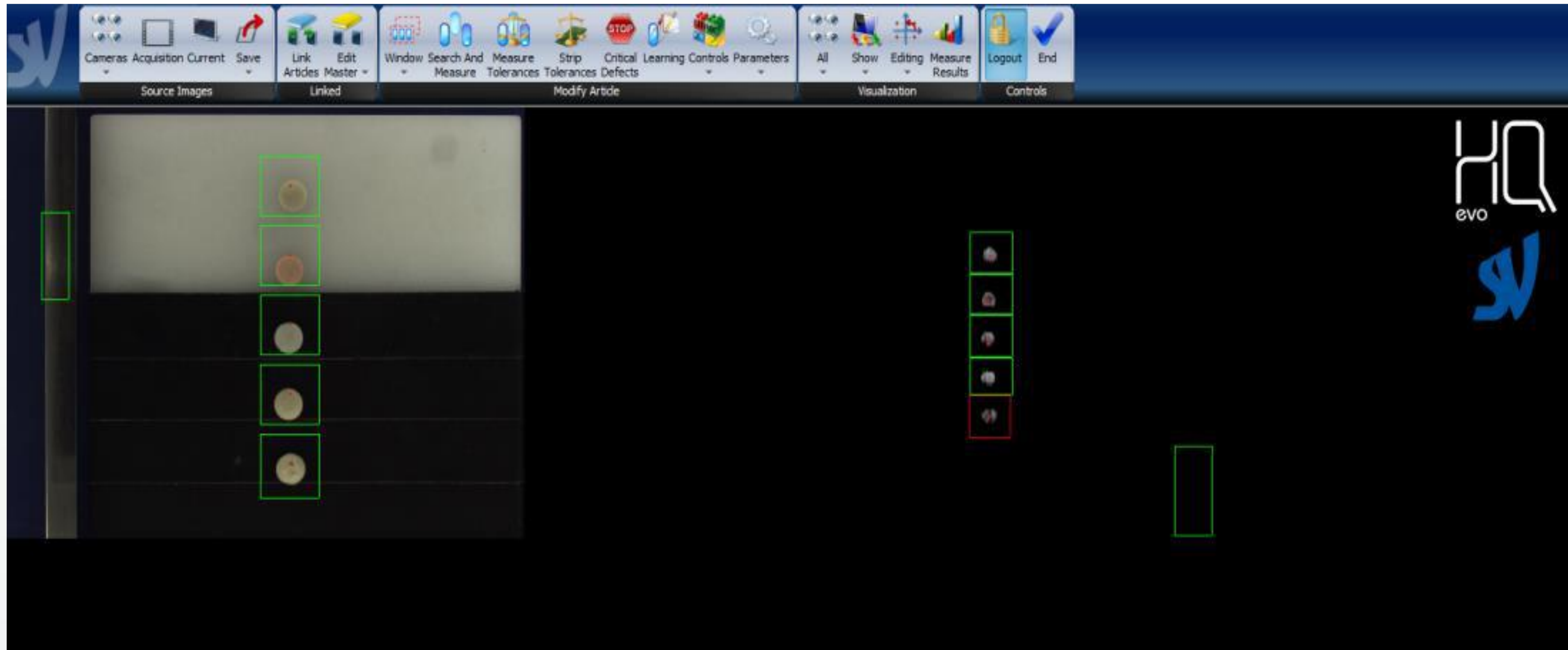
Double check – Visual inspection and dosage content control

HarleNIR - Tablet coating inspection



Without
Coating





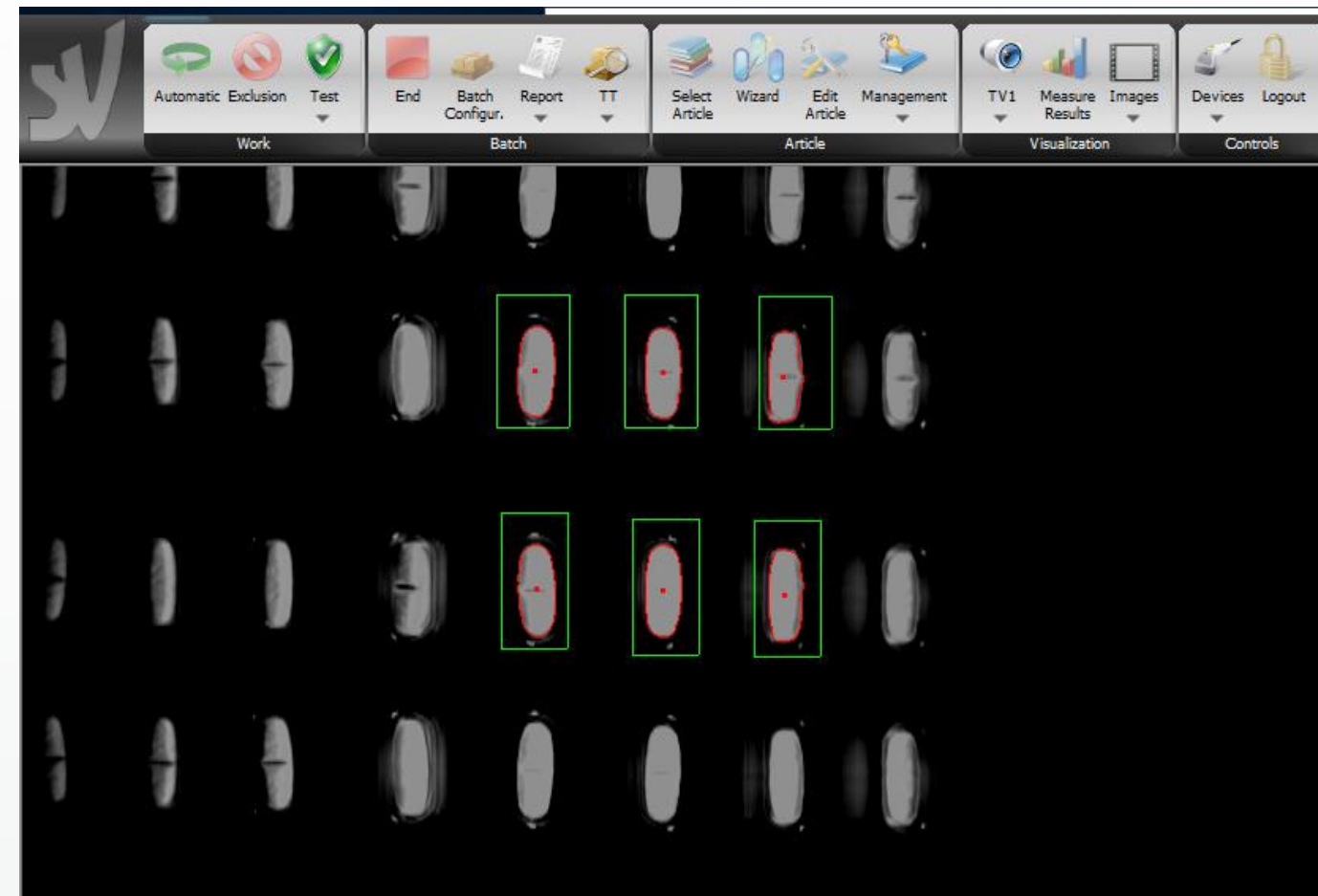
Distinction of product with missing coating

HarleNIR - API Content uniformity

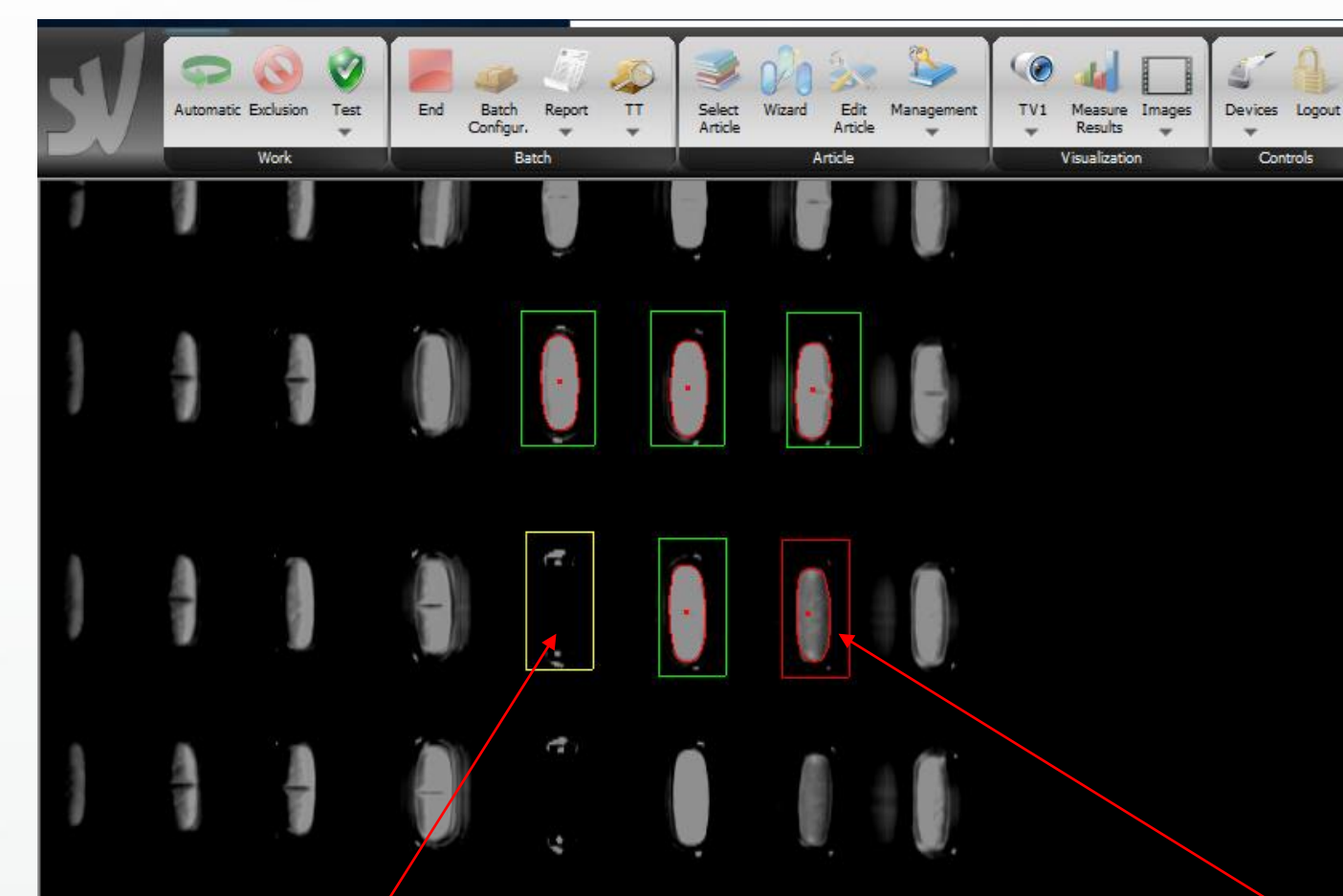
A different gray intensity level reveals foreign tablets



Customized light source
Linear Halogen bulb



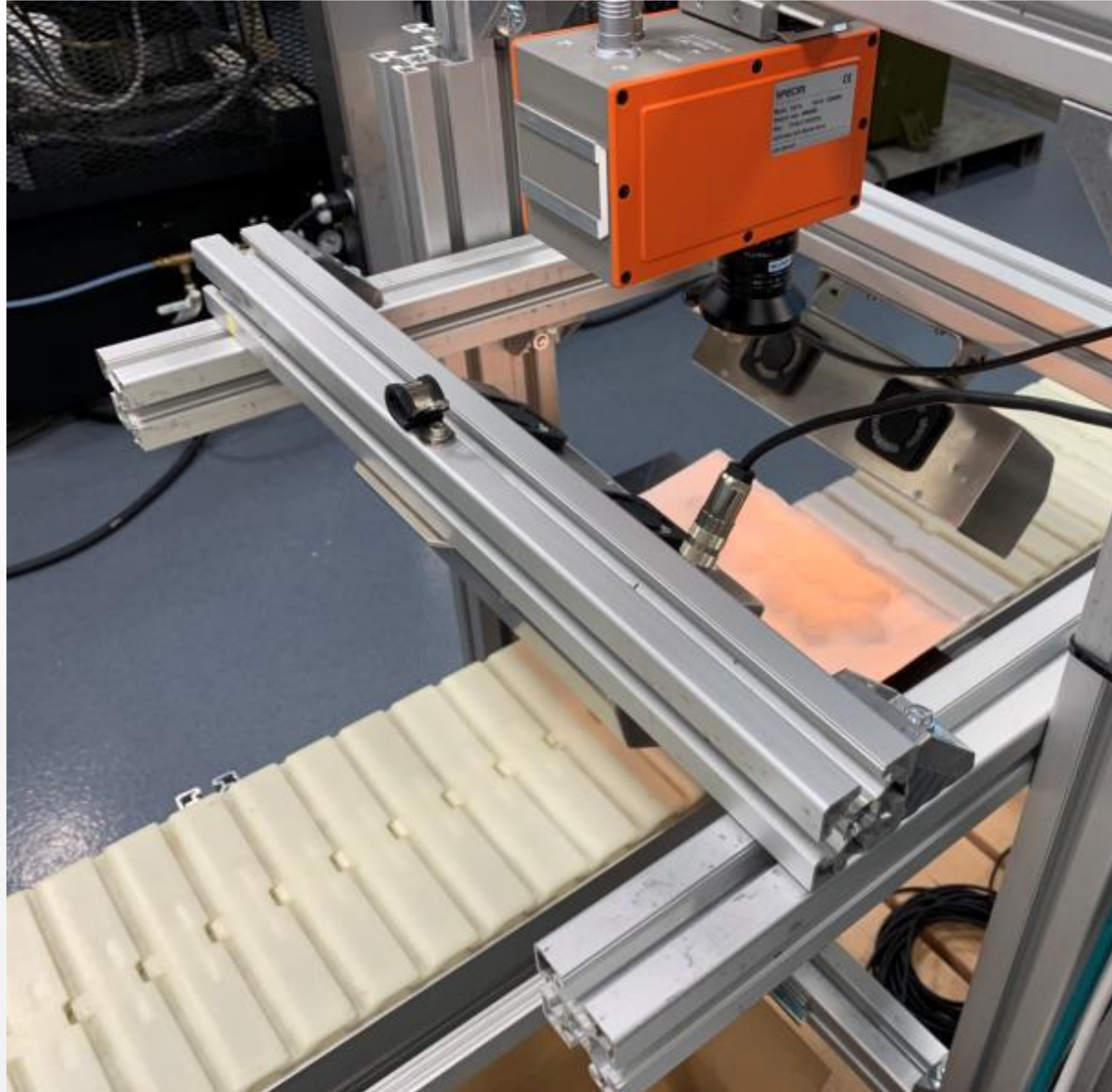
Good blister



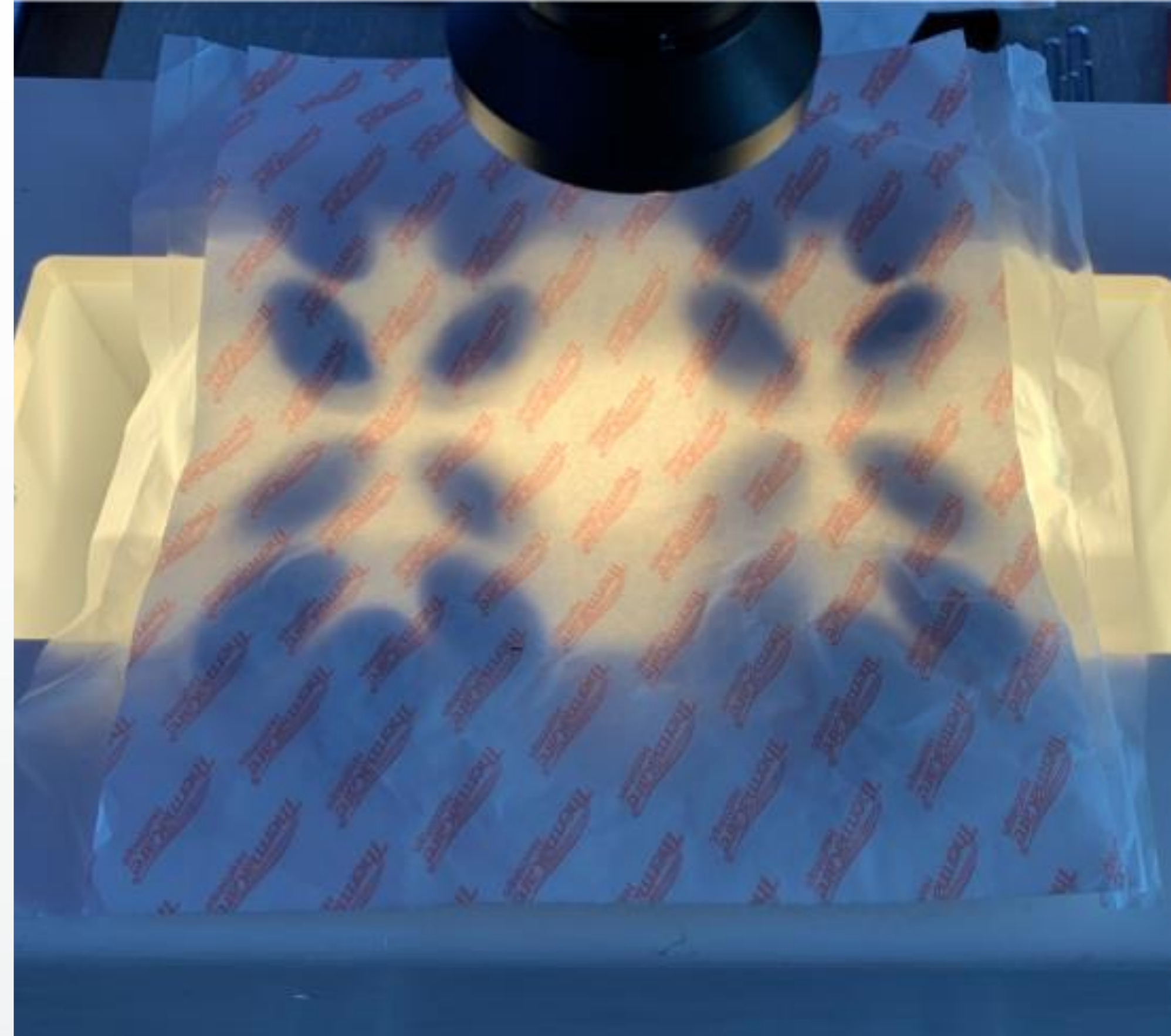
Missing tablet

Blister with Mix-up

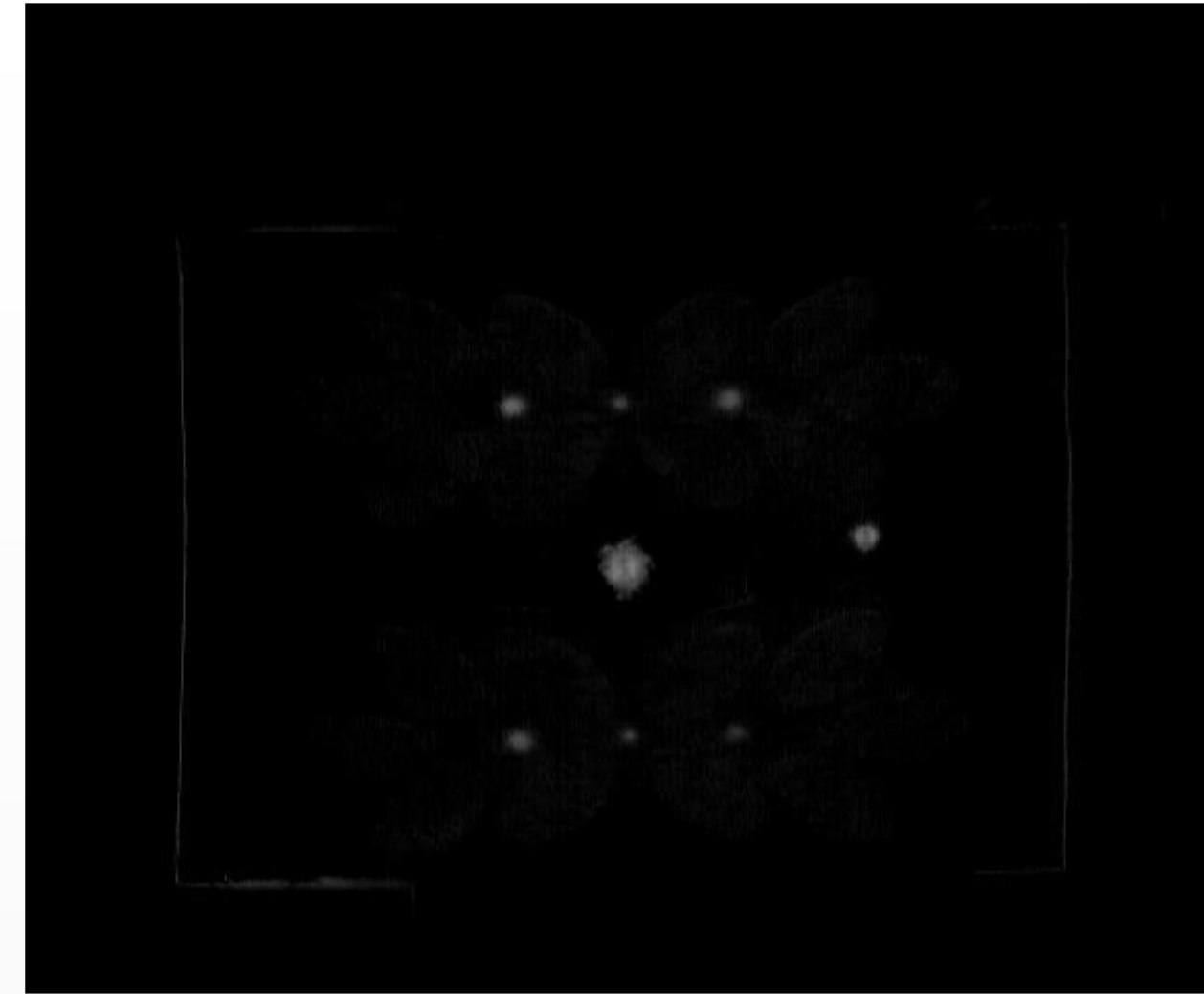
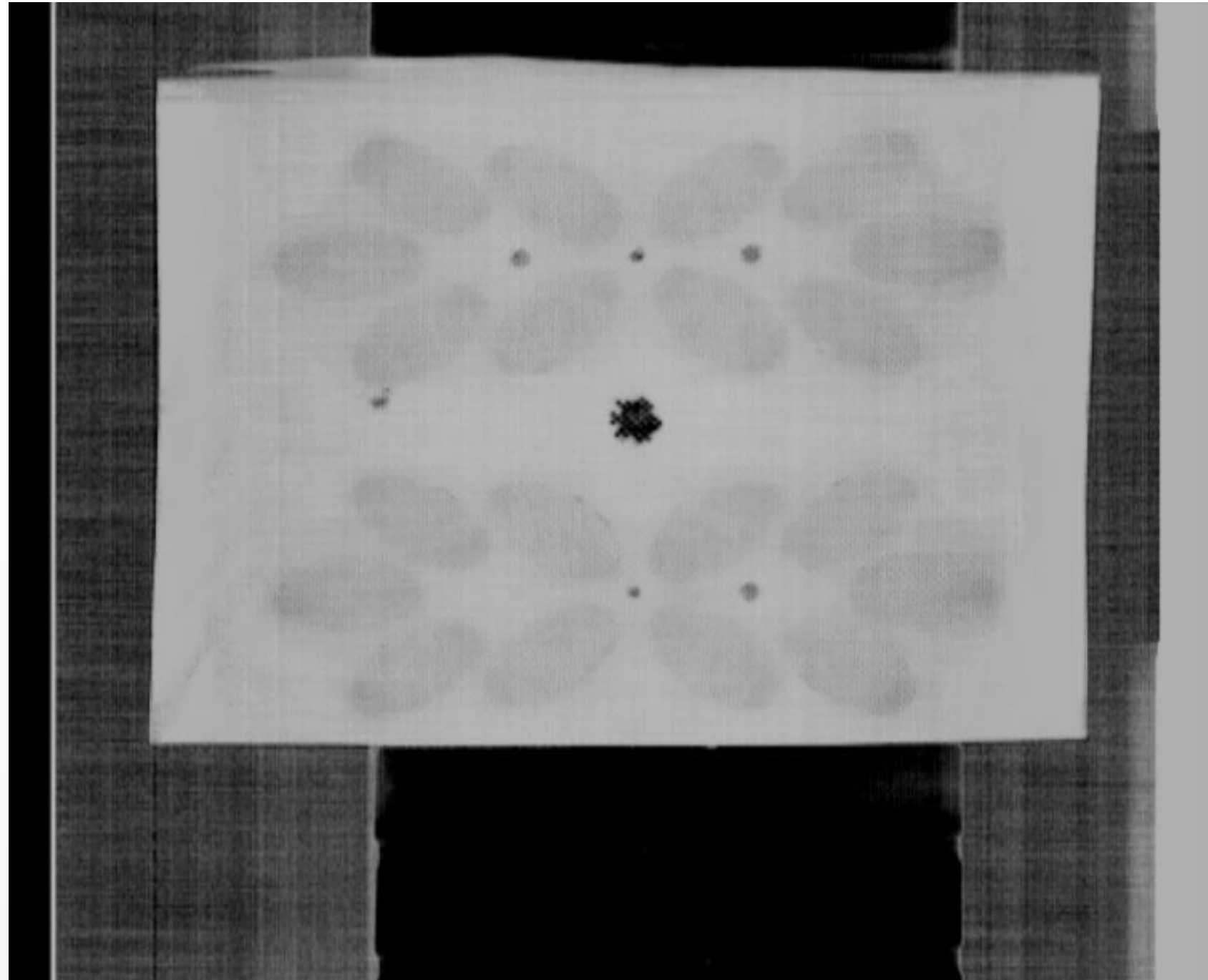
HarleNIR - Moisture measurements



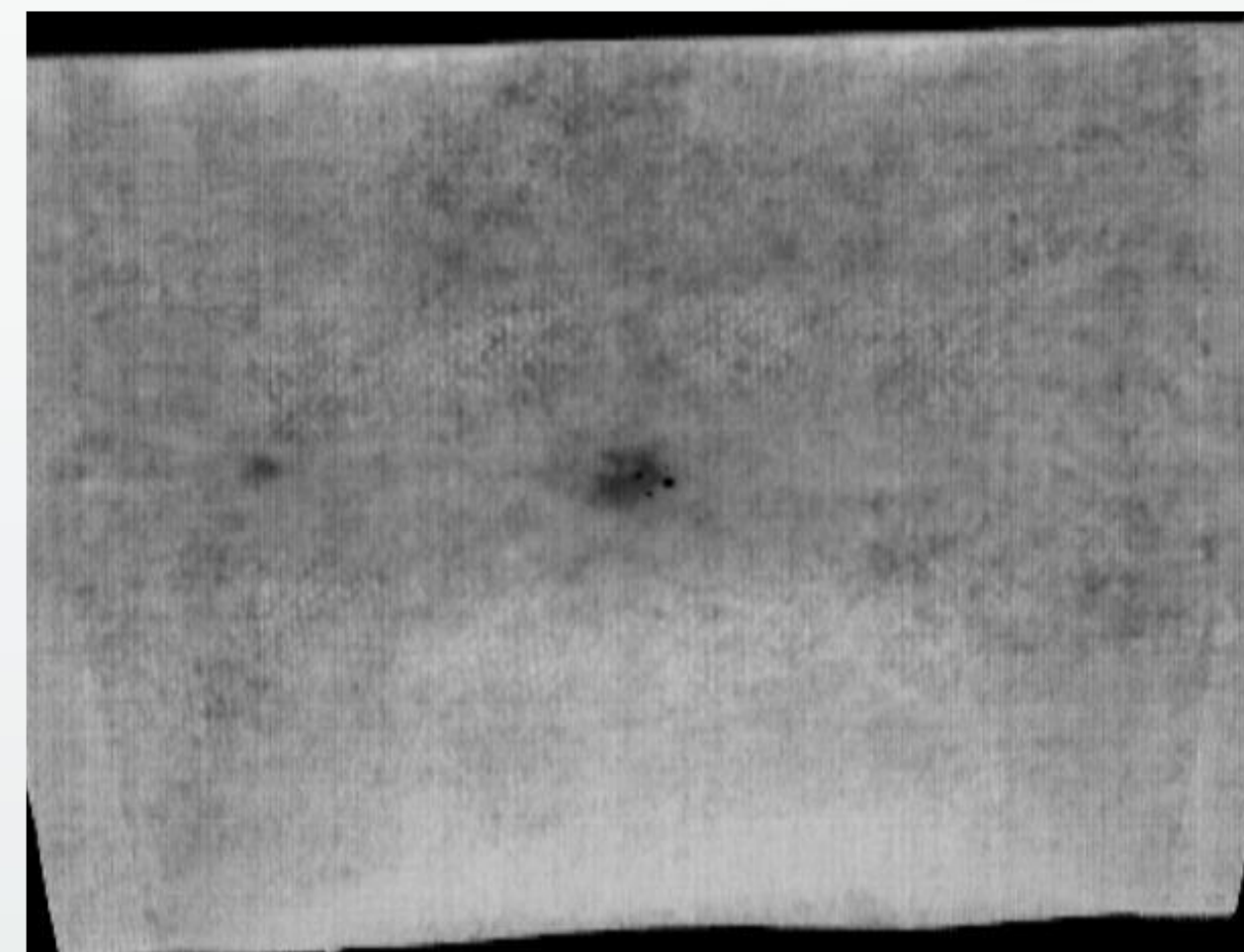
Measurements in reflection

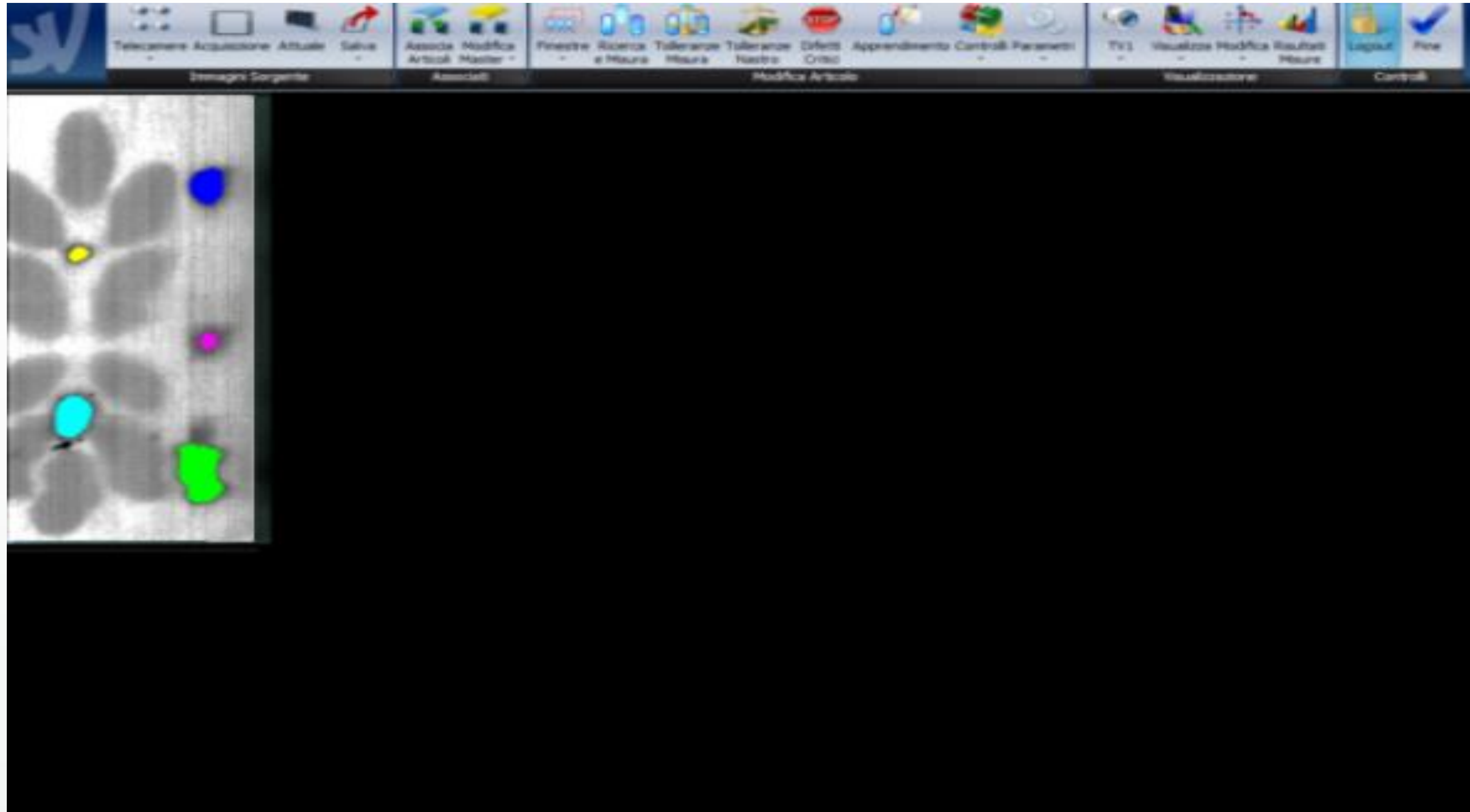
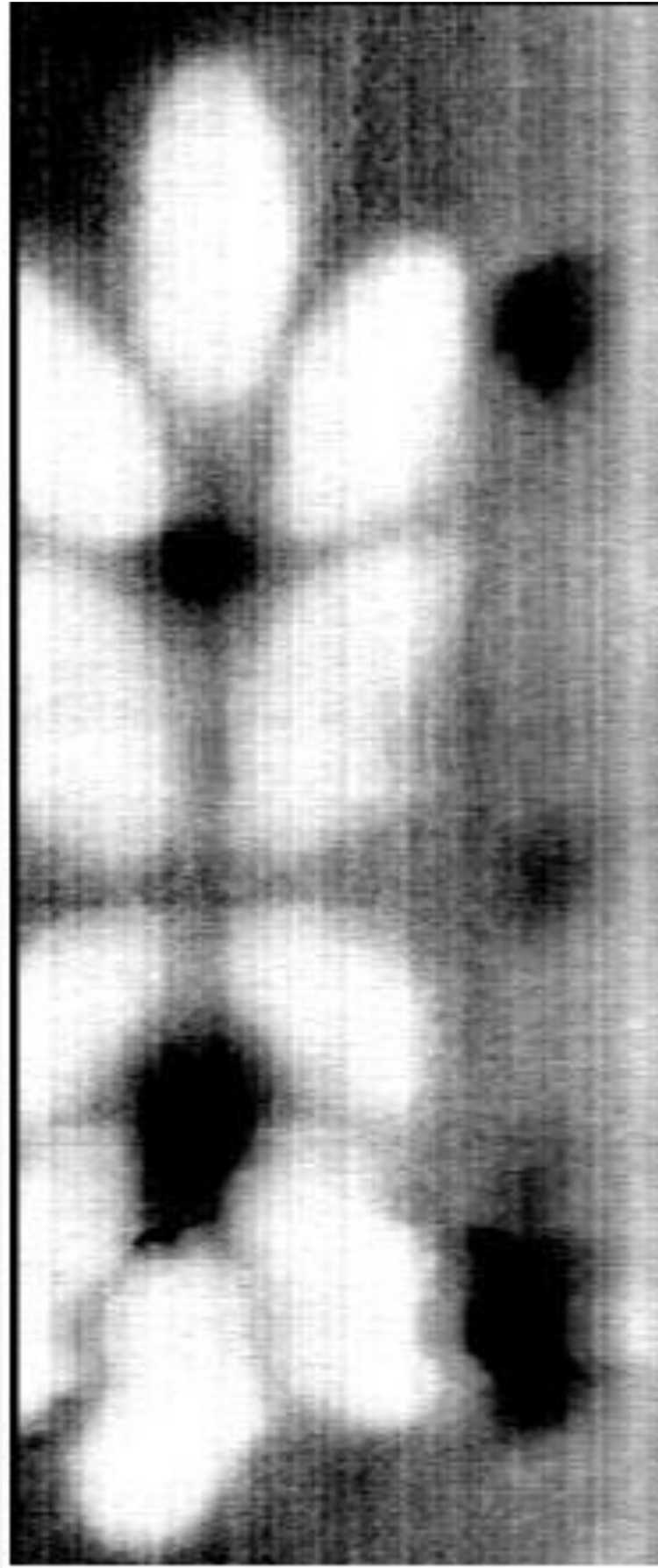


Measurements in transmission



Transformation from
reflection to absorption

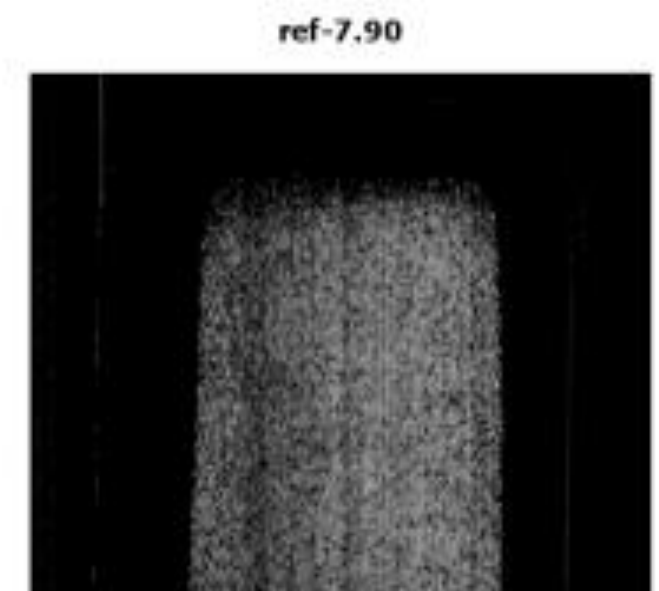
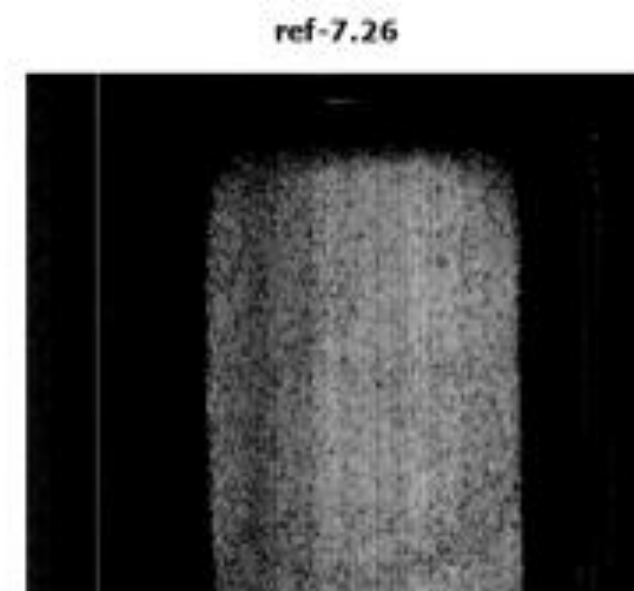
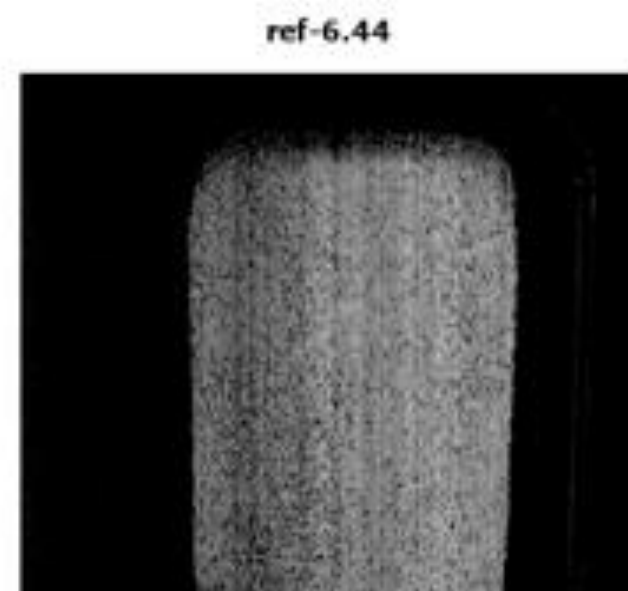
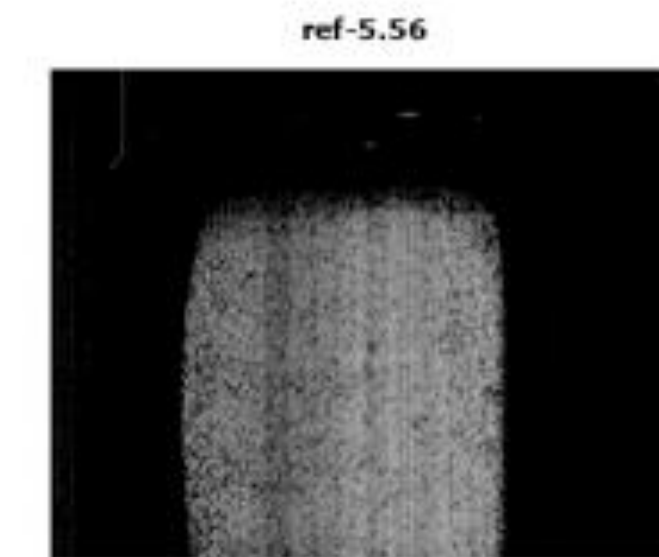
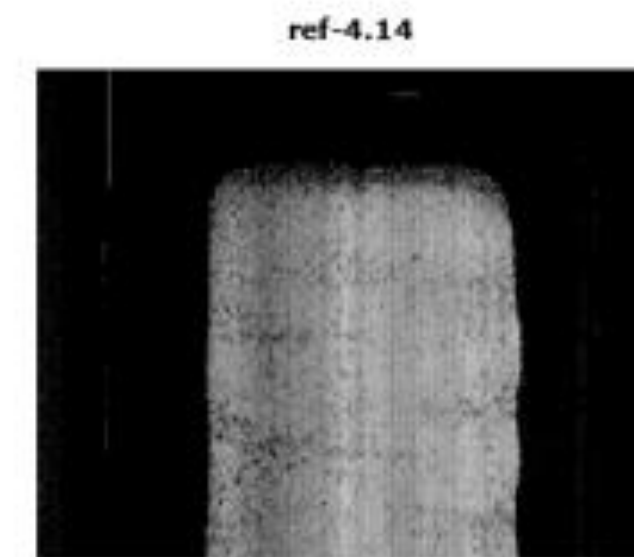
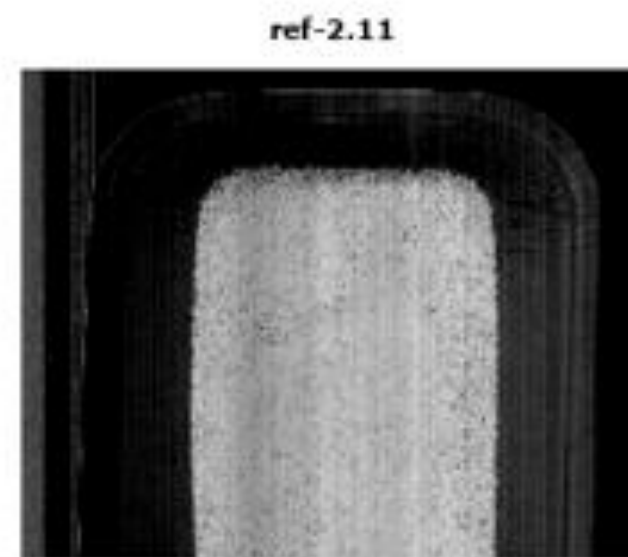


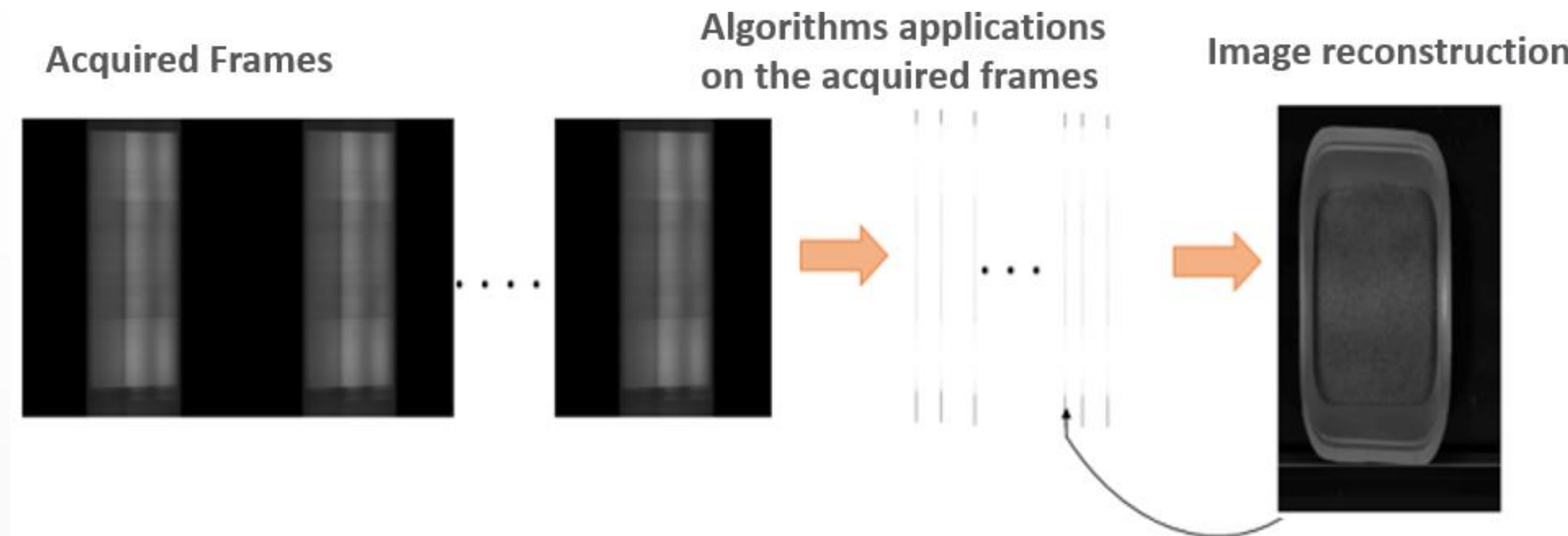


HarleNIR - Other applications & Inspection of ceramic material

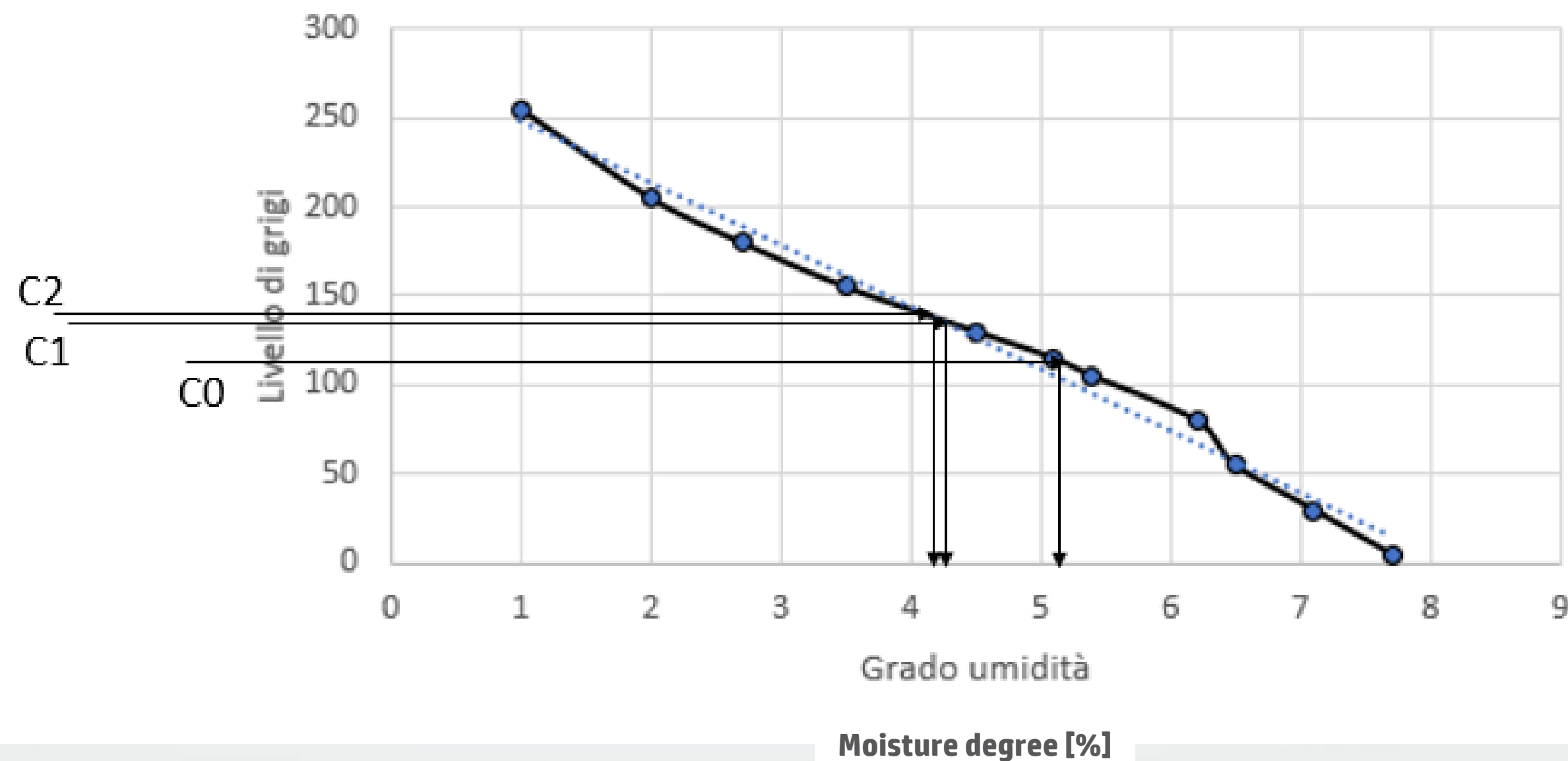


Moisture content of ceramic powder





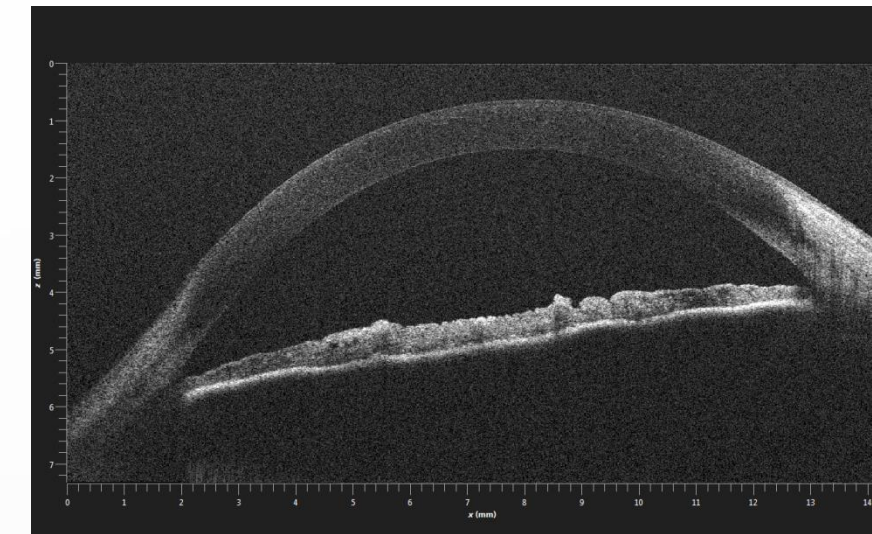
Calibration curve
obtained by a
thermobalance



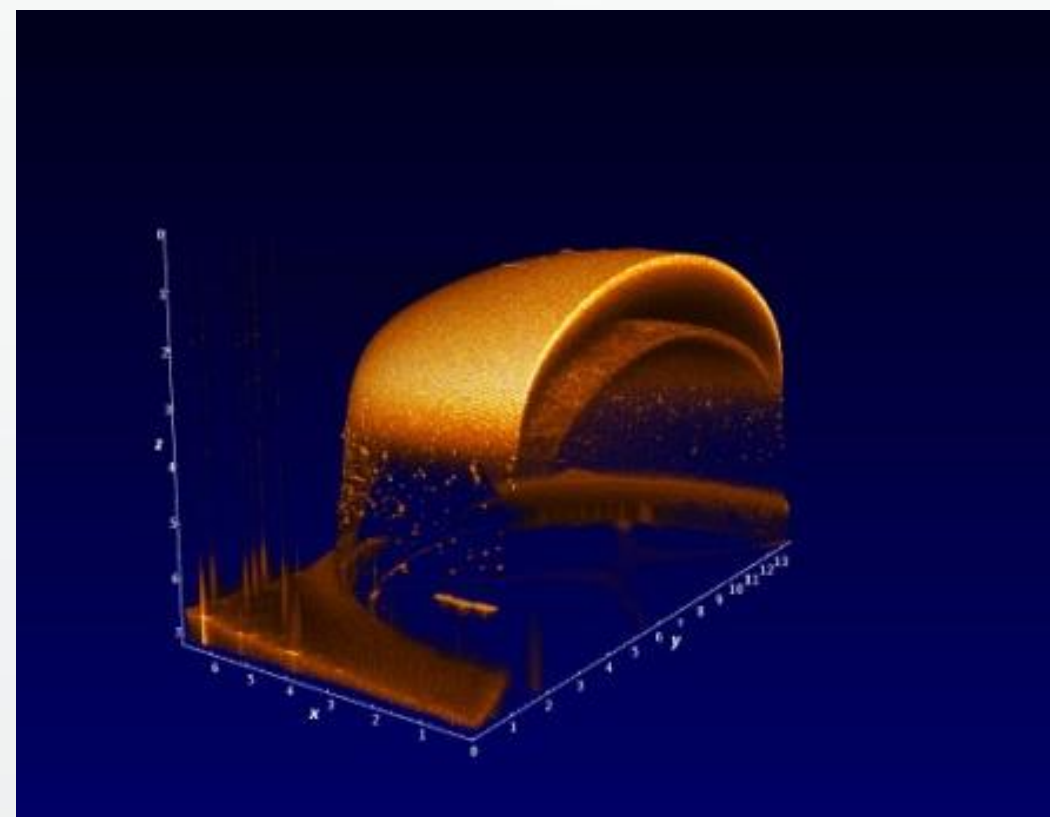
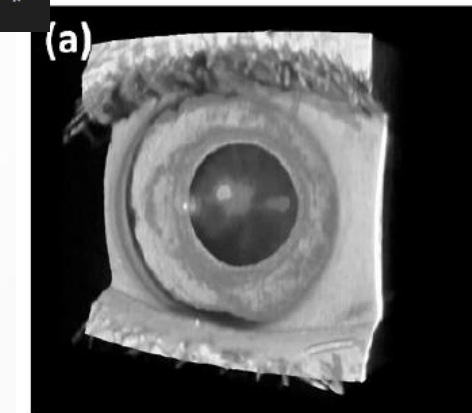
Optical Coherence tomography

OCT is an optical imaging technique that is:

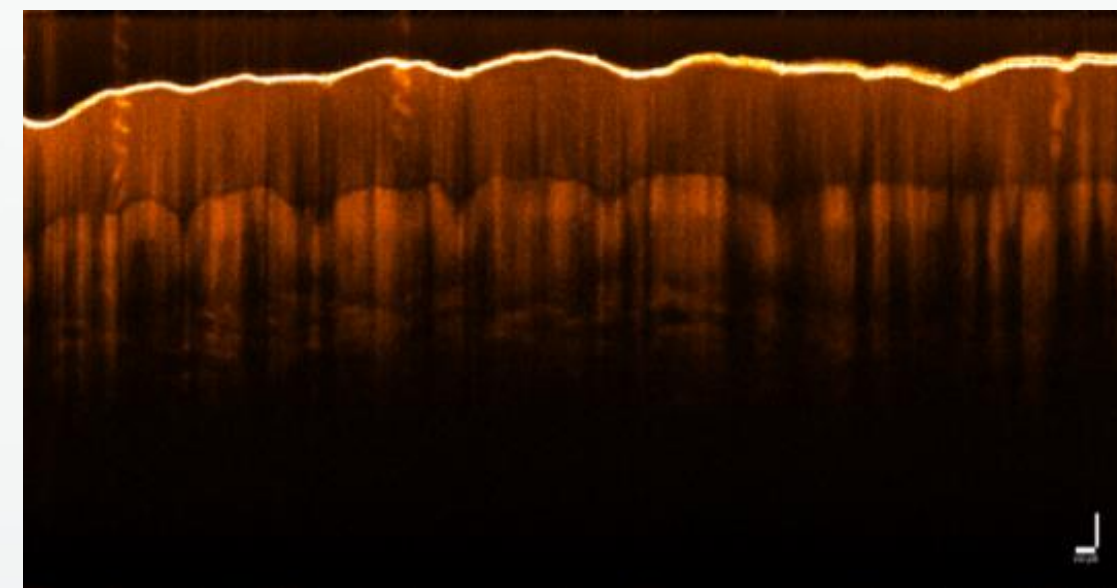
- Fast
- Very sensitive
- Non-contact
- Non-destructive
- Provides a resolution on the micron scale
- Provide a cross-sectional images with an high penetration depth
(Not for all materials)



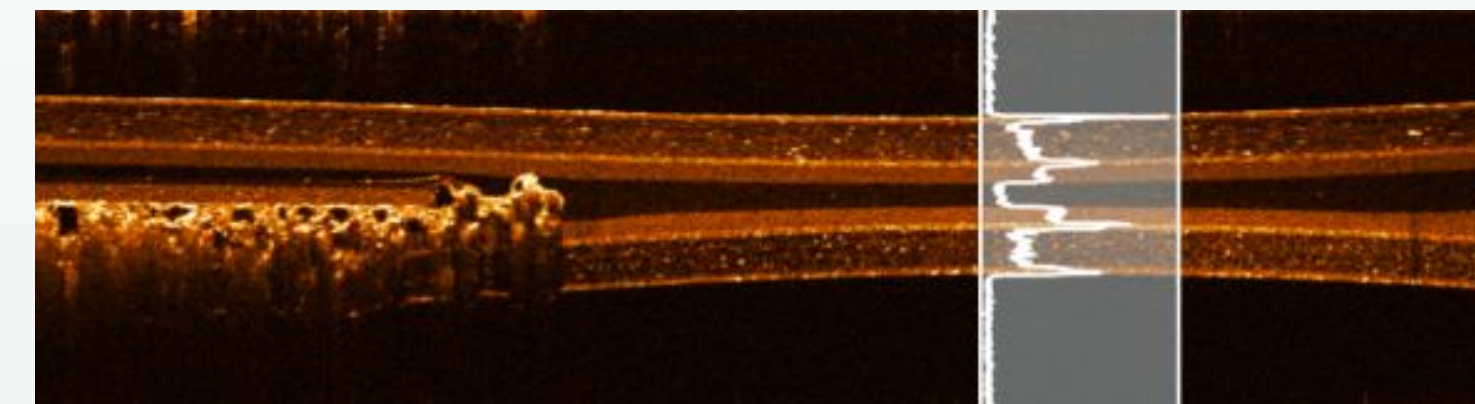
OCT - Human eye inspection



OCT 3D image of a tablet
inside the blister



OCT image of fingerprint



OCT image of thin plastic film

How does OCT work?

OCT is based on white light interferometry

Probe beam is focussed into sample

Light is back-scattered from different structures

A Michelson interferometer is used to measure the travelling time of photons

Signal on the detector

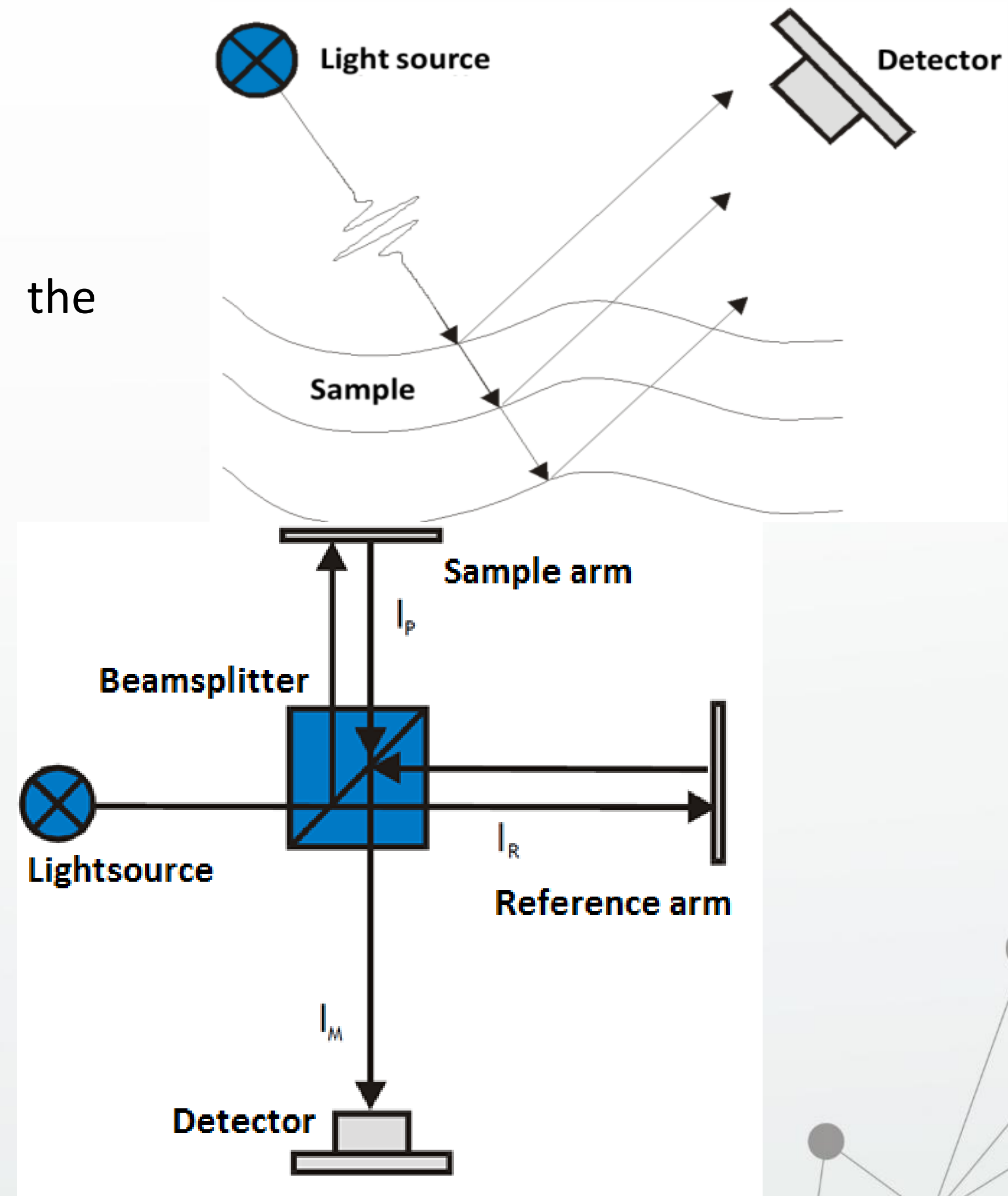
$$I = I_P + I_R - 2\sqrt{I_P I_R} \cos\left(\frac{2\pi}{\lambda} \Delta l_{opt}\right)$$

I_P : Intensity sample light

I_R : Intensity reference light

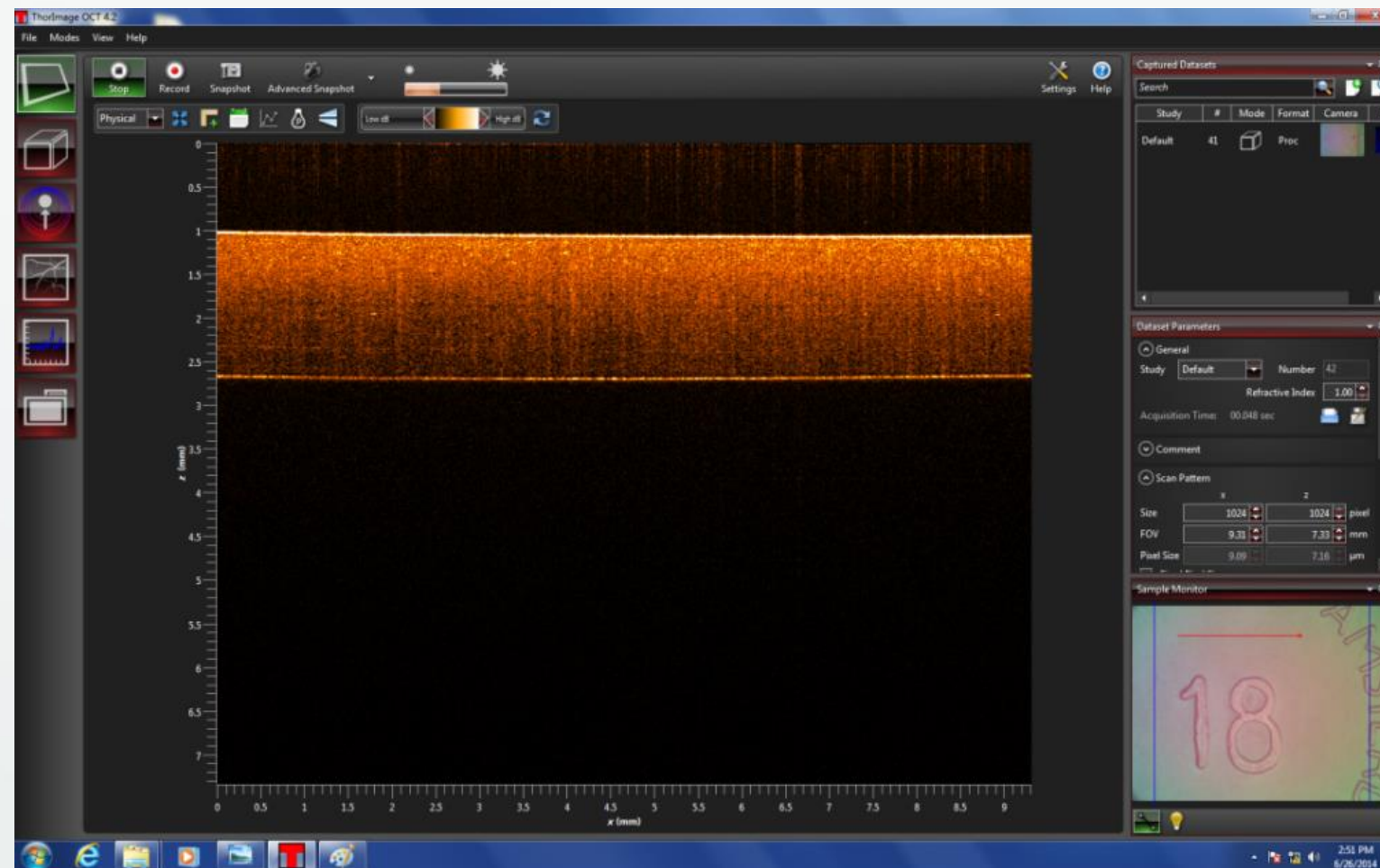
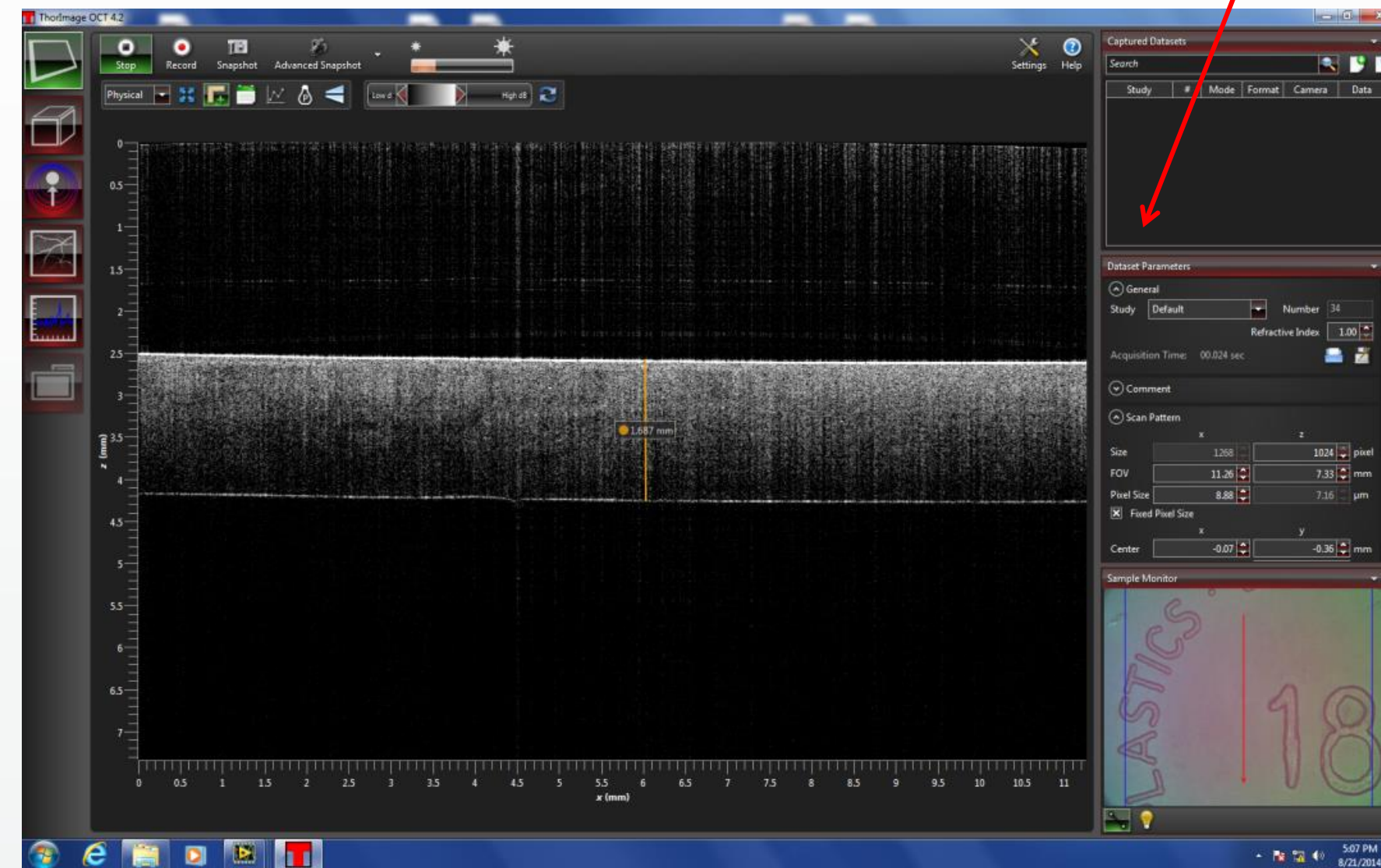
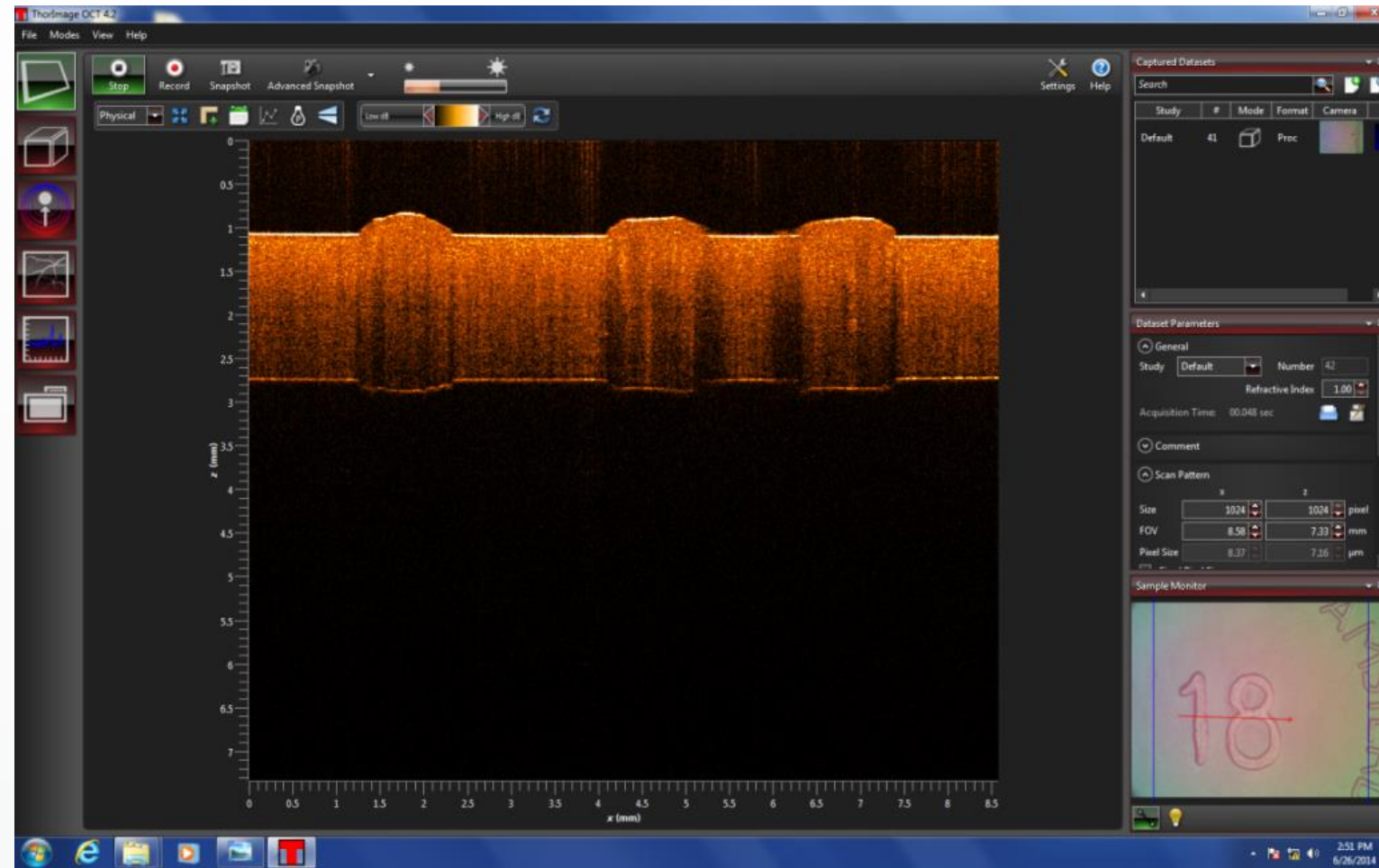
Δl_{opt} : Optical path difference

λ : Wavelength

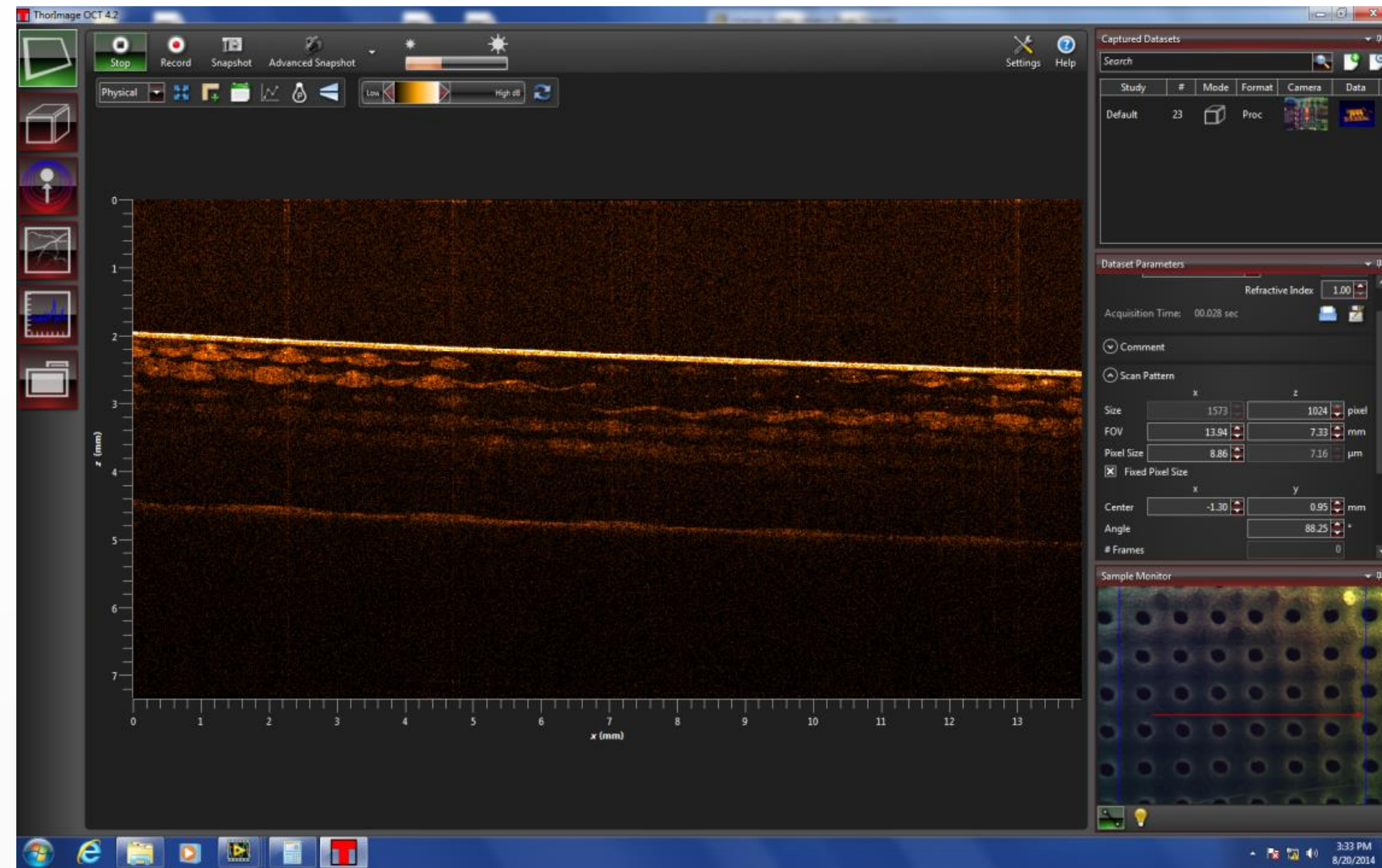


OCT feature: Penetration on materials

Plastic material - **Thickness of 1.6mm**

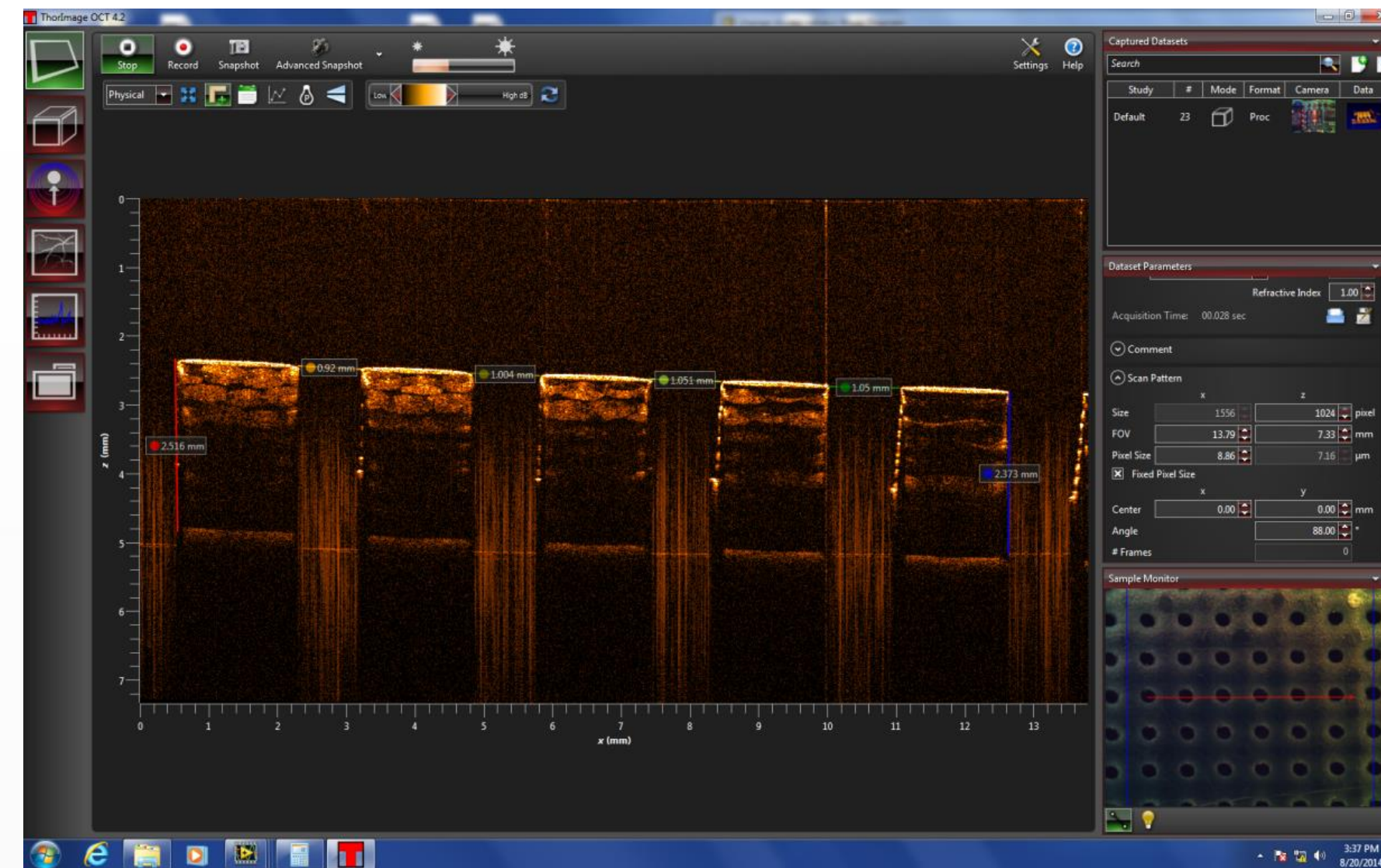


The images represents the section of the sample along the red line



The images represents the section of the sample along the red line.

Thickness and distances measurements can be performed.

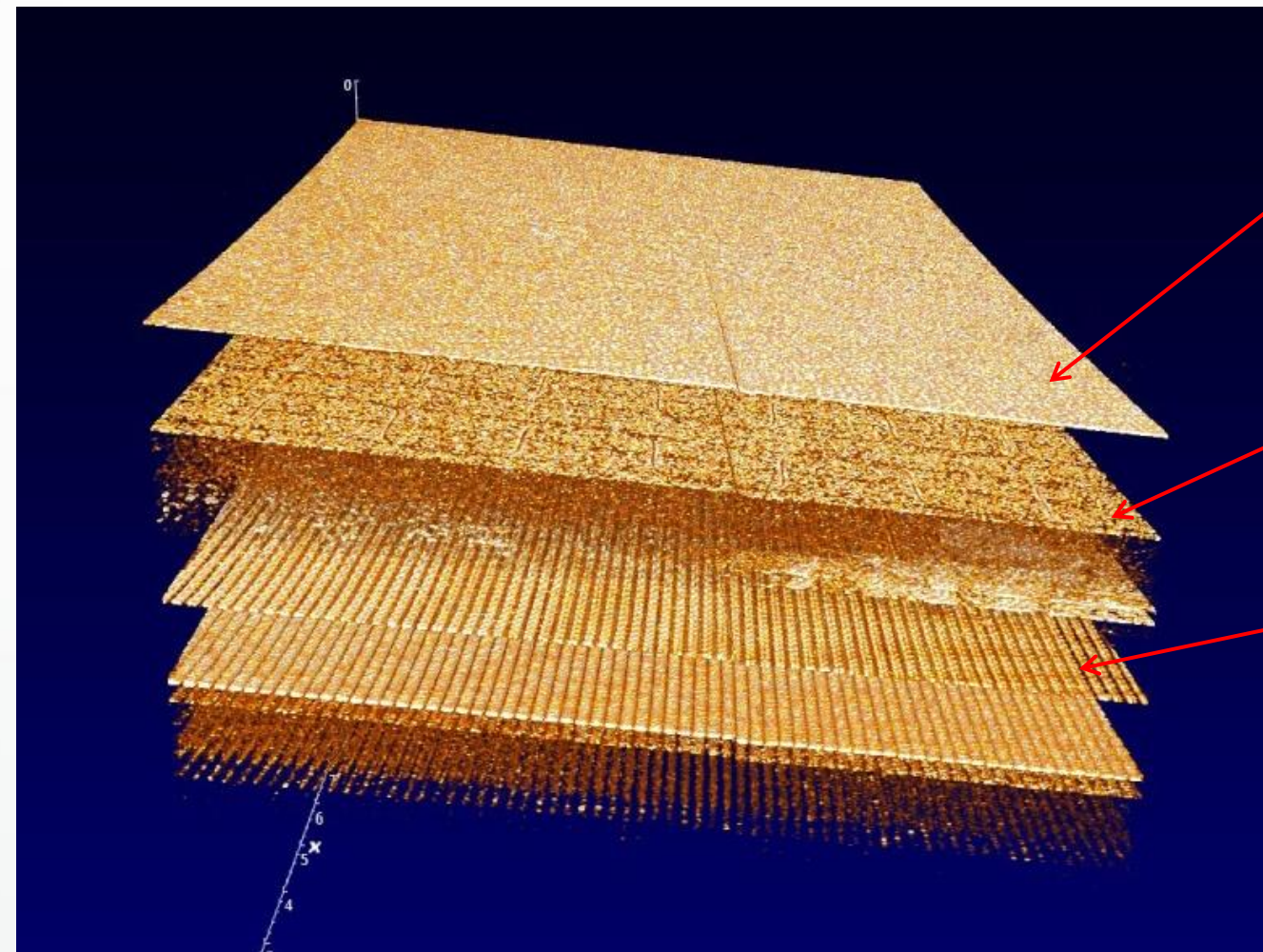


Printed circuit board – the inner structure is well visible. Structural analysis can be performed.

Possibility to verify the presence of unbonded and unwelded layers.

OCT applications: electronics

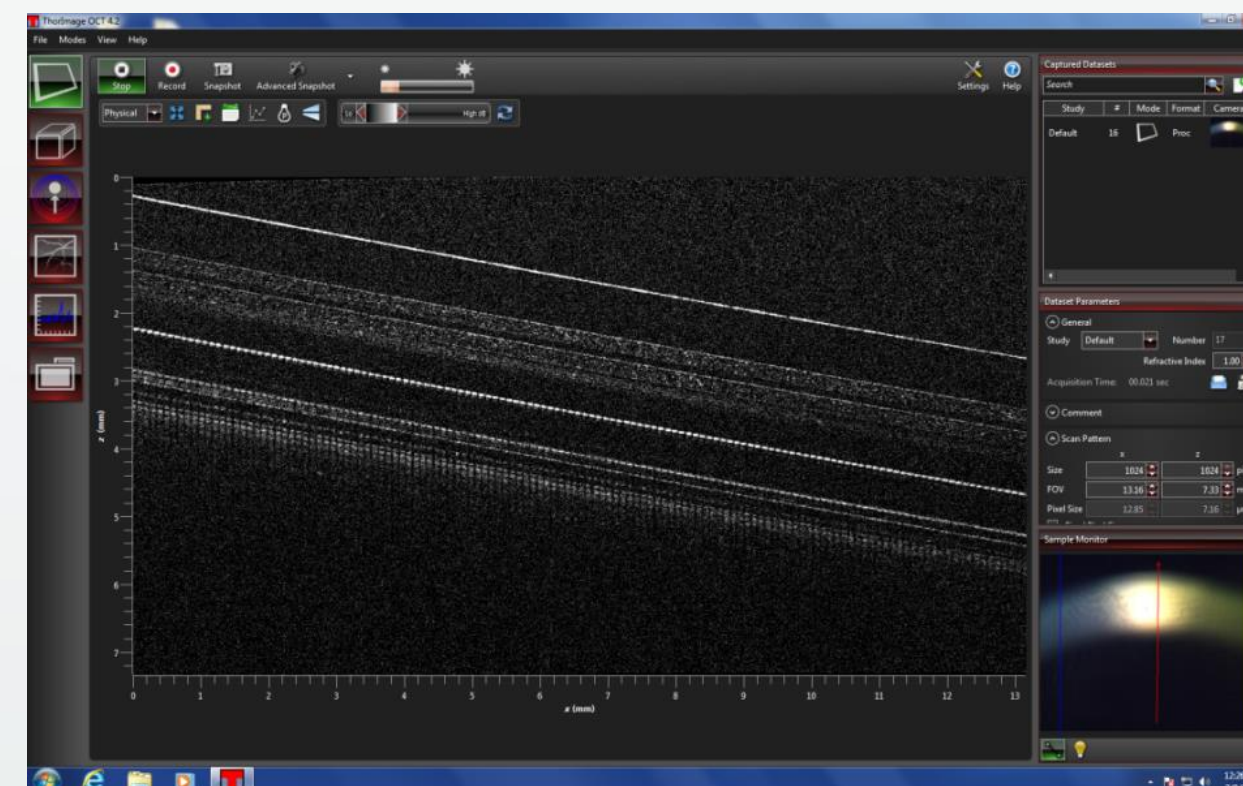
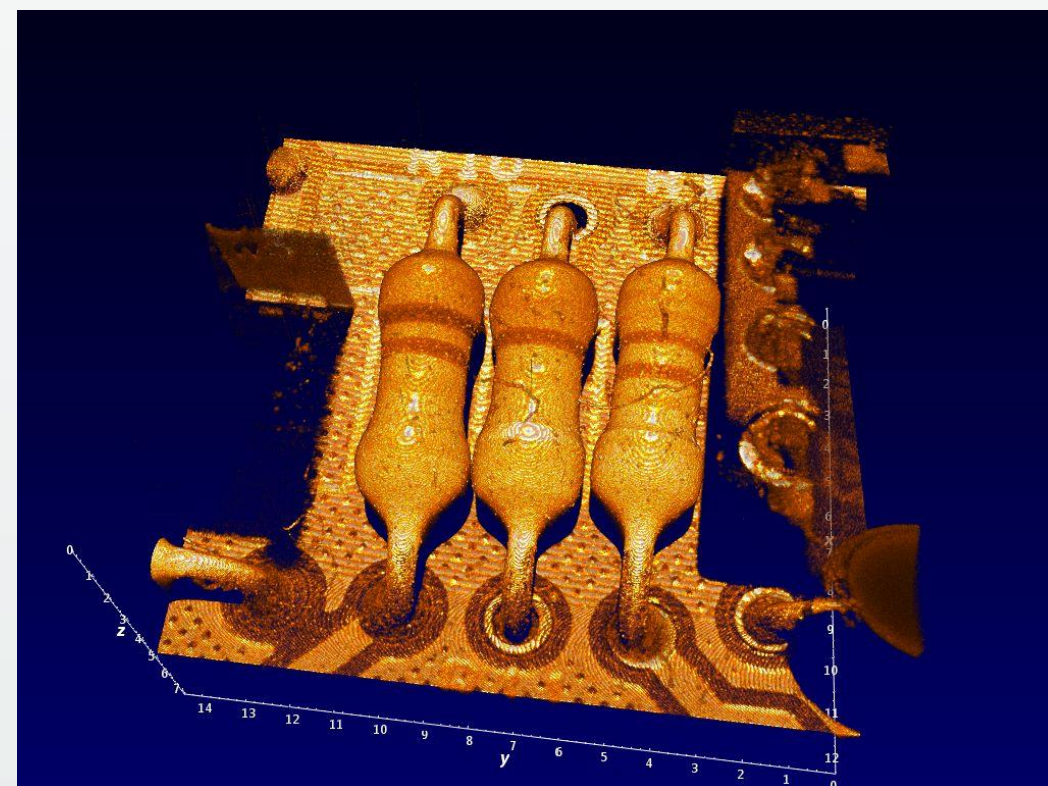
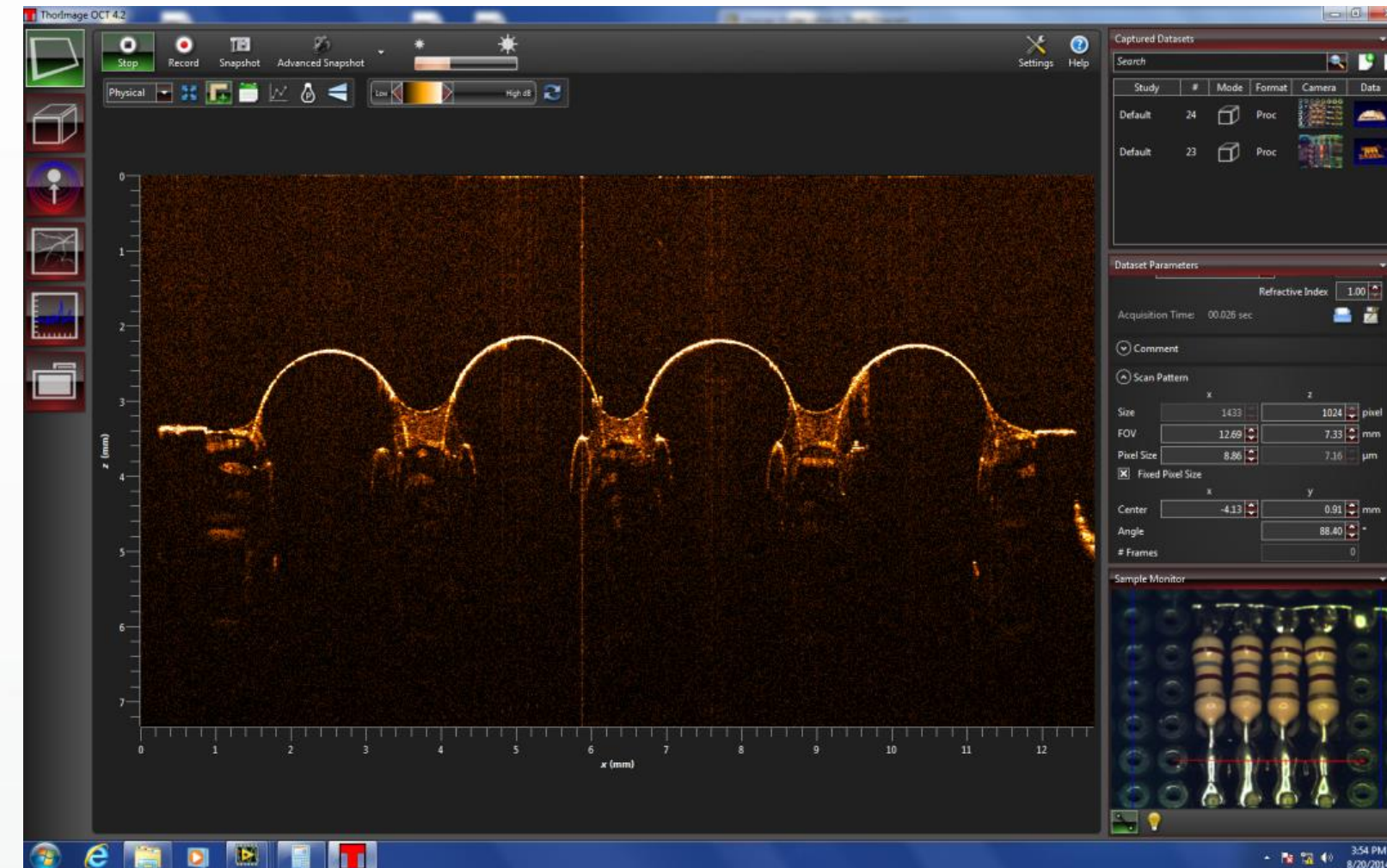
Mobile phone inspection



Screen

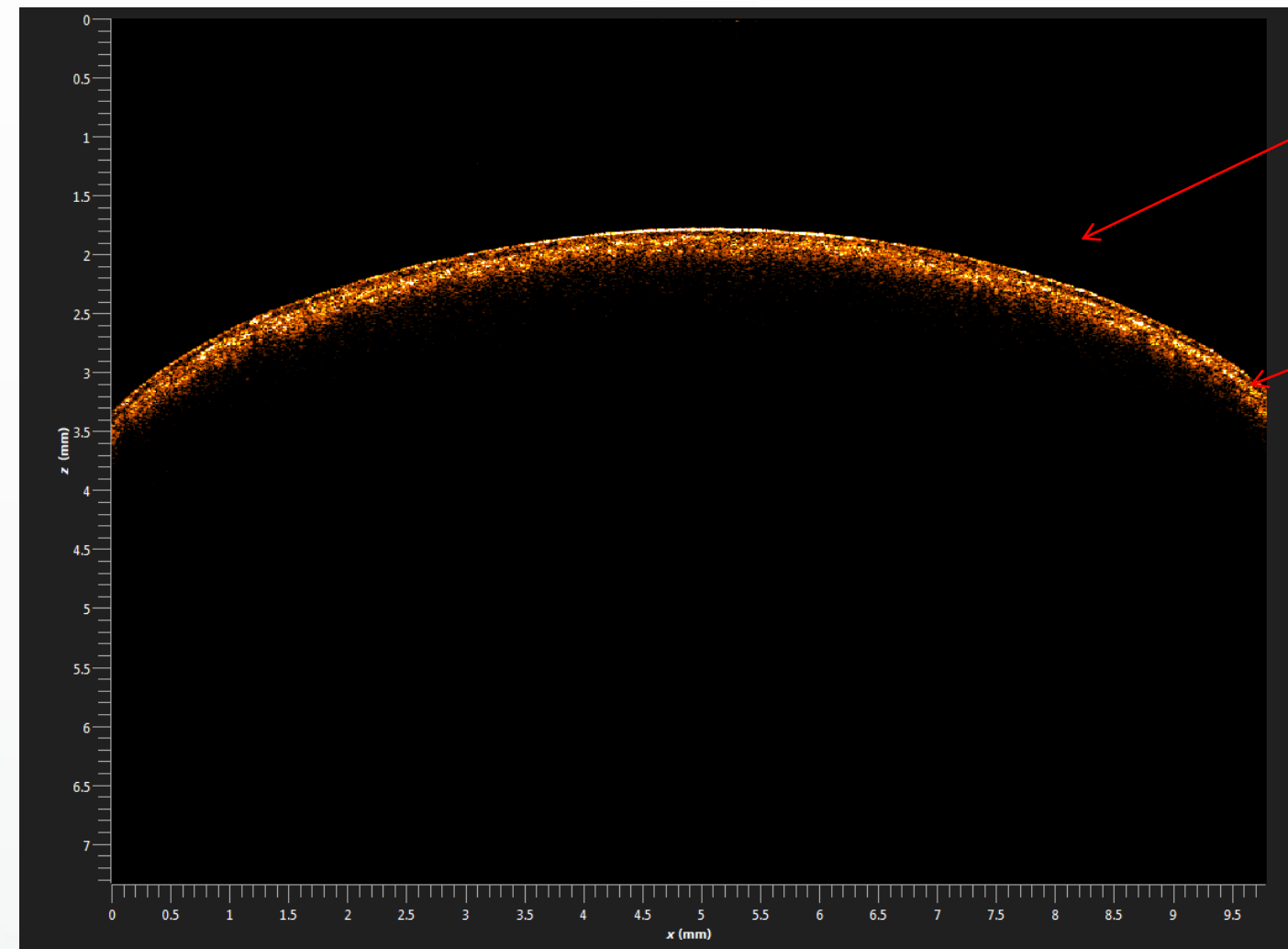
Touch screen
circuits

Pixels



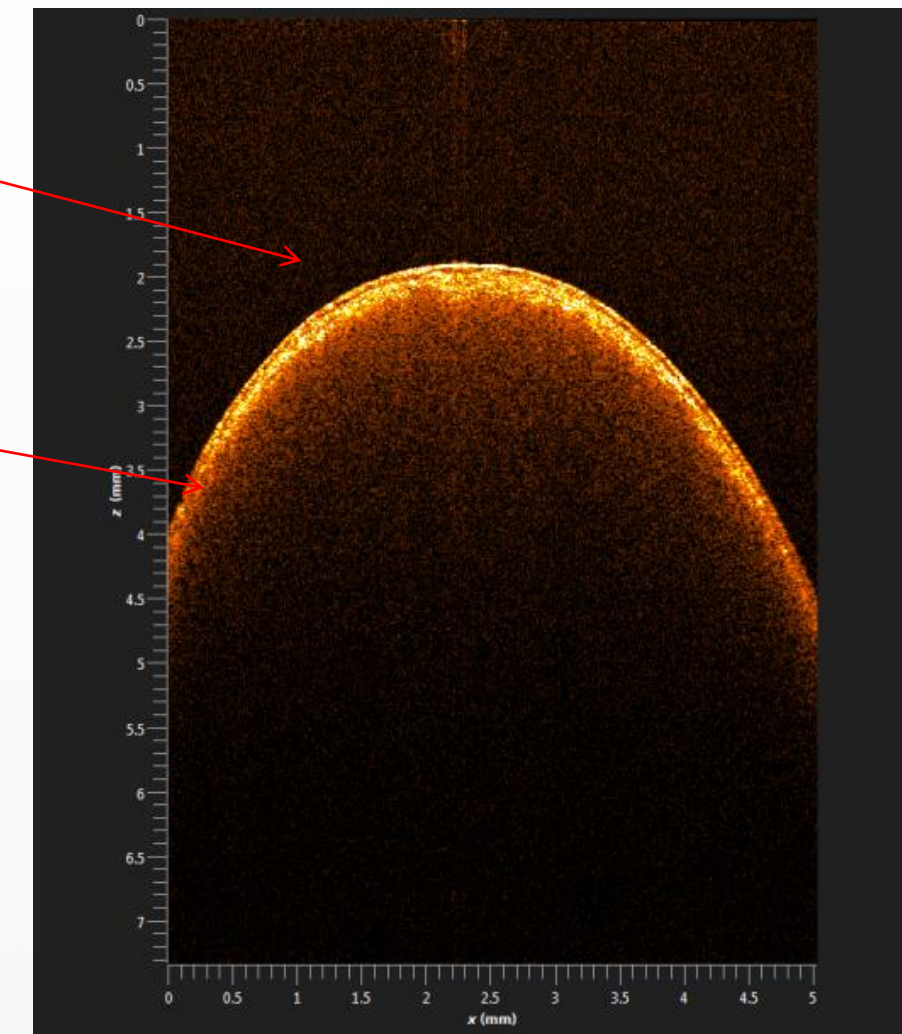
OCT applications: pharmaceutical/medical

Iboprufen tablet

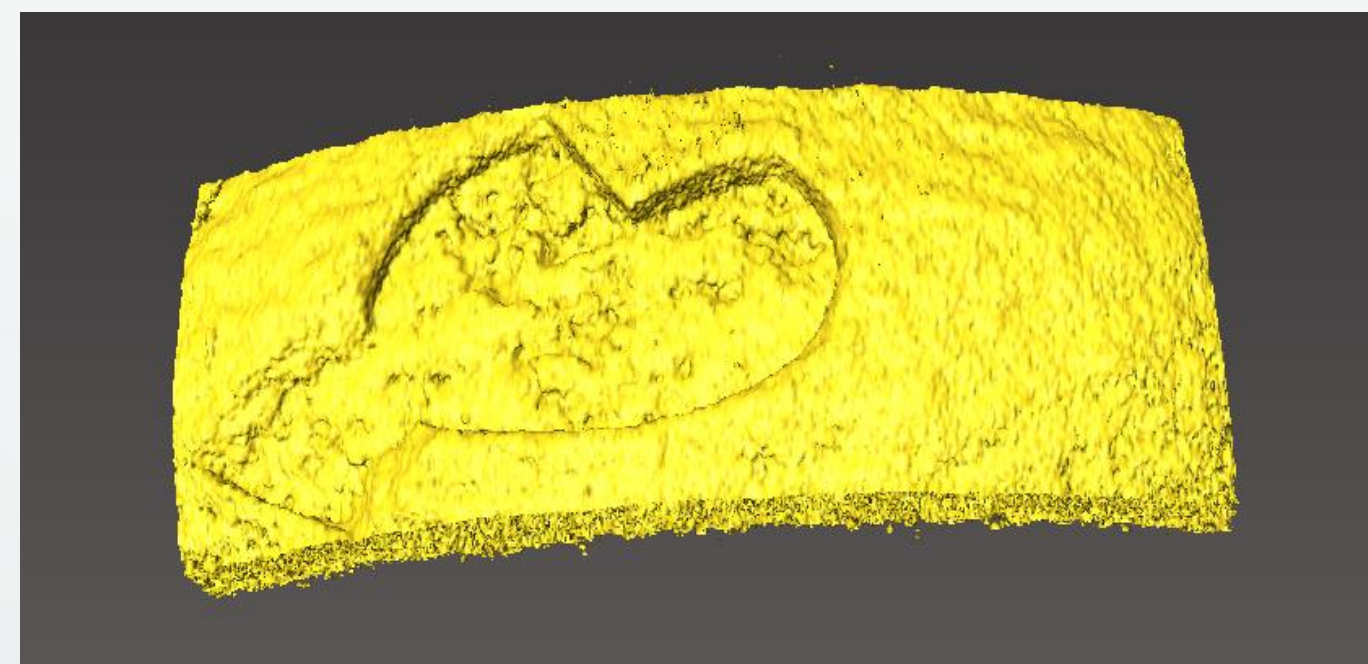
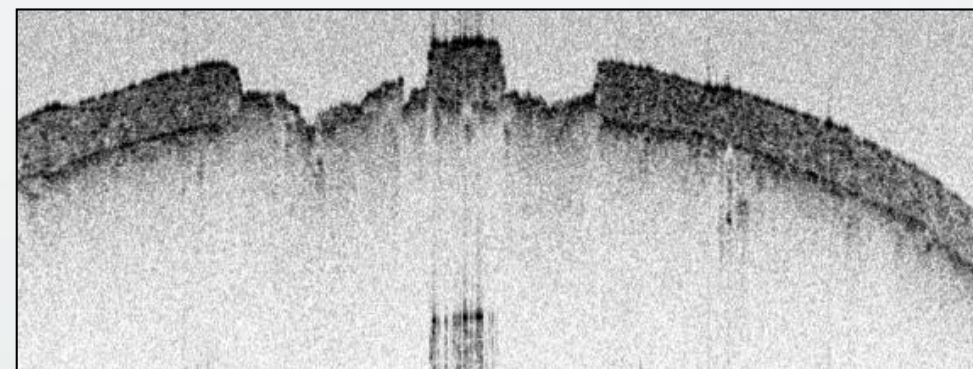
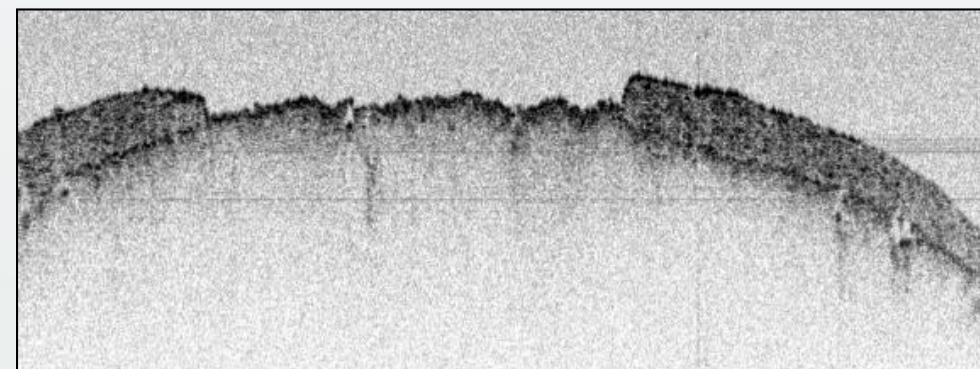
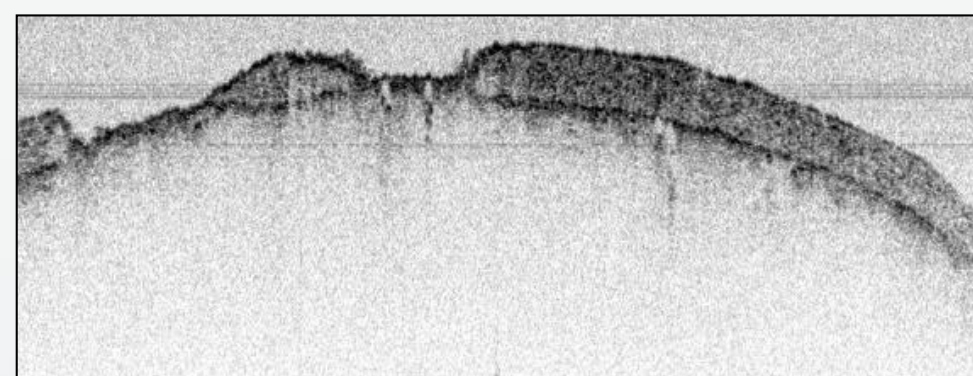
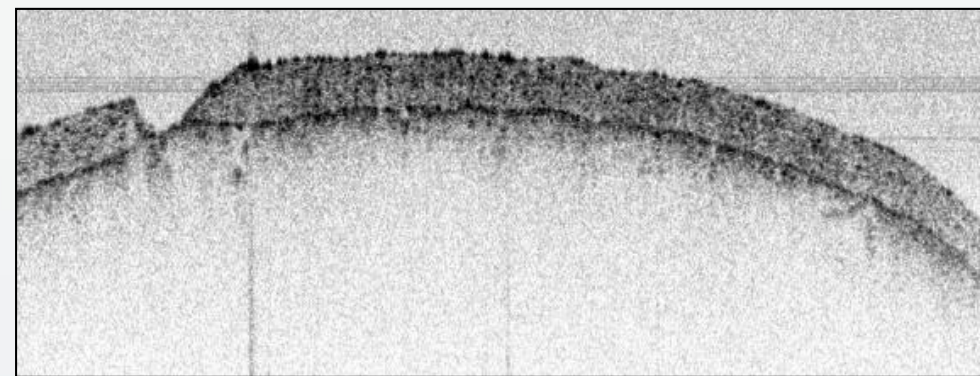


Coating

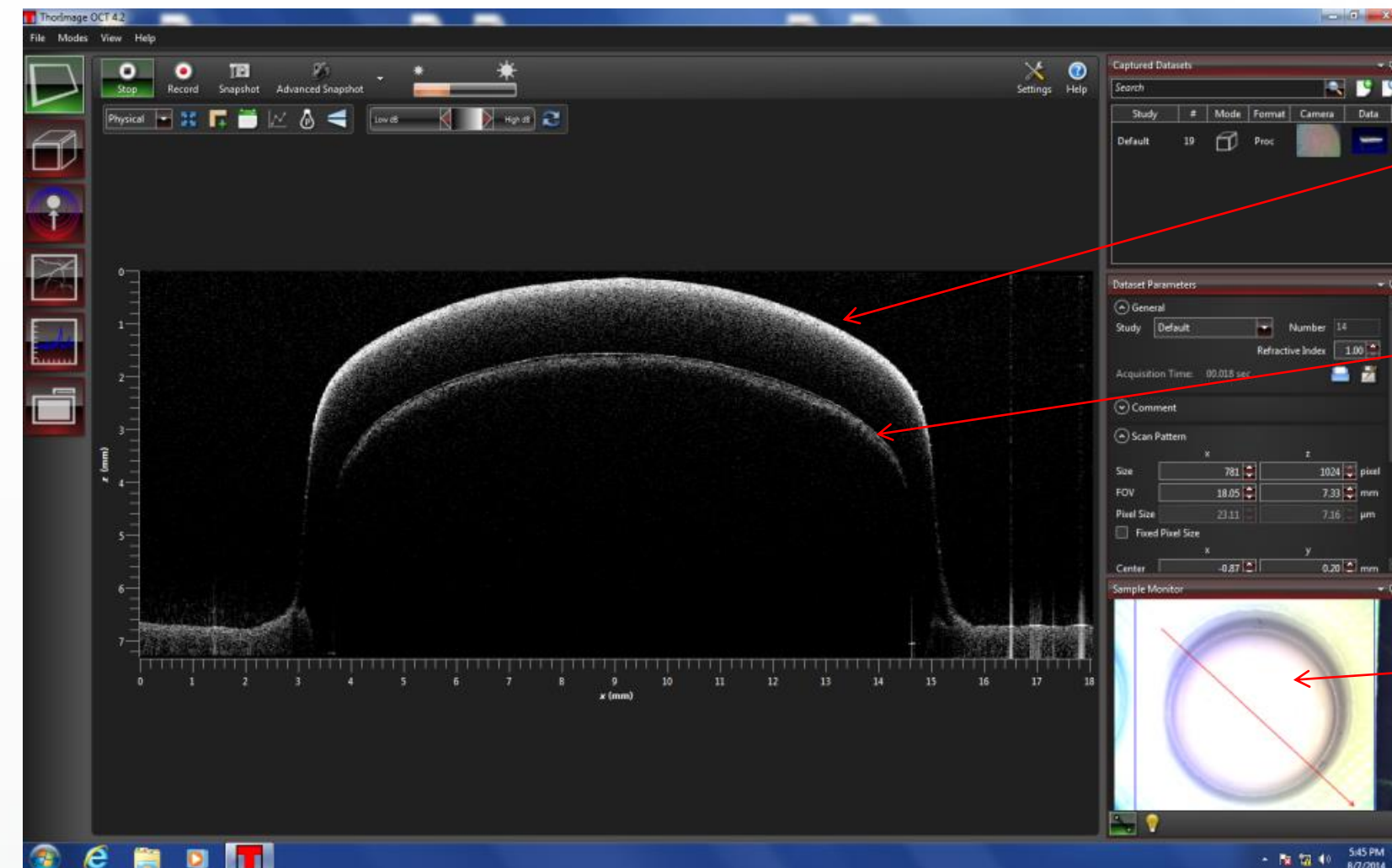
Inner
structure



Defects on the coating



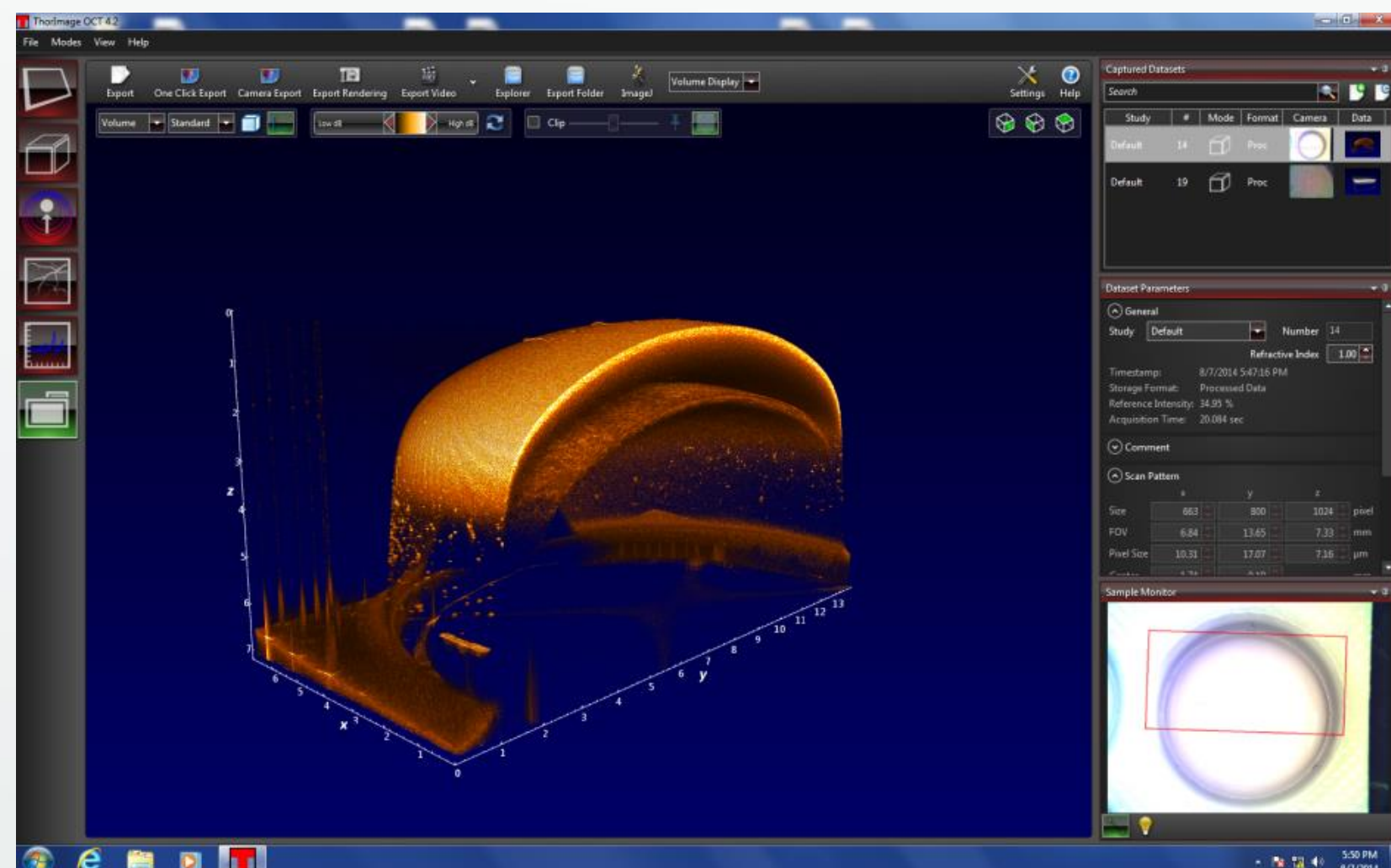
Iboprufen pill inside the blister



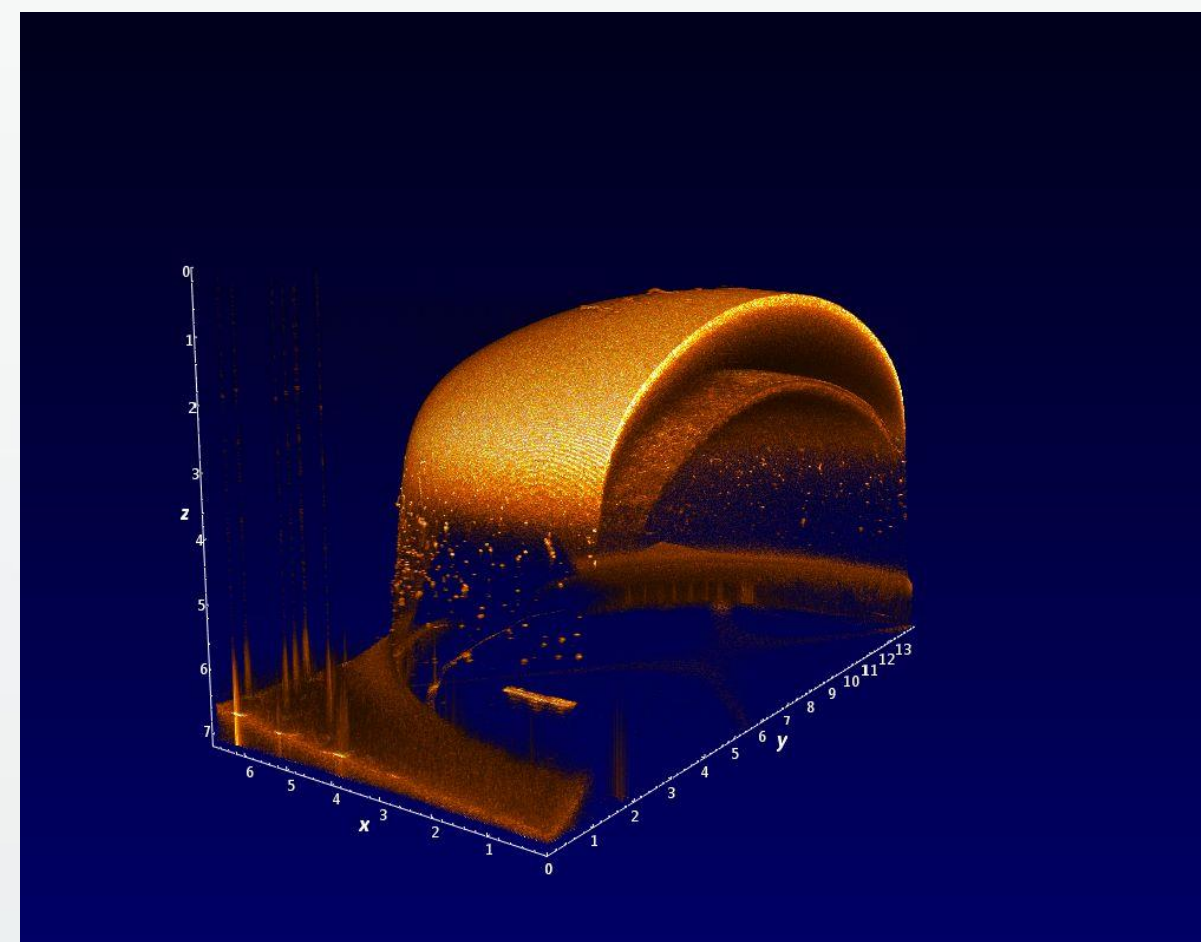
Blister surface

Scan line

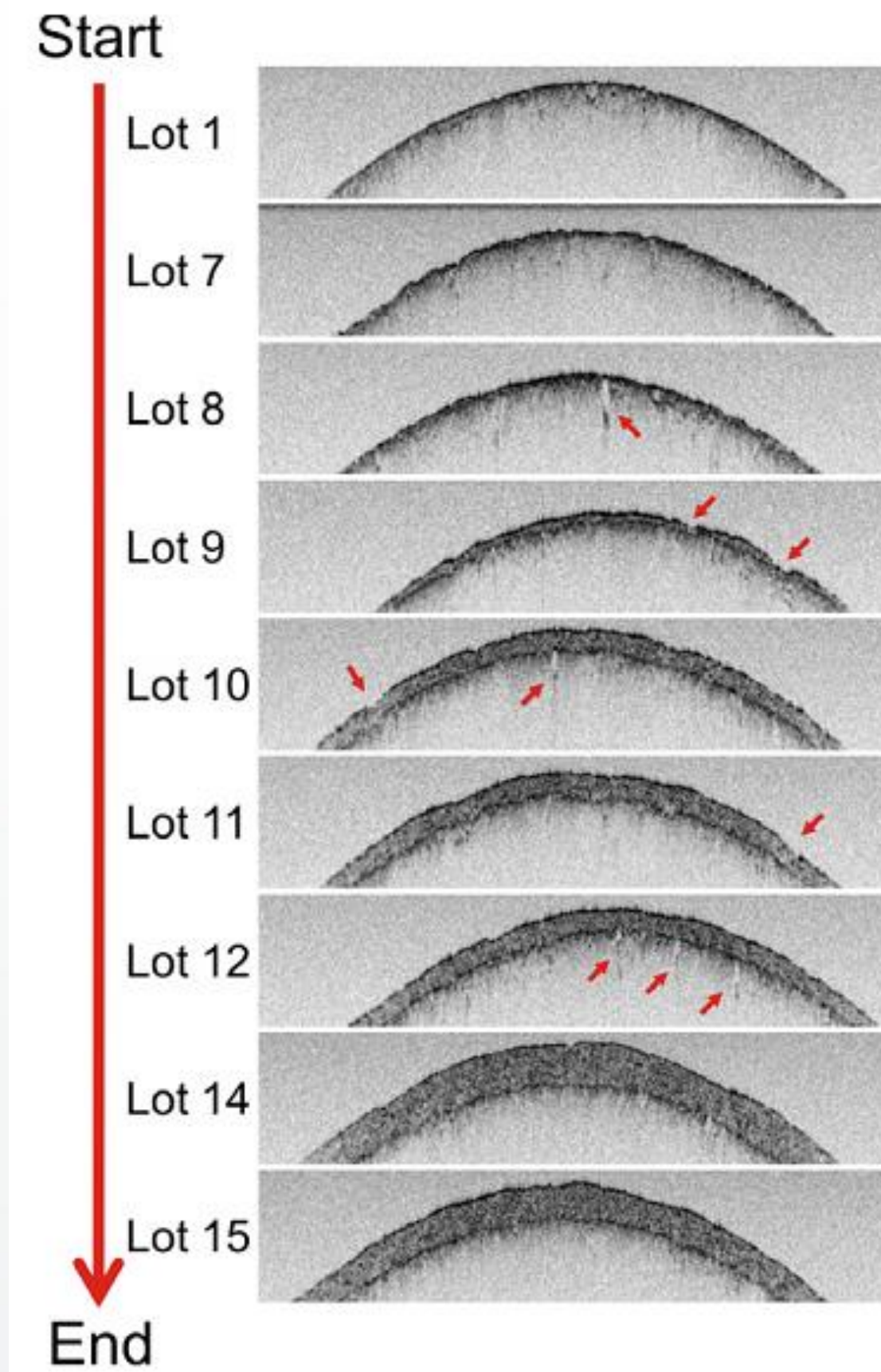
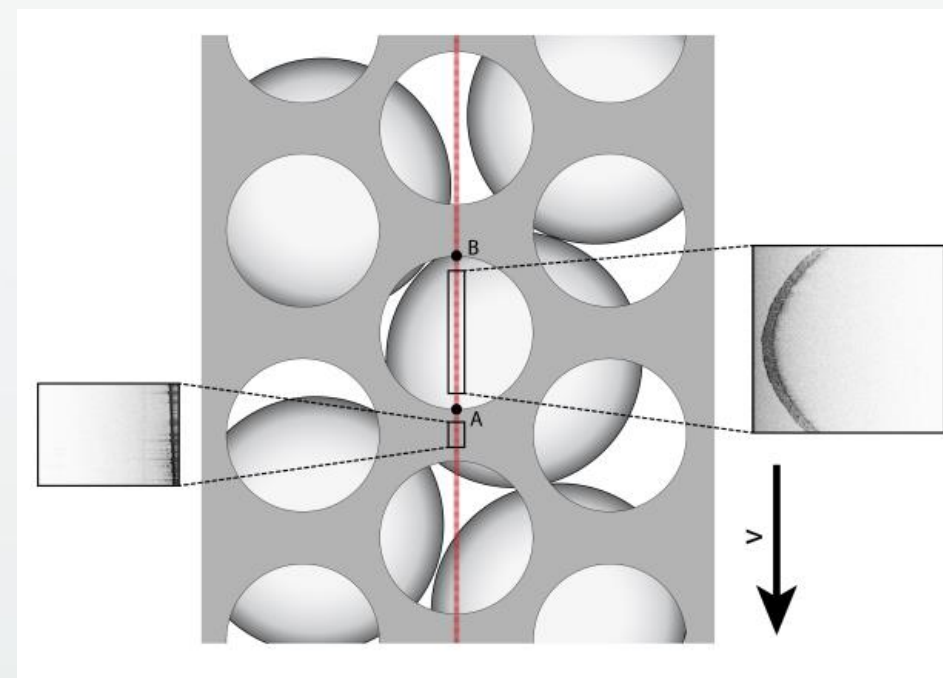
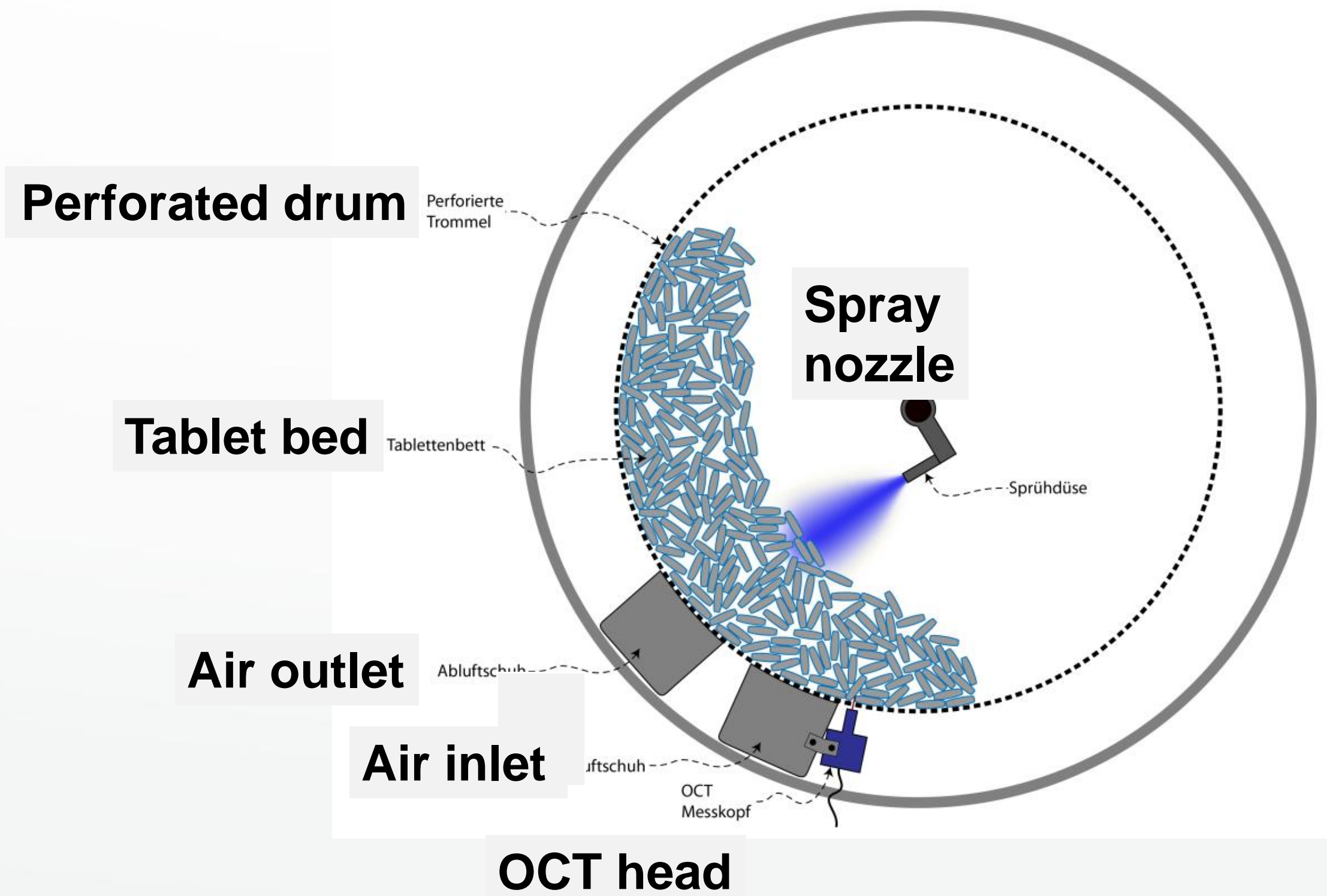
Possibility to control the presence of the pill inside the blister



Iboprufen tablets surface

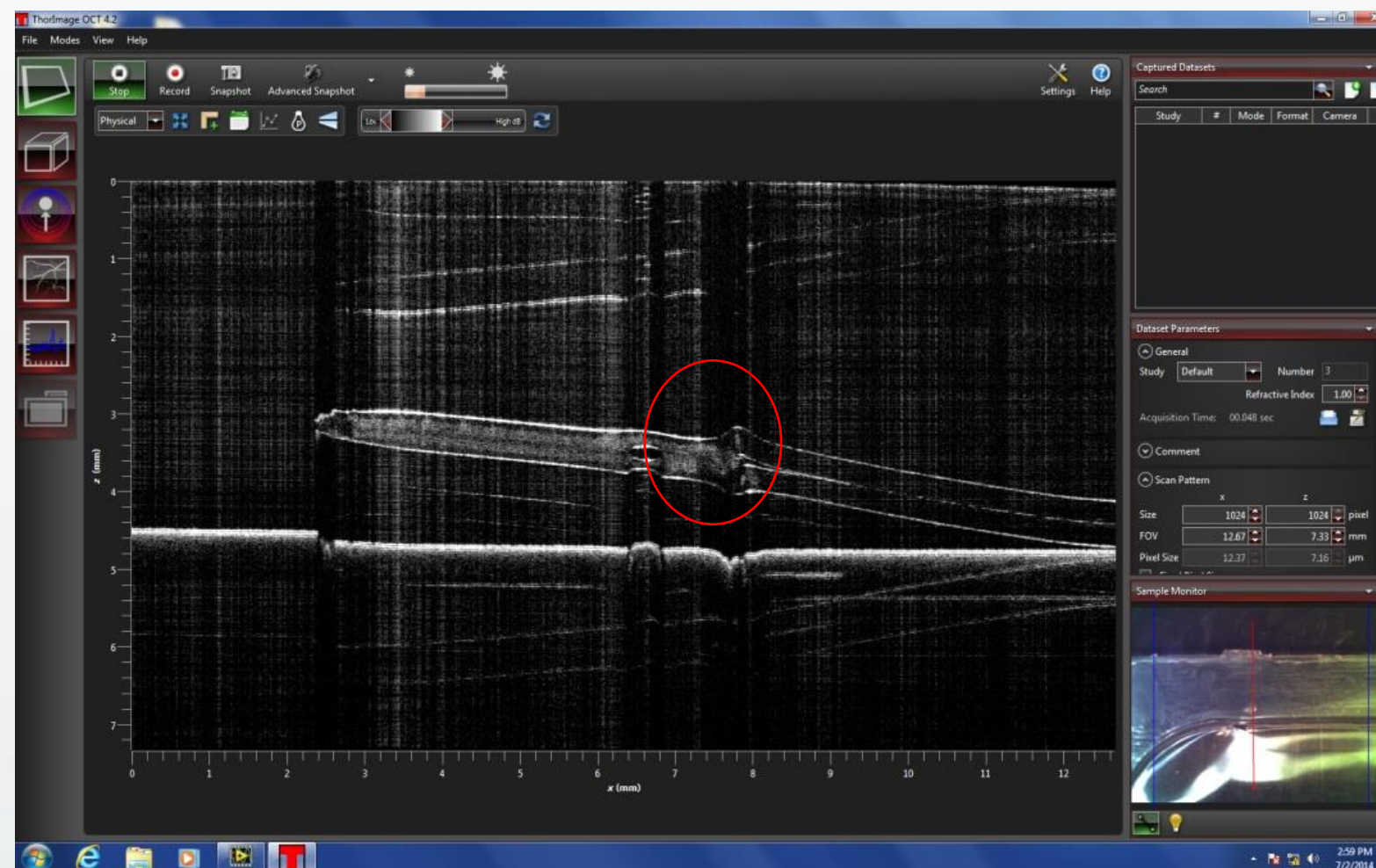
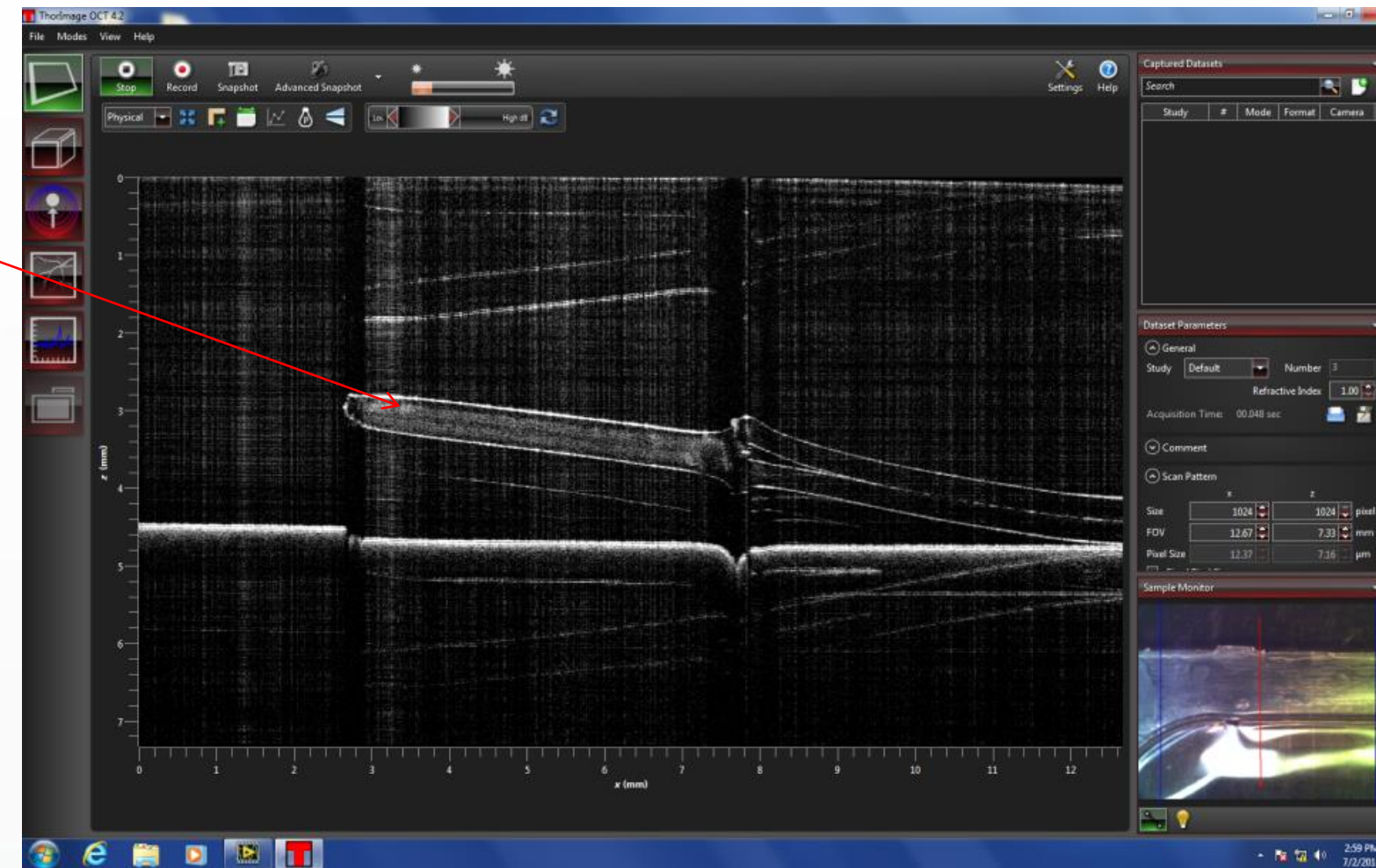
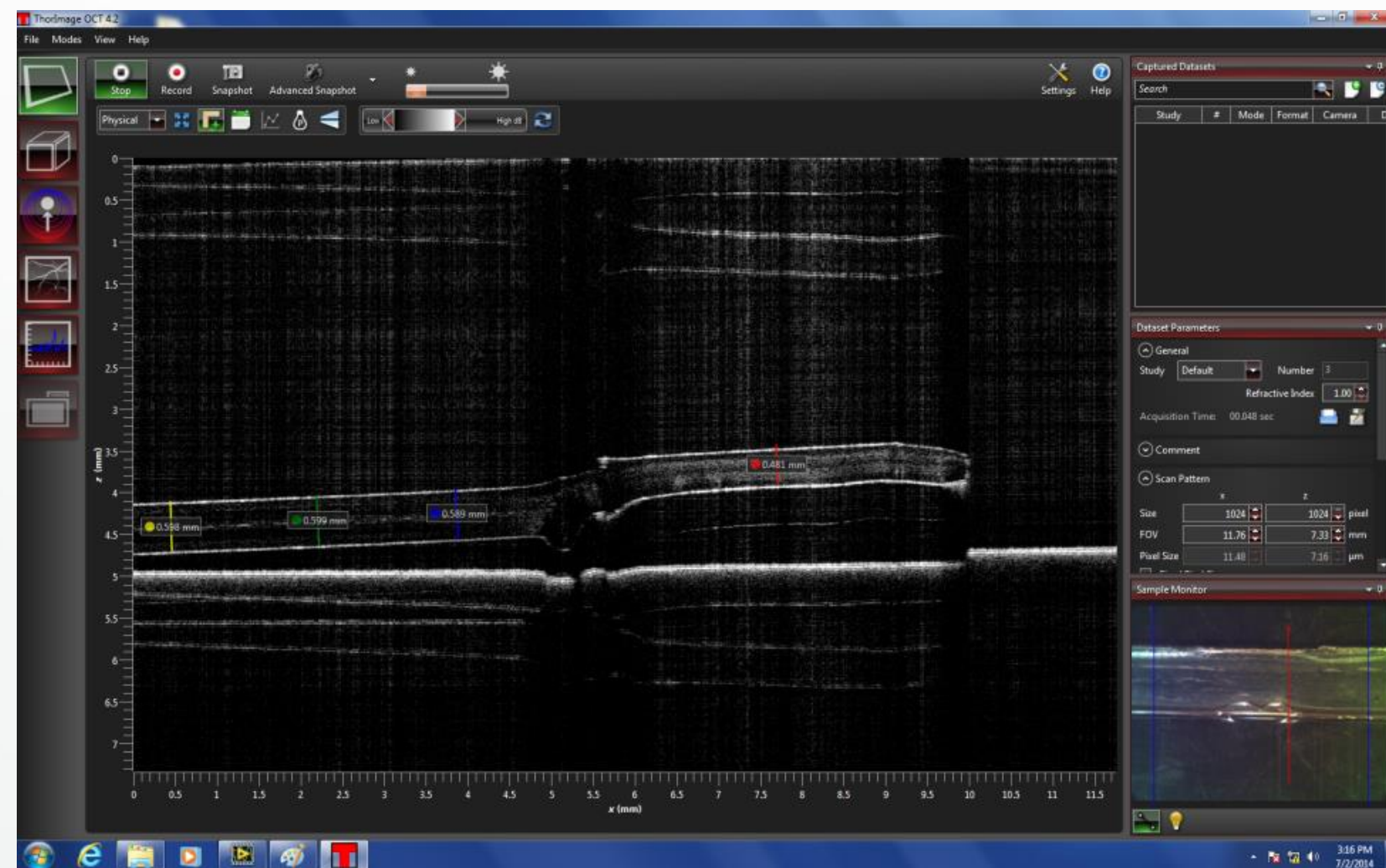


Inline monitoring of the coating growth



Inspection of welded plastic bags for medical applications

The changes on the “white color”
Is an indication of the quality of
the welding

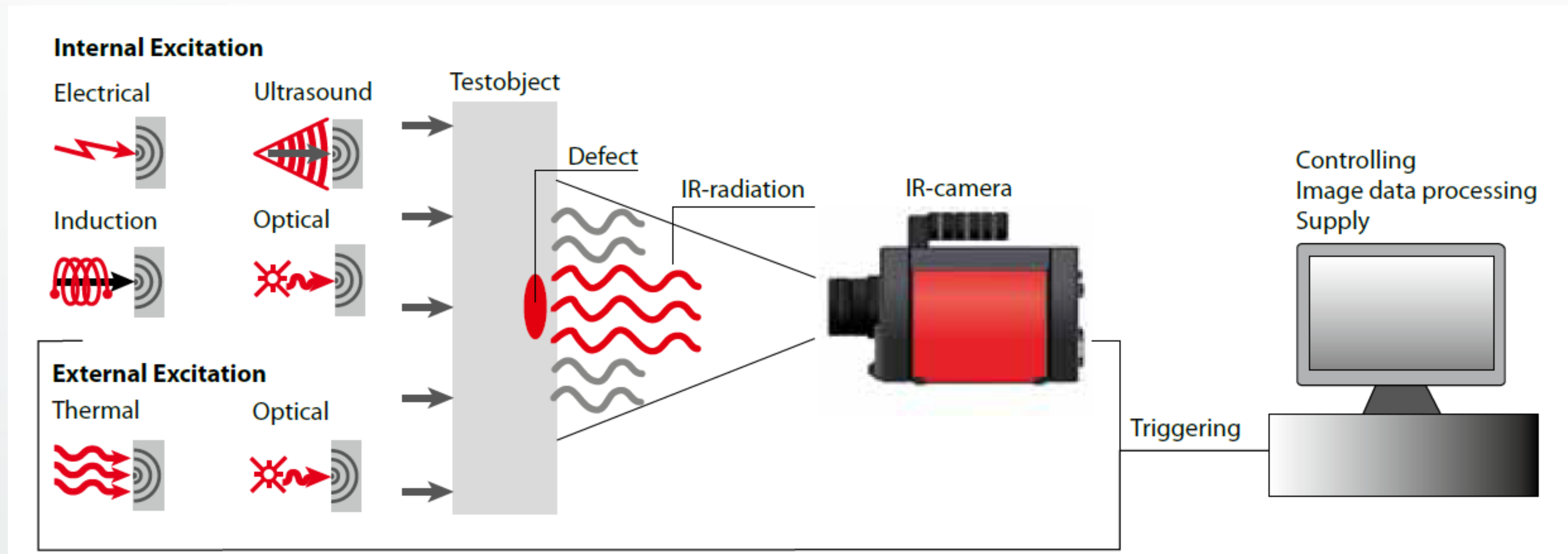


An Automatic inspection system for the
presence of bubbles was developed

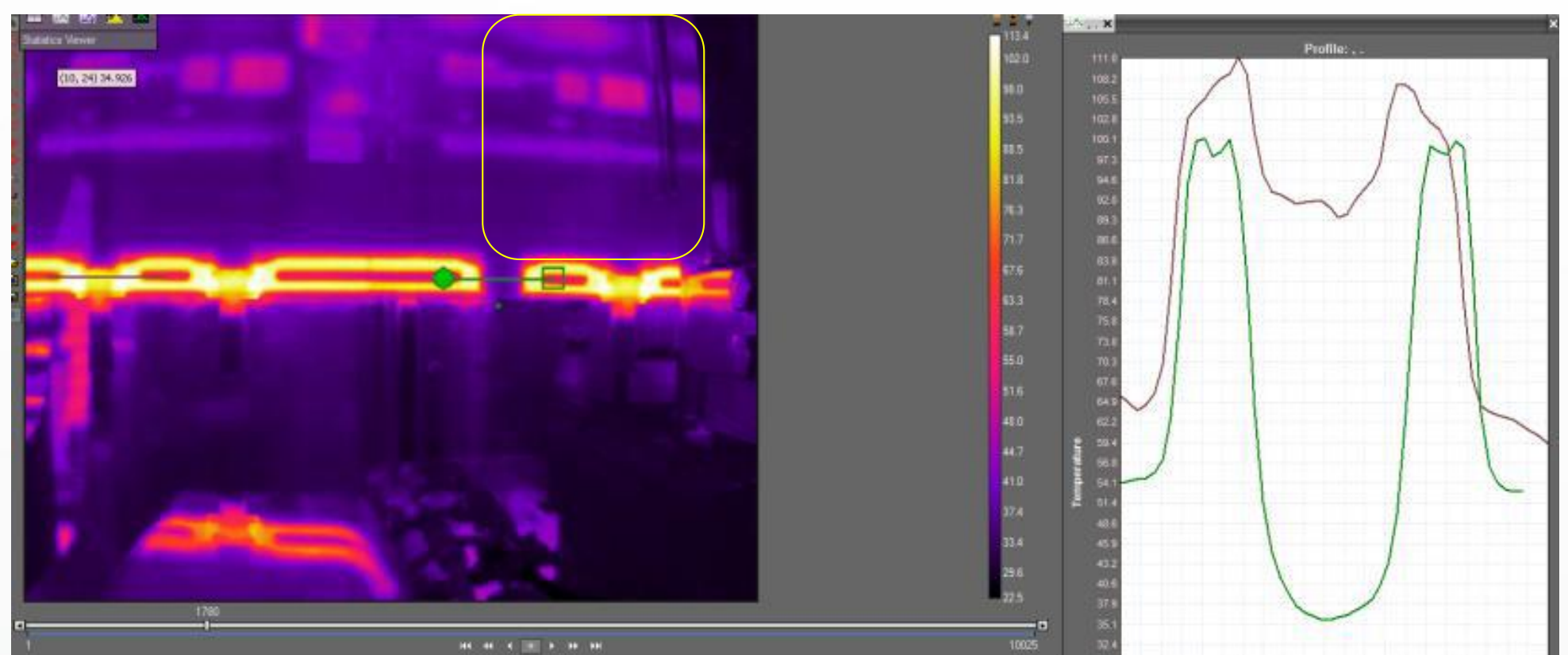
Active thermography

Active thermography is an imaging procedure for non-destructive material testing.

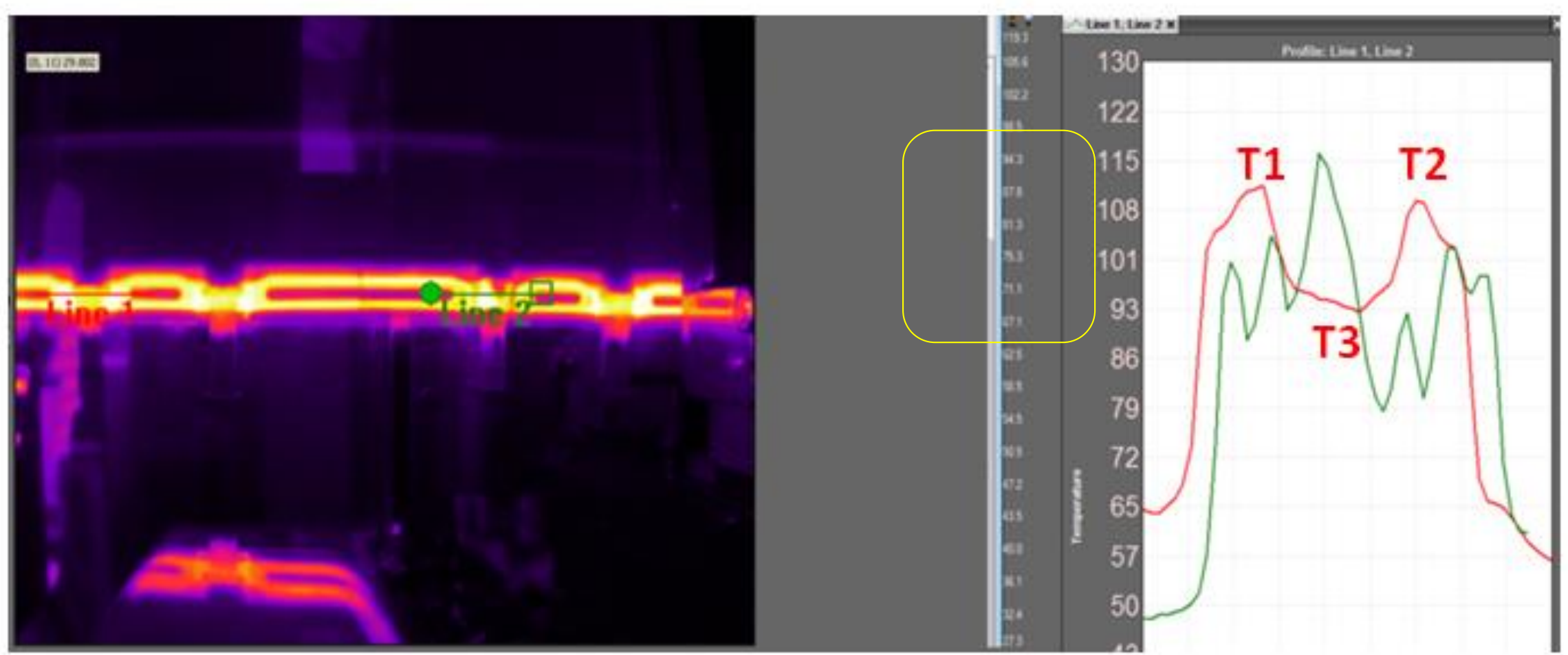
A heat flow is induced by an energetic excitation of the test object, which can be done in a transmissive or a reflective setup. The resulting heat flow is influenced by interior material layers and defects. These inhomogeneities can be captured on the object surface by high-precision thermal cameras.



Monitoring of the single bag - example of data extraction



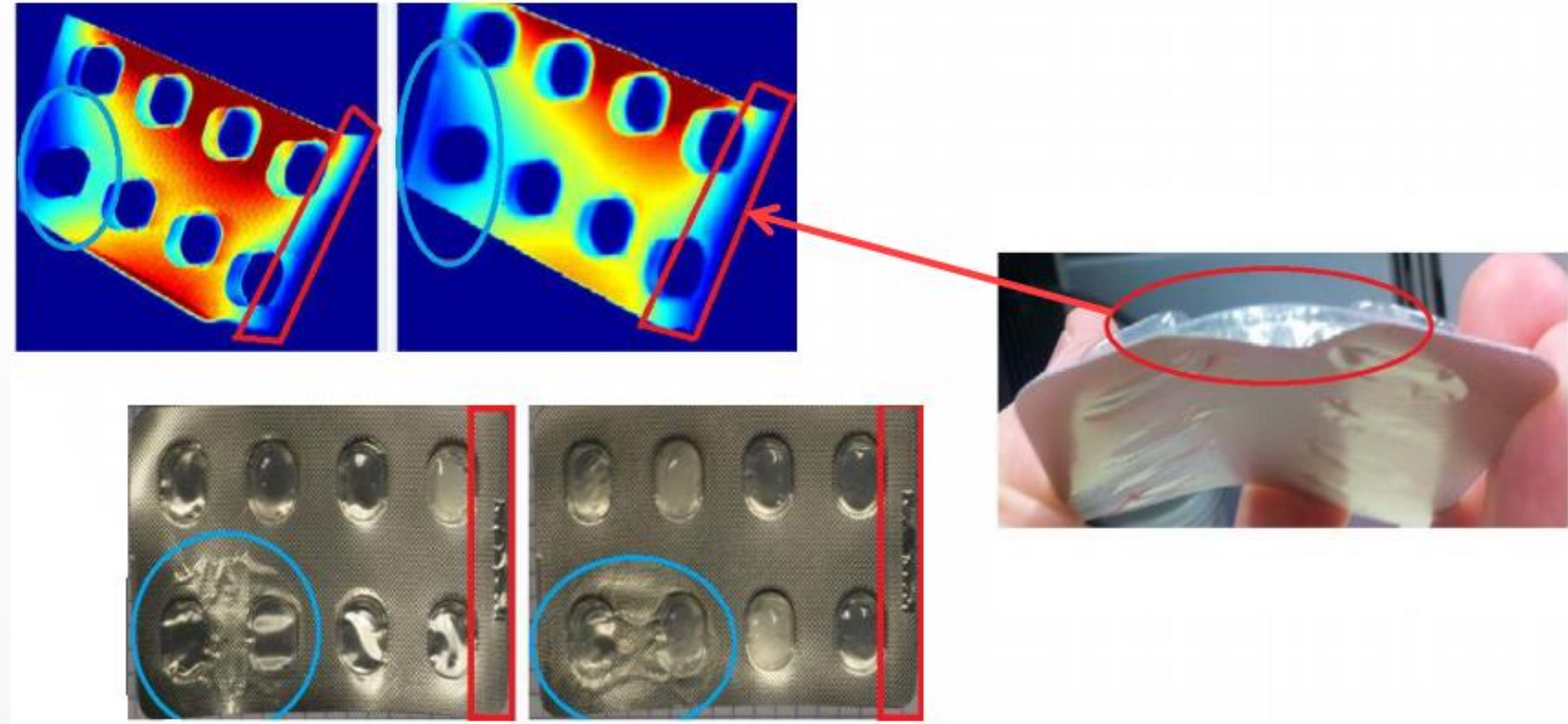
Example of temperature profile for a bag with and without port.



Example of temperature profile For a bag with rotated port.

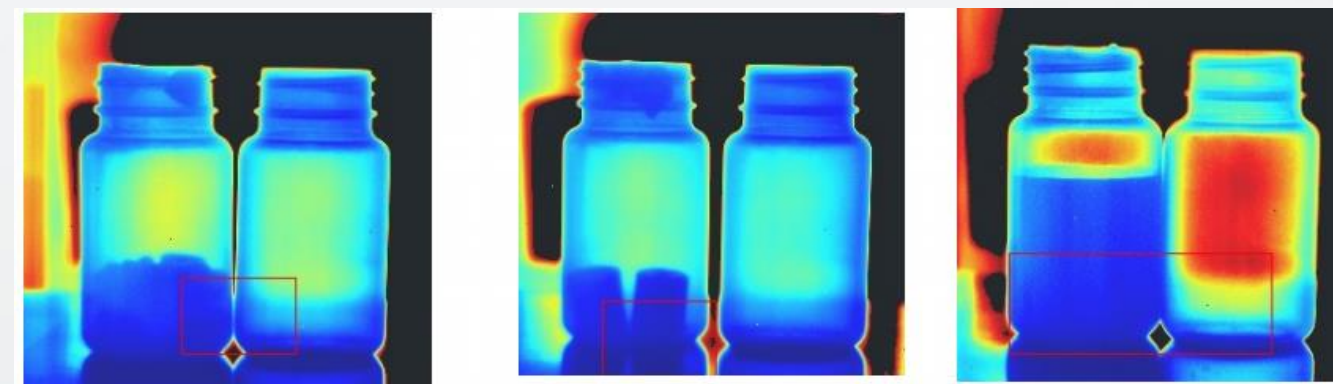
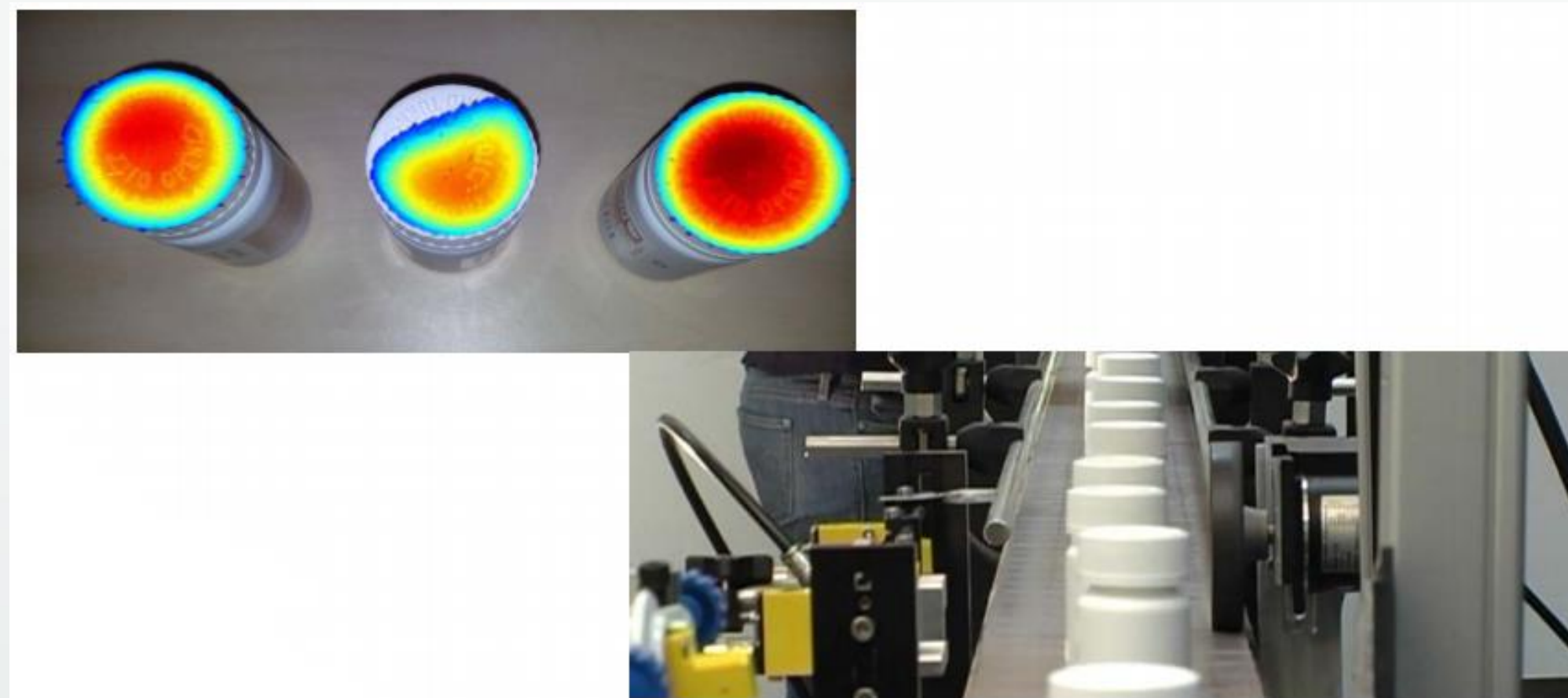
Blister and Bottles sealing monitoring - Inline monitoring

Dynamic Infrared Vision



Advantages of DIR Technology:

- Real-time testing of 100% of the products
- Real-Time process monitoring
- Full records for every products
- Very high throughput → no product slowdown
- Non-destructive, non-interfering

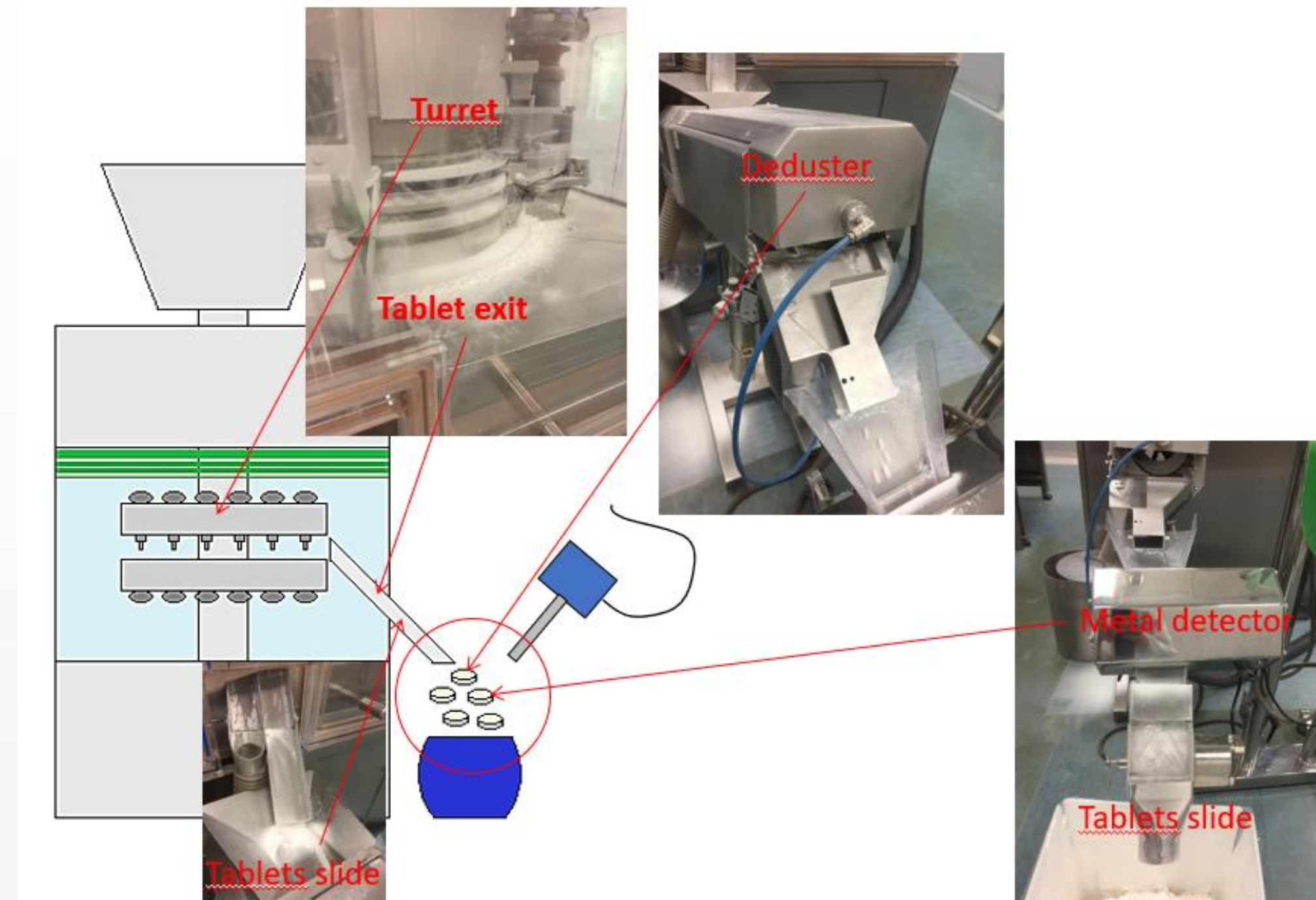
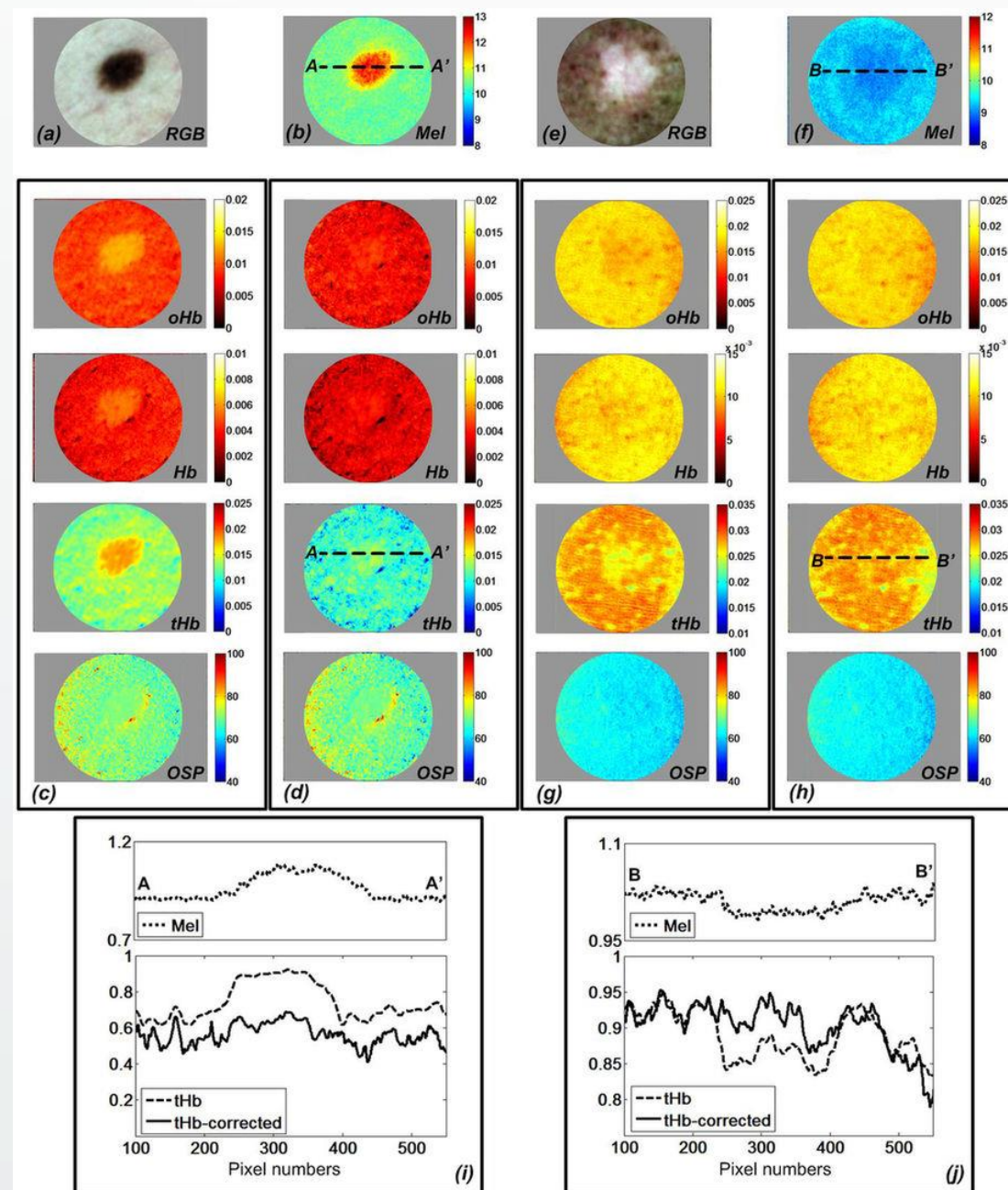


Optical spectroscopy

Suitable for point-by-point inline inspection

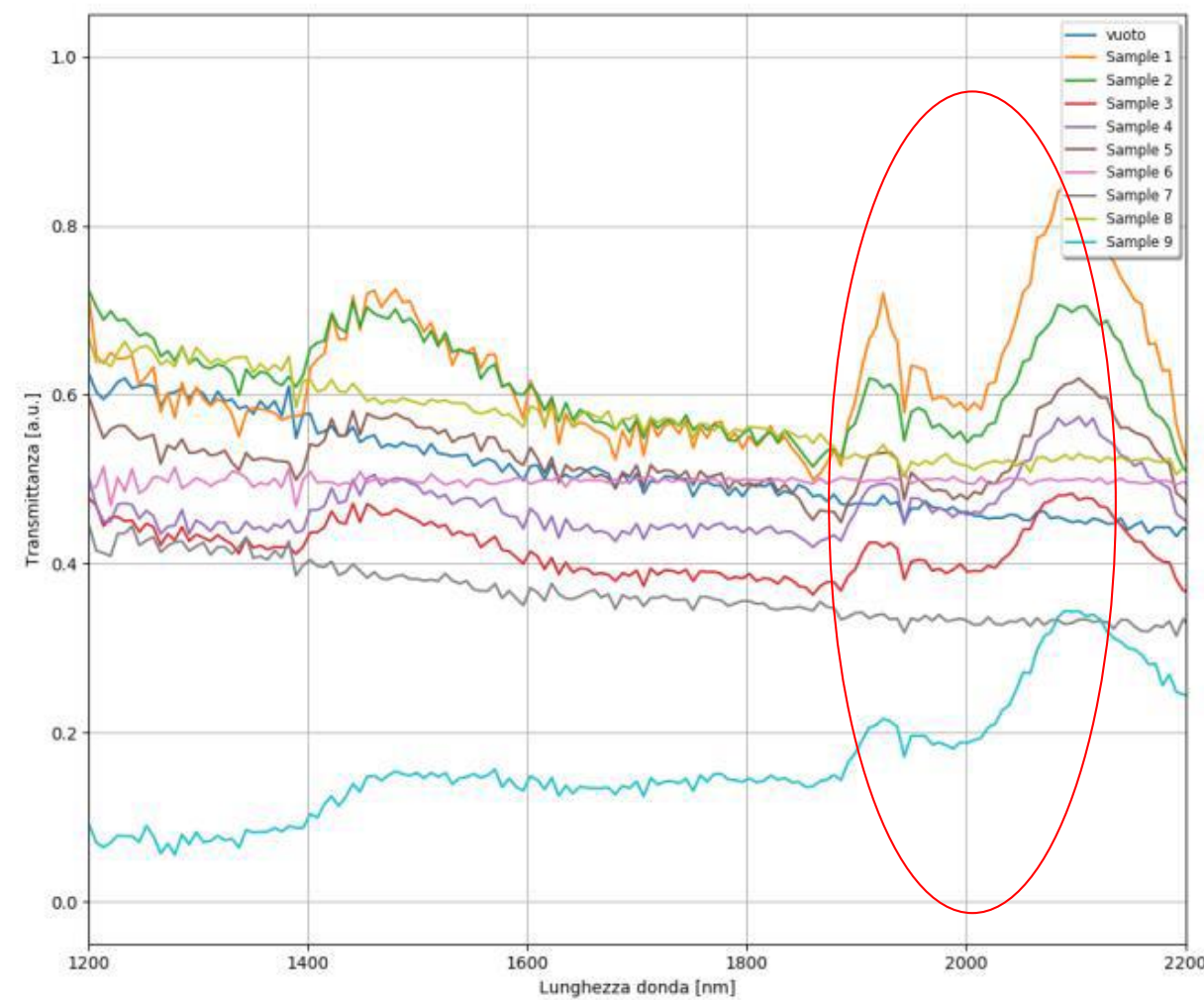
What we can measure?

- API Content
- Moisture
- Crystalline Structure
- POINT BY POINT Measure!

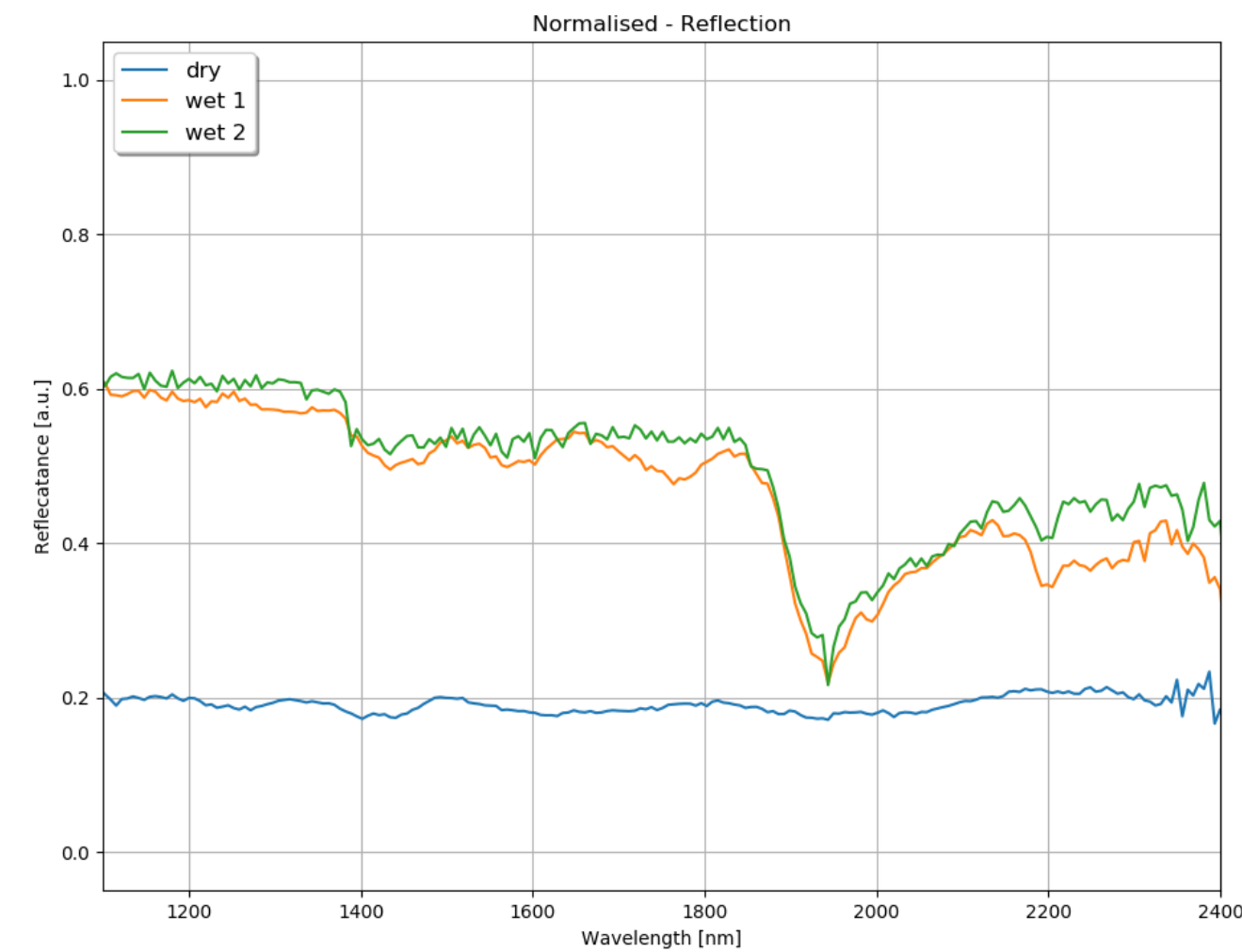


Miniaturisation and high speed acquisition

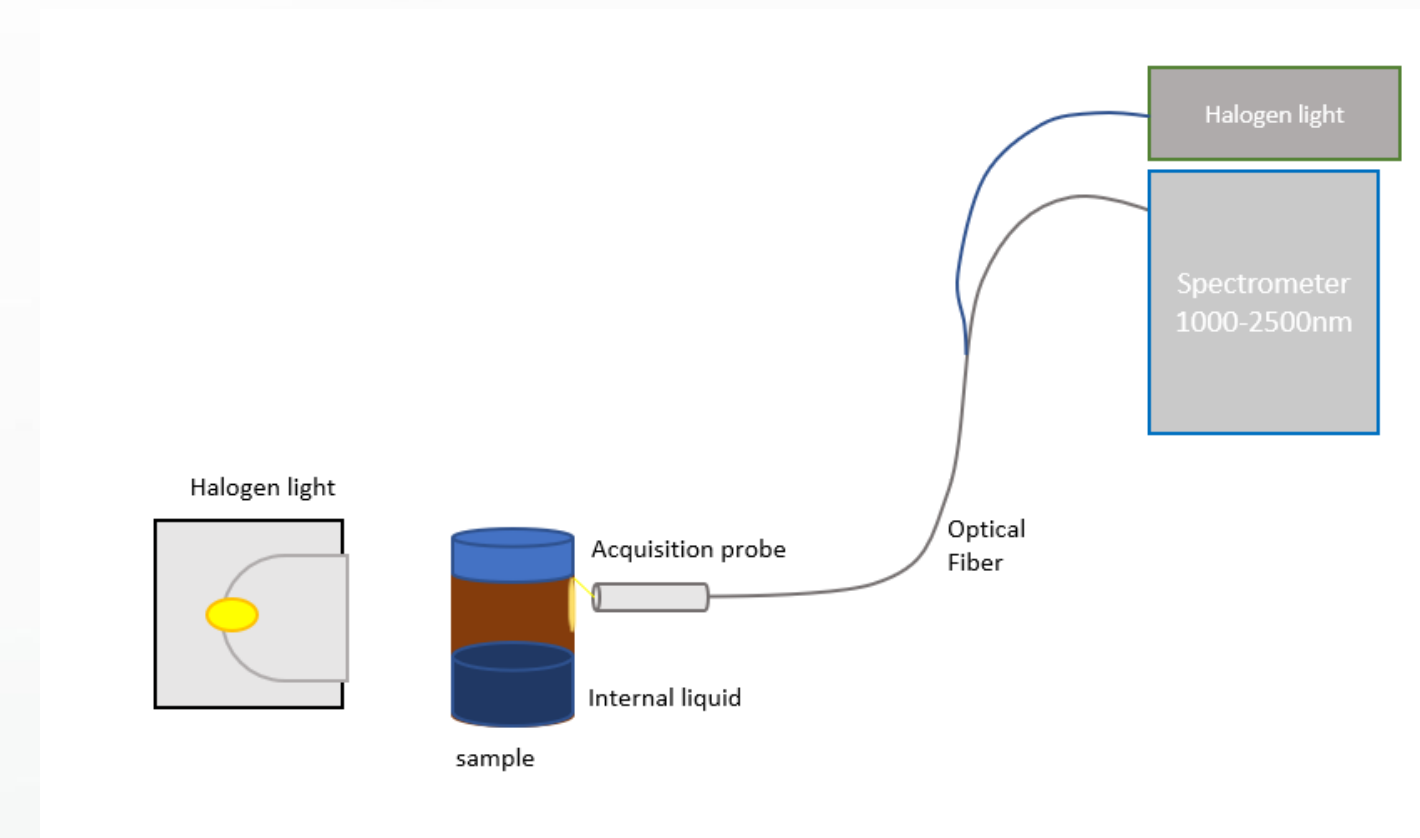
Optical spectroscopy



CO₂ determination on vials.
The absorption peak of the
CO₂ at 1920nm is well visible



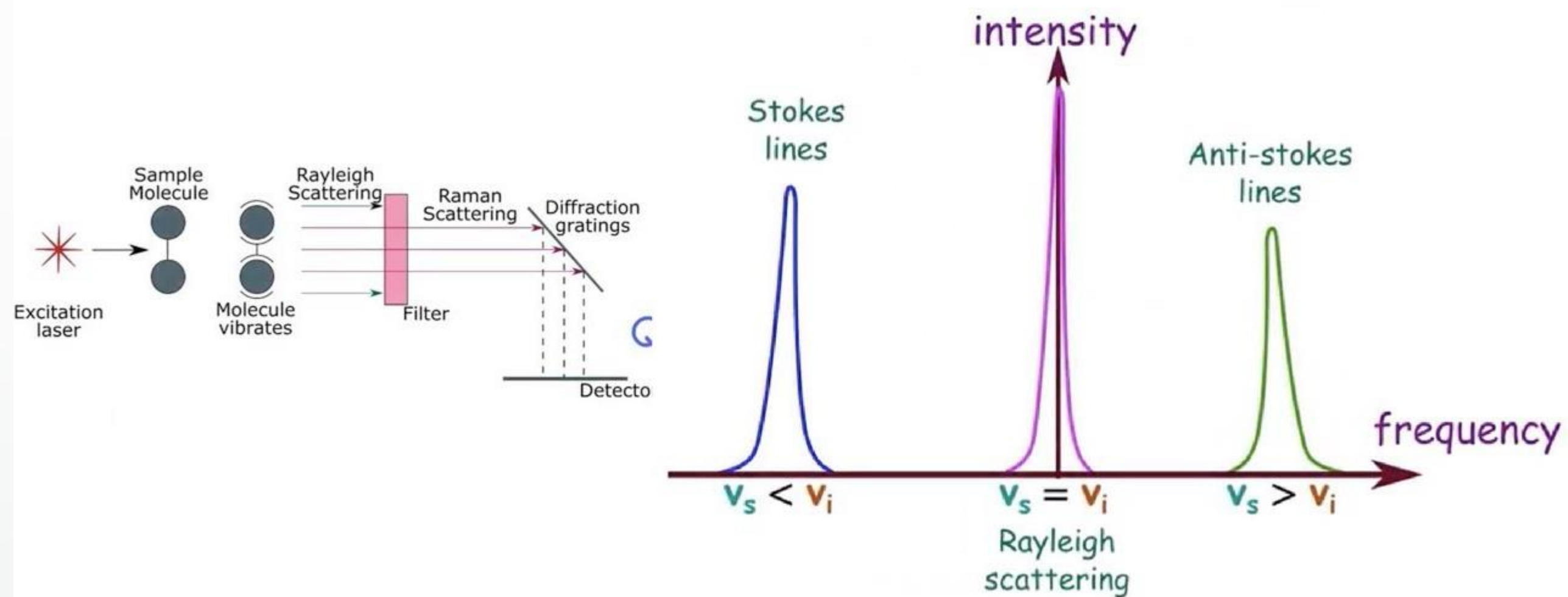
Moisture measurements
on Lyo cake
The absorption peak of the
water at is well visible



Measurements performed
in transmission mode

Raman spectroscopy imaging

Suitable for point-by-point inline inspection

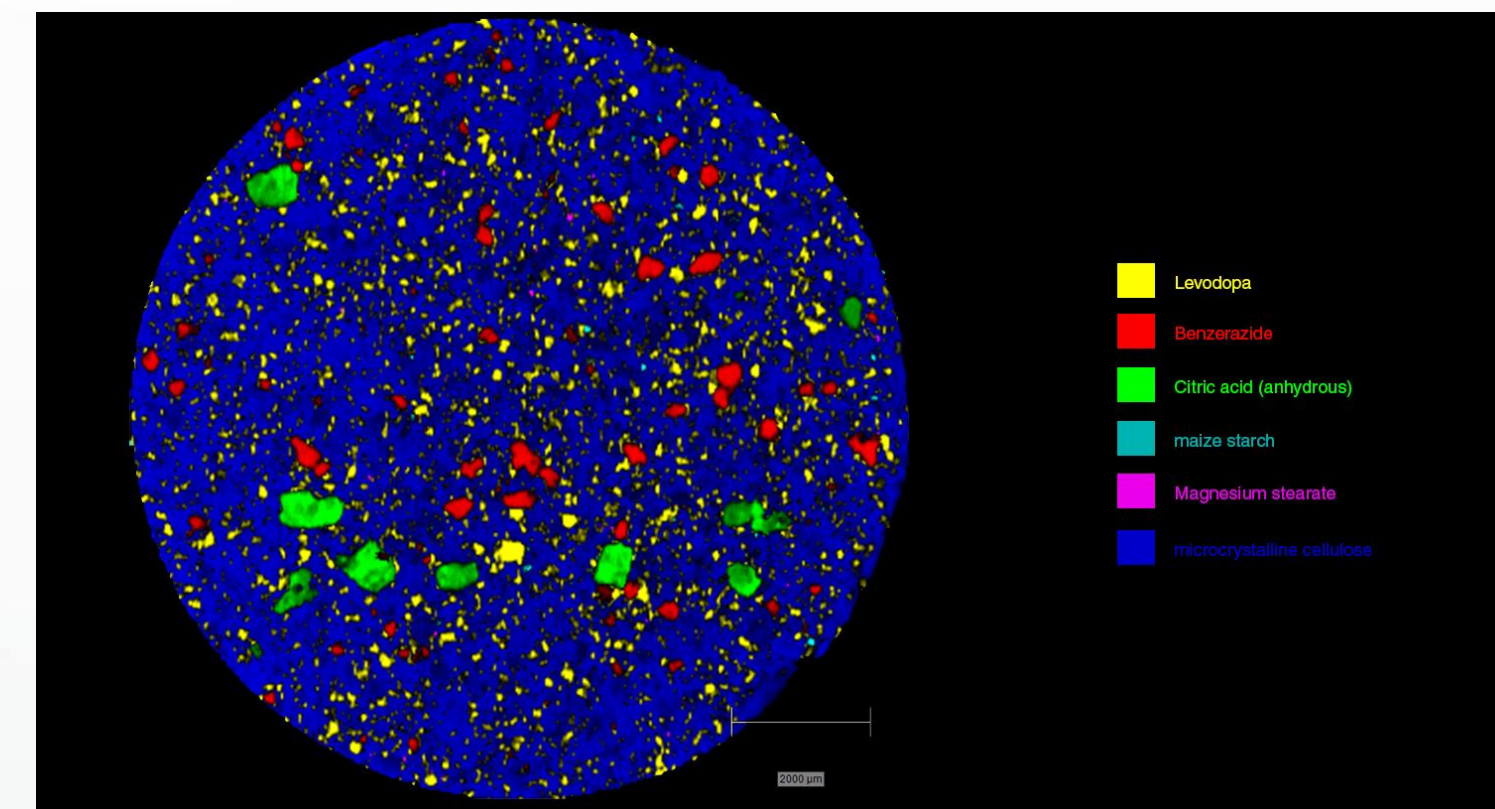


Laser wavelength used for Raman spectroscopy:

532 nm → Green

785 nm → Red

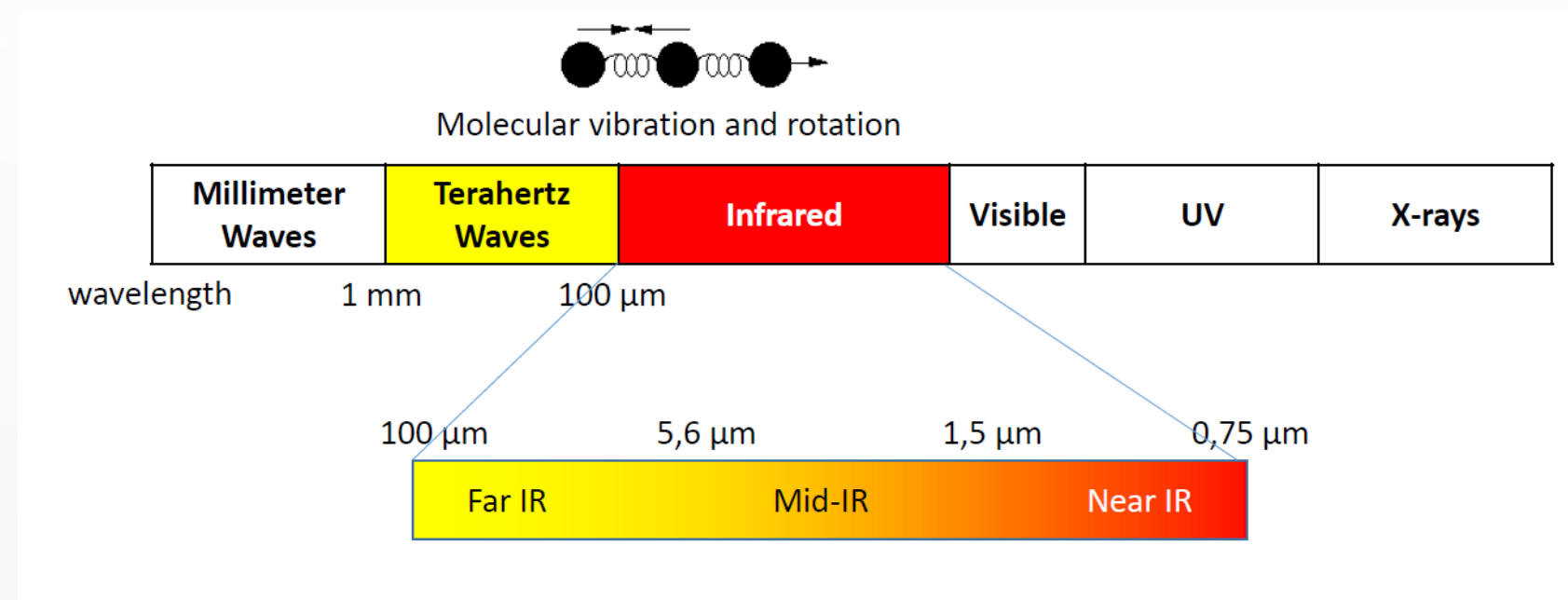
1064 nm → Infrared



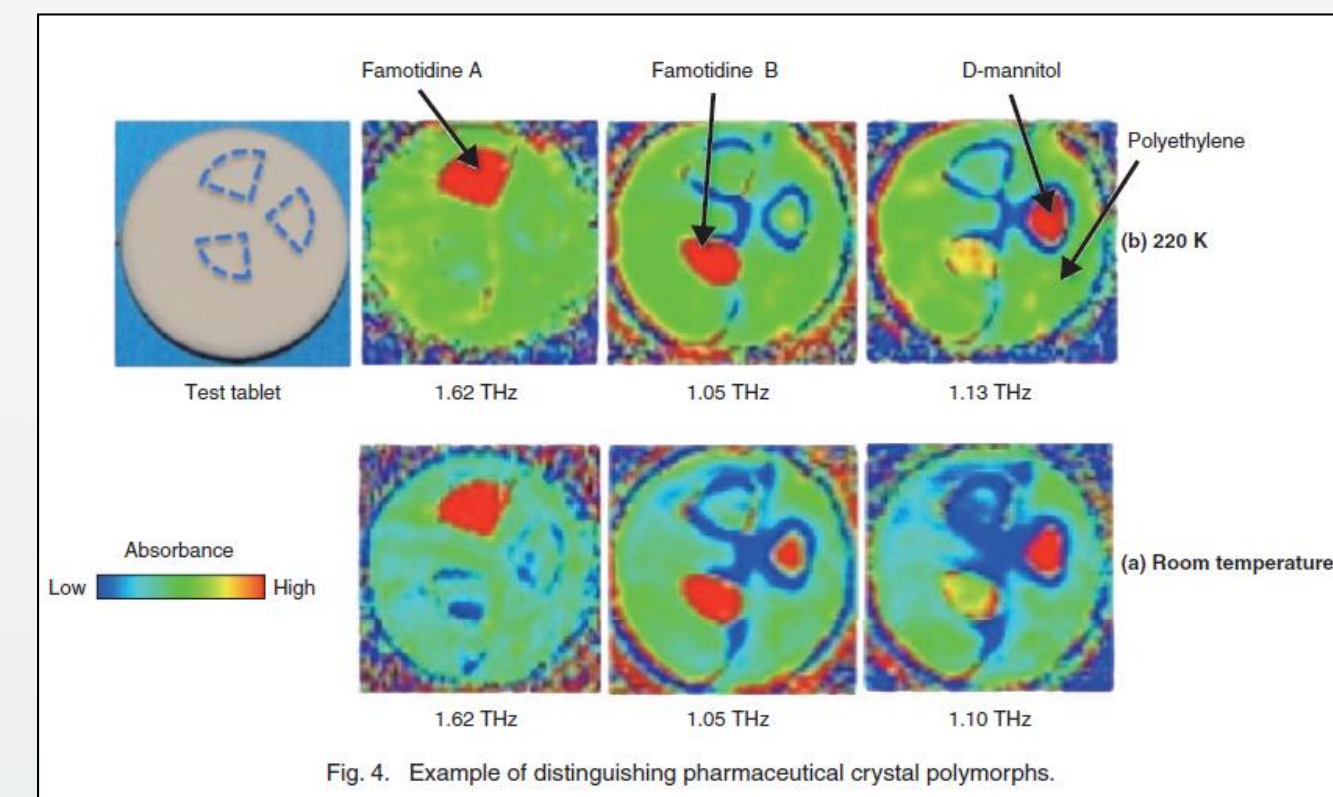
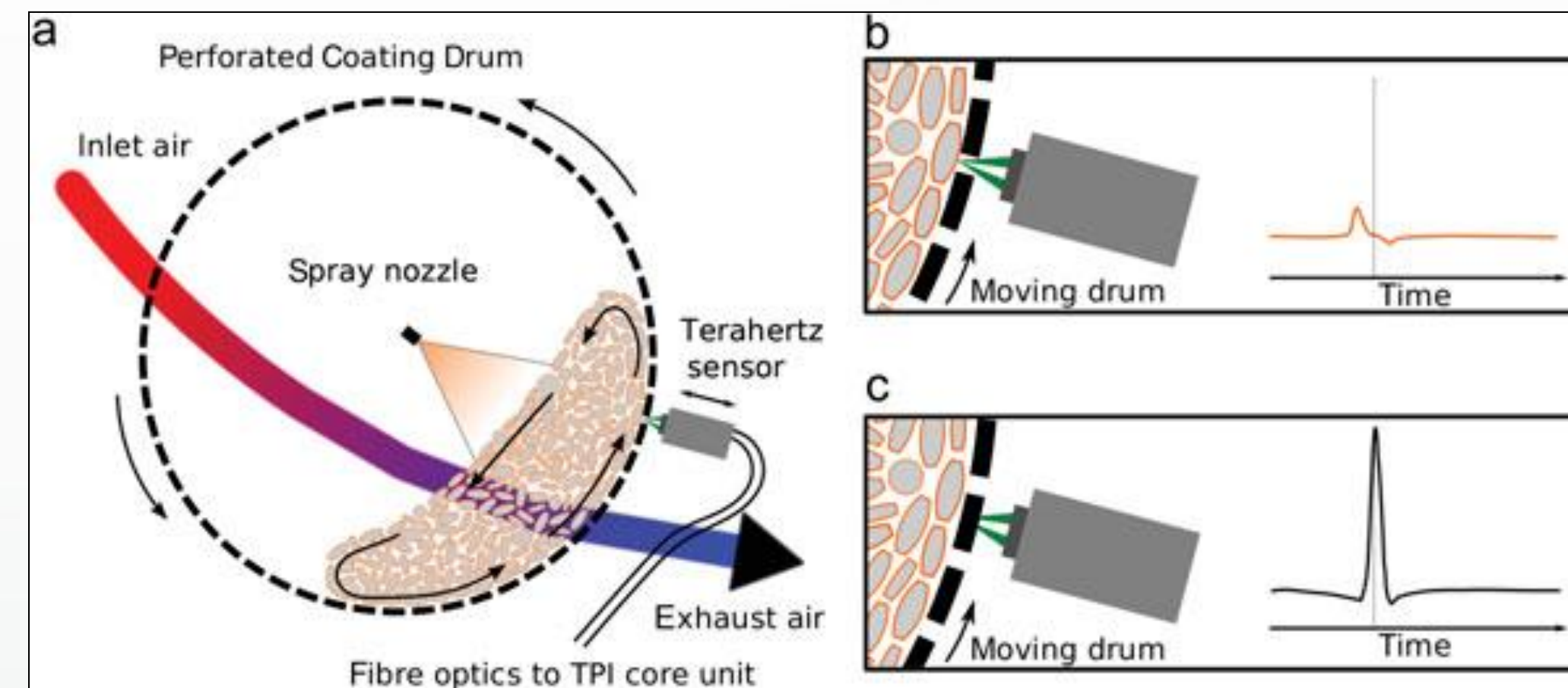
Long time acquisition

Terahertz imaging

On the THz range (300 GHz to 3 THz) and on the Infrared range (3 THz to 190 THz), the which molecules exhibit molecular vibrational and rotational modes, which enable to identify and quantify products compounds.

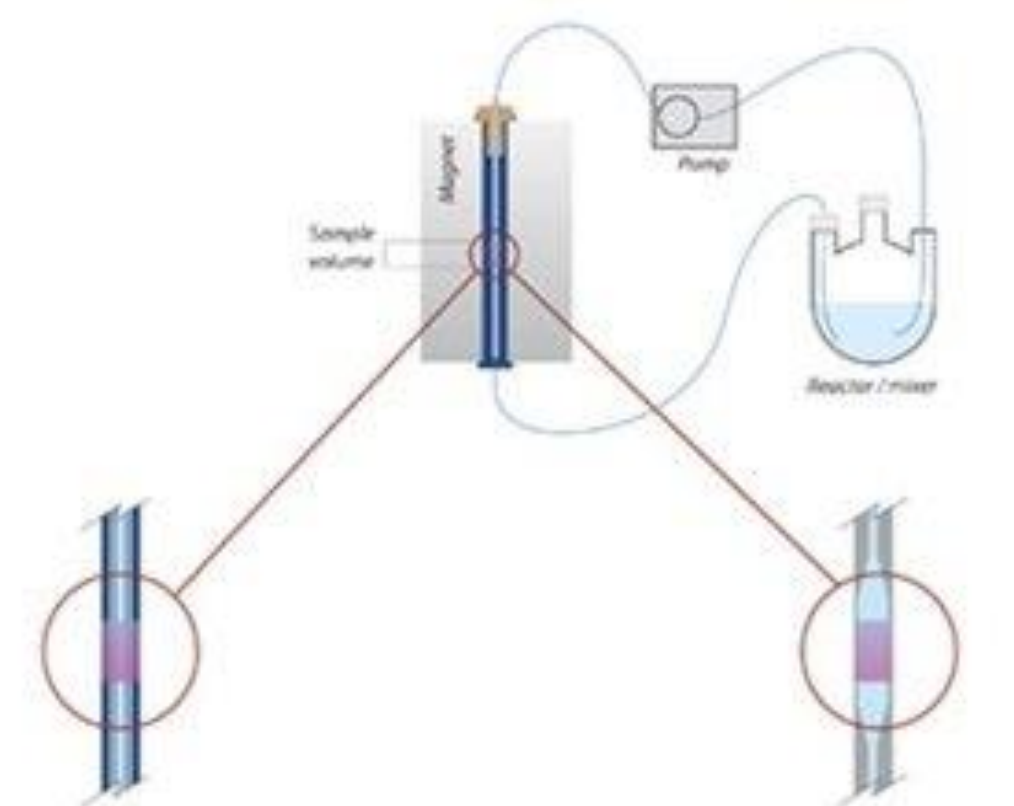
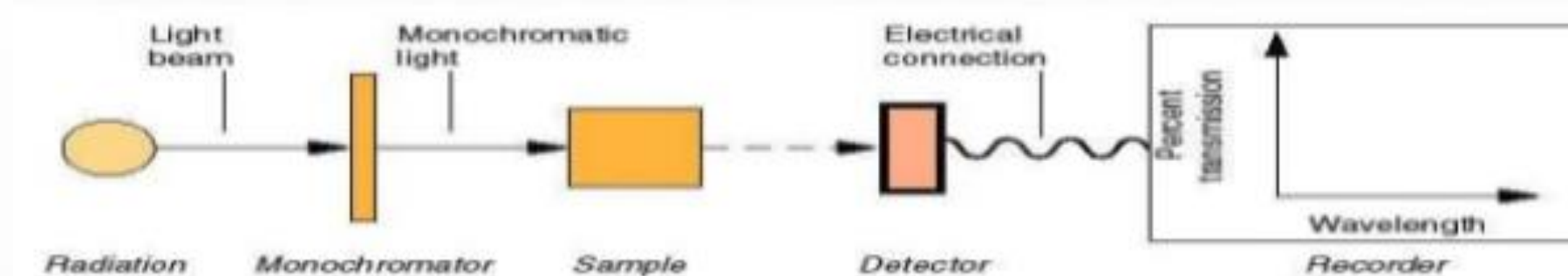
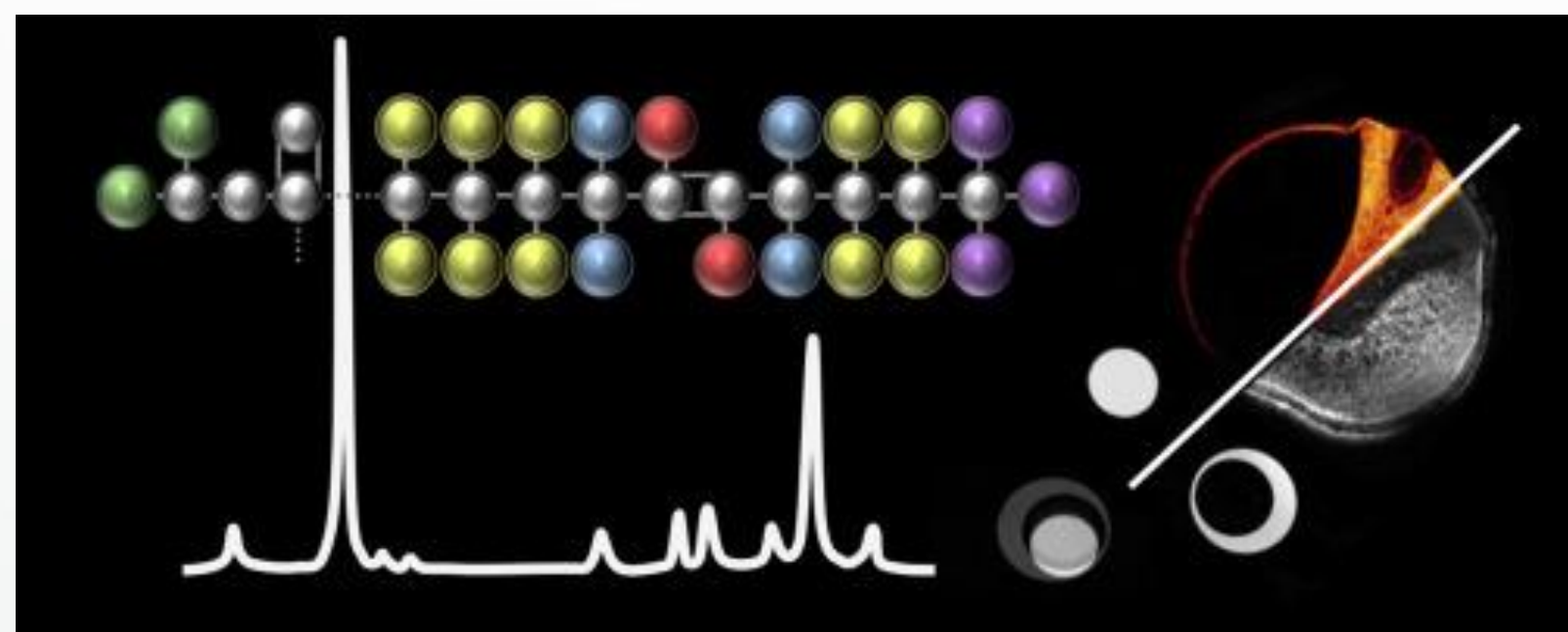


Terahertz radiation corresponds to frequencies between the microwave and infrared regions of the electromagnetic spectrum: 300 GHz to 10 THz, or wavelengths of 1mm to 1 μm .



Nuclear Magnetic Resonance

NON-DESTRUCTIVE spectroscopic analysis method based on the magnetic properties of the nuclei of some atoms and isotopes. Possibility to extract information on the structure of the molecules and monitor the synthesis reactions and drug formation.

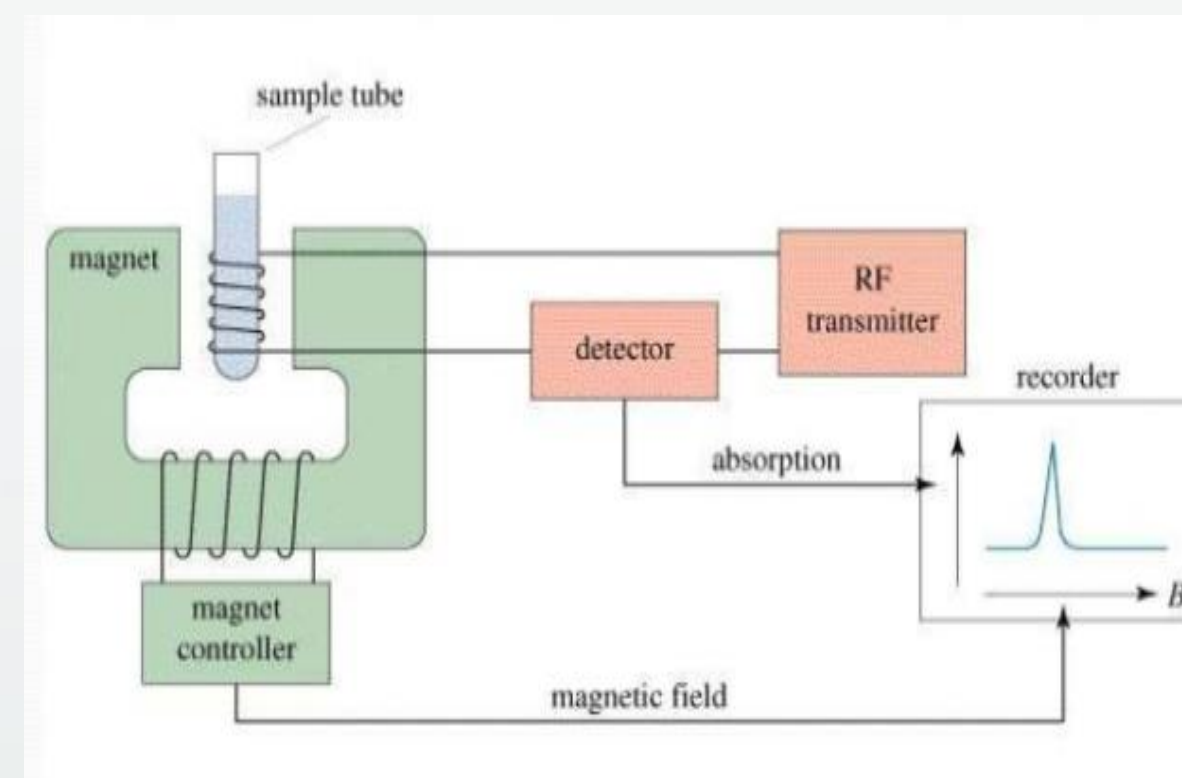


Linear response

Orthogonality

Signal Variance

Structural info



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