ParticlePro

Project Images and Exploitation outline

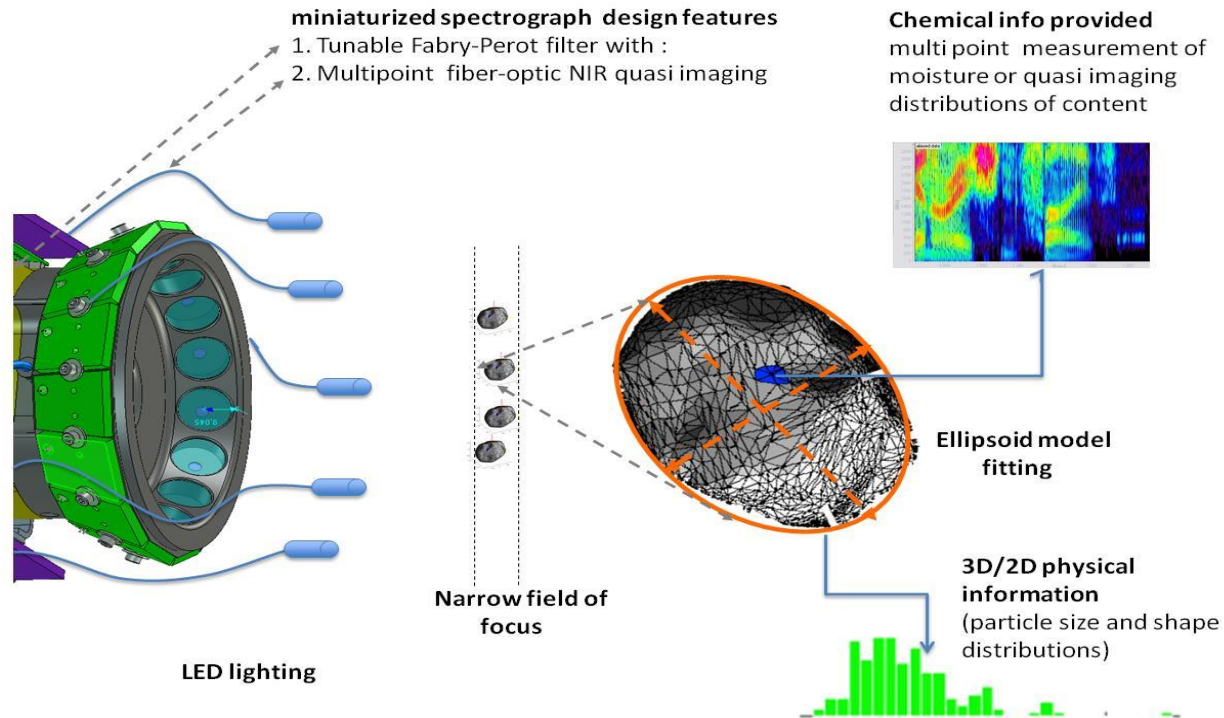# Project proposal.

miniaturized spectrograph design features
1. Tunable Fabry-Perot filter with :
2. Multipoint fiber-optic NIR quasi imaging

Chemical info provided
multi point measurement of
moisture or quasi imaging
distributions of content

Ellipsoid model fitting

3D/2D physical information
(particle size and shape distributions)

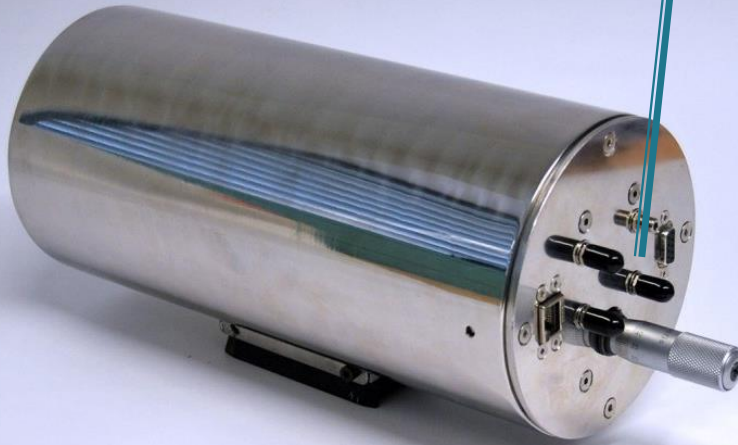**Narrow field of focus**

LED lighting

Image above from section B1 of the DoW illustrates the expected foreground Proposal for the ParticlePro system.

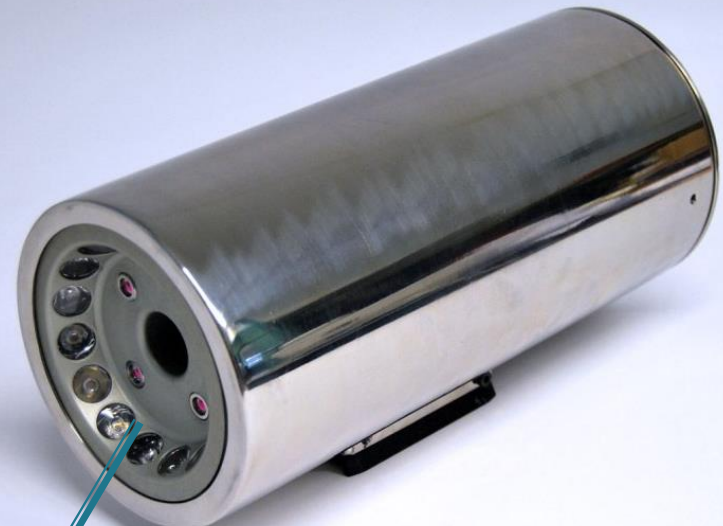# Inline particle-sizer with integrated fibre optic probes

ParticlePro

- Stainless steel exterior

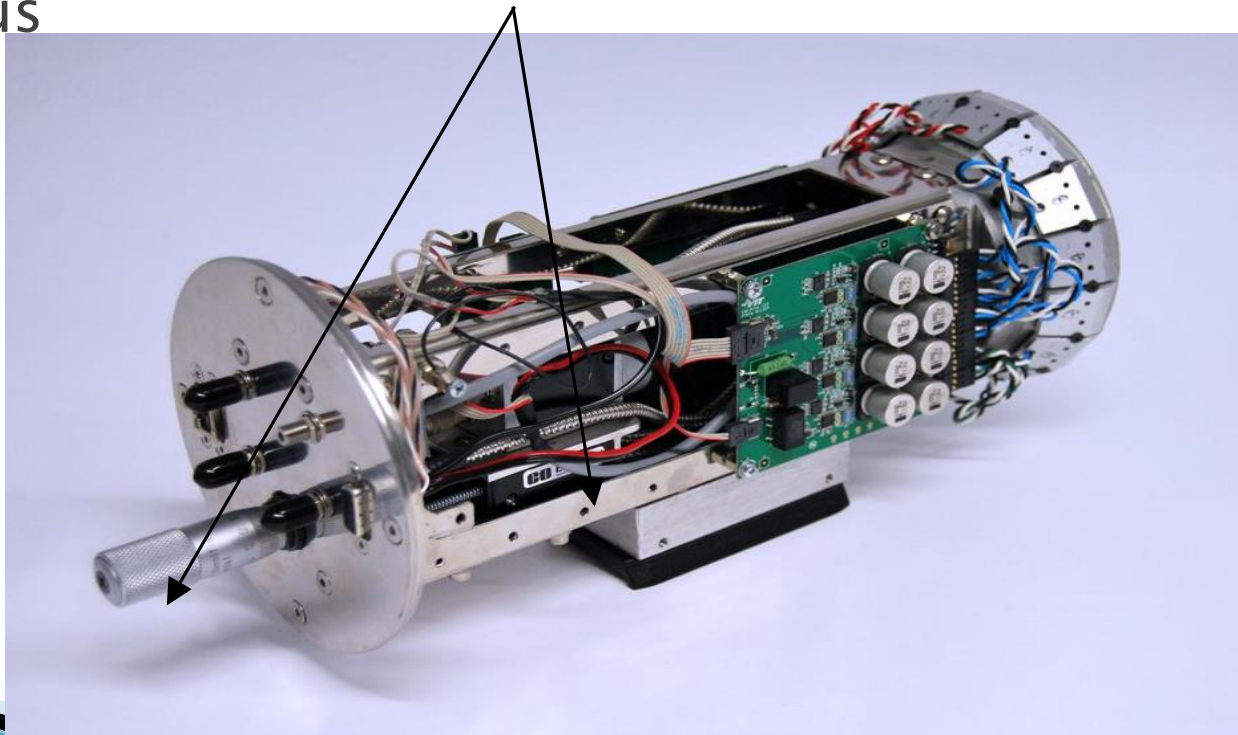Particle sizer with Integrated probes and collimated lenses.

Particle sizer LEDs and Collimated lenses for fibre probes

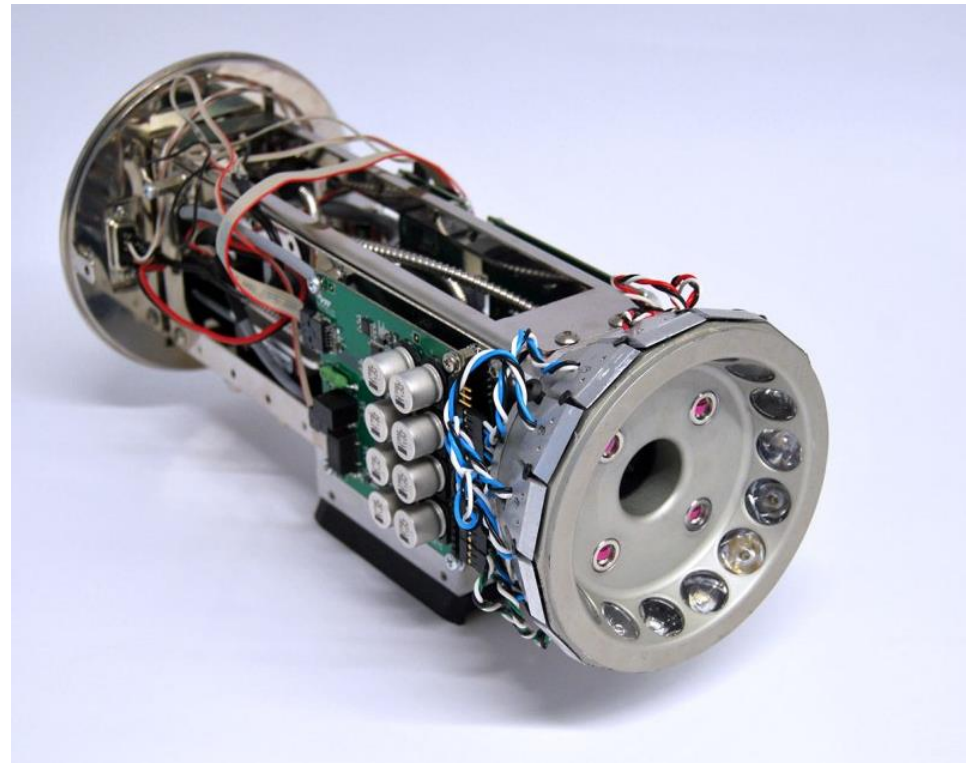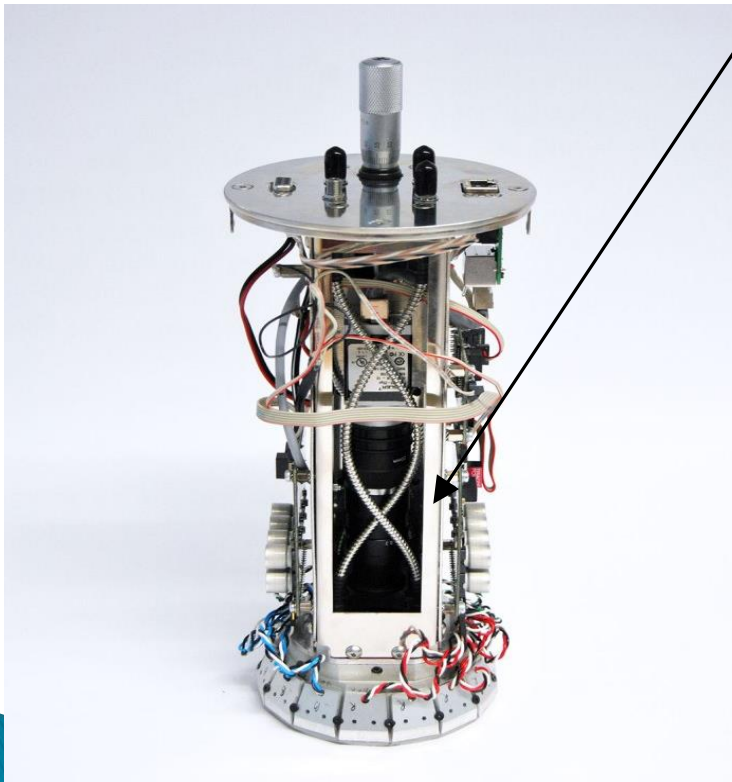# Inline particle-sizer with integrated fibre optic probes

ParticlePro

- Compact size enabled by switch to small optics by VTT
  - **Camera and lens**
- Manual movement stage with external screw to adjust focus

Inline particle-sizer with integrated fibre optic probes

▸ Fibre-optic probes integrated with the particle-sizer

Ownership of foreground
(breakdown by contribution)

	Participant Name		INNOPHARMA		SIGMOID		SERVIPLAST		RIKOLA		EXENS		TAKEDA	
Participant Number		1		2		3		4		5		6	
Project result breakdown	Description	Type of Exploitation	Remuneration	Type of Exploitation	Remuneration	Type of Exploitation	Remuneration	Type of Exploitation	Remuneration	Type of Exploitation	Remuneration	Type of Exploitation	Remuneration
1a	ParticlePro pre-competitive prototype available for further demonstration	Ownership	137,974.50	Ownership	34,493.70	Ownership	31,358.10	Ownership	47,036.70	None	17,310.20	Preferential use and access	13,065.25
1b	Stastical validation of the system for providing spatial measurements of moisture and materila identify from granules and agglomerates	Ownership	137,974.50	Ownership	34,493.70	Ownership	31,358.10	Ownership	47,036.70	None	17,310.20	Preferential use and access	13,065.25
1c	Knowledge for the scale up of the chemometric models and algorithms	Ownership											
1d	Knowledge of the optoelectric and micro electric modules of the system.	Ownership	122,168.60	Preferential use and access	22,995.80	Preferential use and access	20,905.40	Ownership	62,715.60	None		Preferential use and access	13,065.25
1e	Knowledge for the scale up of the hardware for the precompetitive prototype and the commercial ParticlePro technology	Ownership	183,966.00	Preferential use and access	22,995.80	Preferential use and access	20,905.40			None		Preferential use and access	13,065.25
Subtotal			582,083.60		114,979.00		104,527.00		156,789.00		34,620.40		52,261.00
Total			945,260.00										

Exploitation strategy.

Steps foreseen to ensure

The SMEs can assimilate

And exploit the RTD results.

Envisaged exploitation results
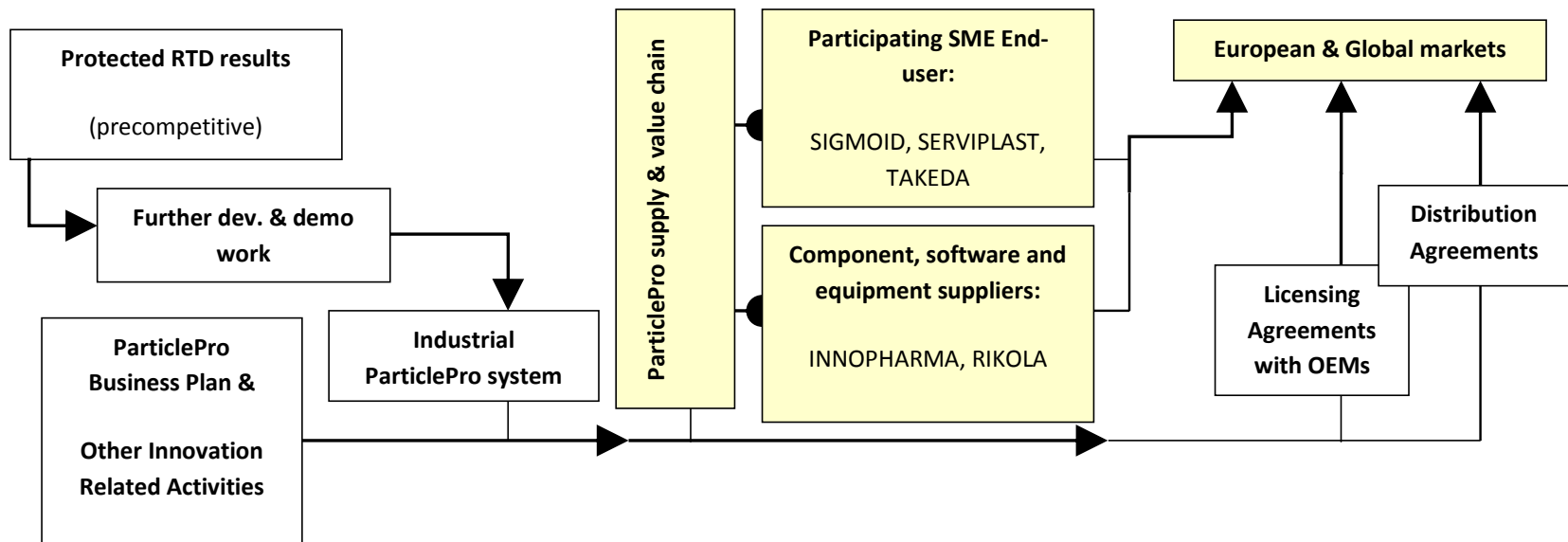
Exploitation strategy.

ParticlePro

Current Eyecon

In order to maximise the market opportunities for the ParticlePro project the system will be offered in modular form. This is to avail of opportunities where existing Eyecon™ customers may want add the MultiEye NIR functionality to their existing capabilities. There will therefore be 3 version of system software.
Software for the operation of Eyecon as a stand-alone system
Software for the operation of MultiEye as a stand-alone system
Software for the operation of both systems through a single user interface.

A similar approach will be adopted with respect to hardware integration. The systems can again be supplied in modular fashion.
As two stand-alone pieces of process analytical technology
Partial integration of physical characterisation and chemical characterisation systems
Full integration of both the physical and chemical characterisation applications.

In addition to these considerations Innopharmalabs need to be cognisant of their current revenue stream for 2015. Currently Innopharmalabs has an inventory level to meet the first half demand for the current Eyecon™ technology. This will determine the timing of the launch of the foreground of the project. This is currently planned for end of Q2 2015 in conjunction with the Achema exhibition. The strategy would be to move from the current commercially available Eyecon to the version developed during the project. There are a number of items to be addressed before the June exhibition as detailed in the report for deliverable 6.1. These include optimisation of lens performance. Reduction in size of the outside casing and enhancement of the software performance.
This will result in a significant shift in Innopharmalabs current branding position. Innopharmalabs are currently working with a design house to complete a package for the presentation and outer design of the updated Eyecon outer casing.

Eyecon Developed in ParticlePro

Exploitation Strategy

Similarly with respect to the NIR application it is propose to move from the current marketed 4 channel MultiEye to the final version as developed and upgraded as a result of the evaluation trials conducted during the project.
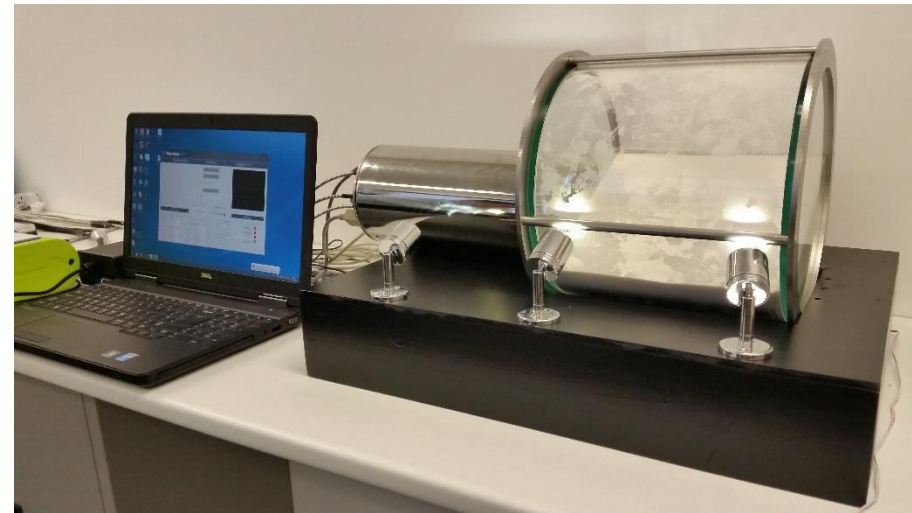
Current 4 channel MultiEye

MultiEye presentation as Designed during the ParticlePro project

Demonstration Rig
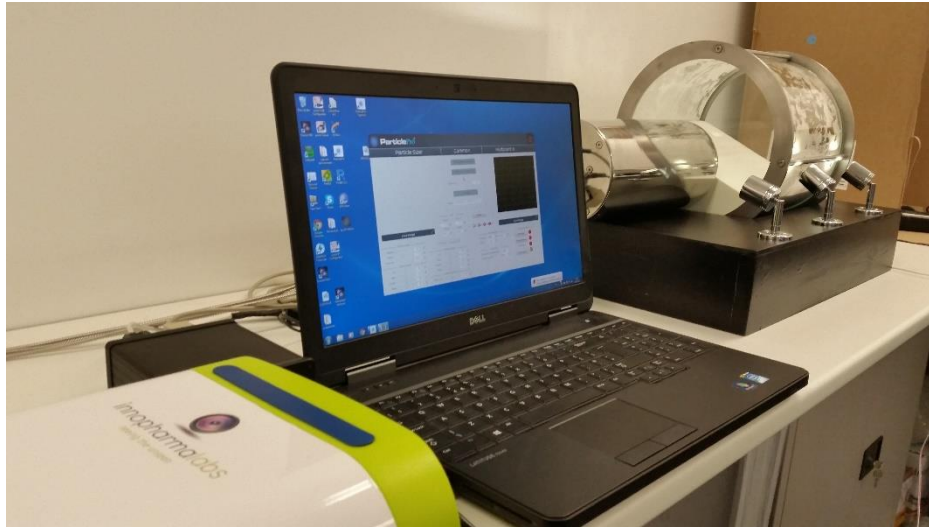
Demonstration rig designed and
Built to exhibit technology monitoring
Moving particles.
This will be upgraded to include a
moisture addition option.

Additional Dissemination

ParticlePro

While the requirement for surface quality determination was not part of the original scope.

This was an area of interest to Sigmoid one of the end user SMEs of the consortium.

To this end research was conducted and the results disseminated at EuPAT6 in Porto Portugal. The following is the slide deck from that presentation.

Toward a PAT solution of measuring particle size and surface texture

Hicham. Rifai

Talk Overview

- Why measure Particle properties
- Particles properties
- Measurement Method
- Results
- Next step

Particle properties affects both the Process efficiency and final product quality for pharmaceuticals

Compression and coating

Blending

Powder flow

Tablet content uniformity

Dissolution rate

Which particle properties are important to measure?

- Size, shape and surface texture of particles are the most important.
- Statistical surface texture methods are used to identify surface texture
- Other properties: Mechanical, charge, microstructure…

D_{min}

D_{max}
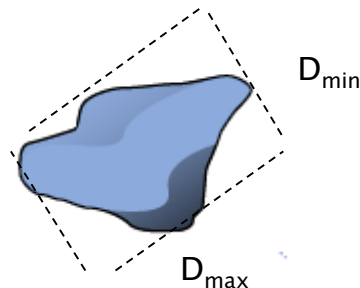
- moving particles imaged using a *flash* imaging technique

- A powerfull short pulse is created

- Particle movement during the pulse is negligible, enables sharp image without blurring
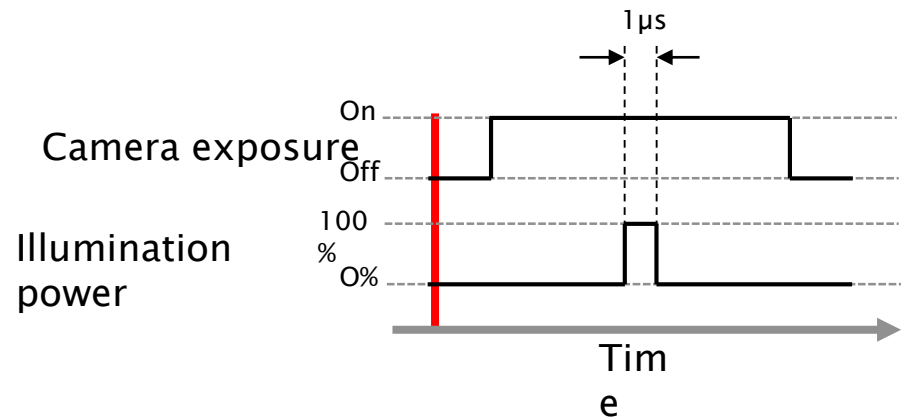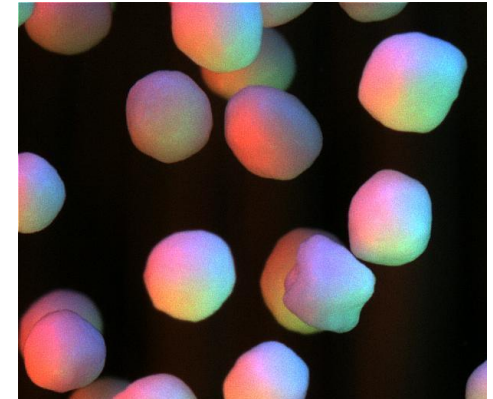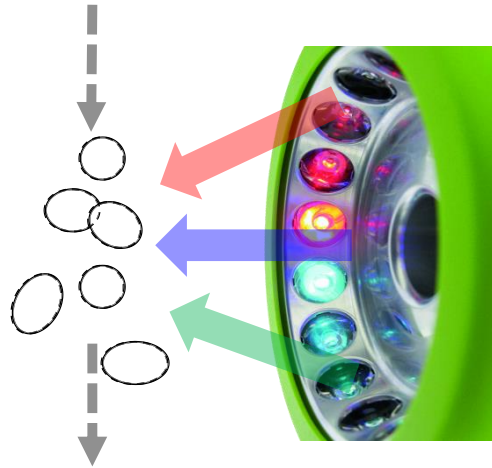
Material used for the experiment

- Microcrystalline cellulose spherical pellets of nominal size 200, 350, 700 and1000μm commonly known as Cellets ®

- To create rough surface particle, chemical etching (HCl) was applied to Cellets ®
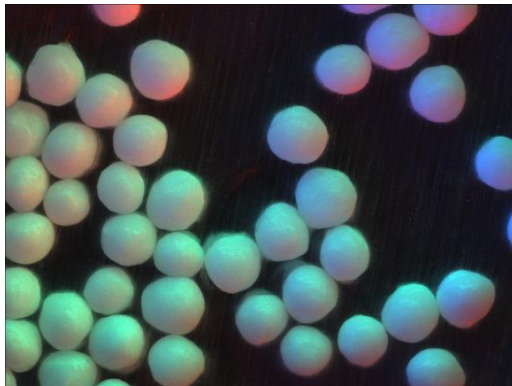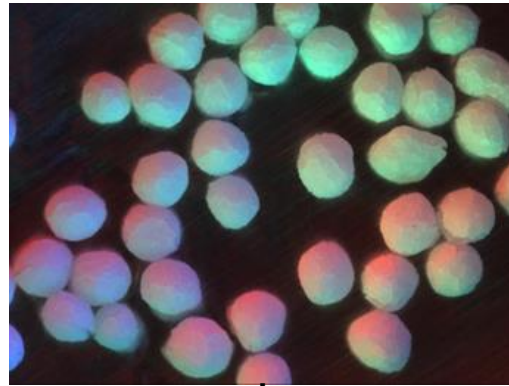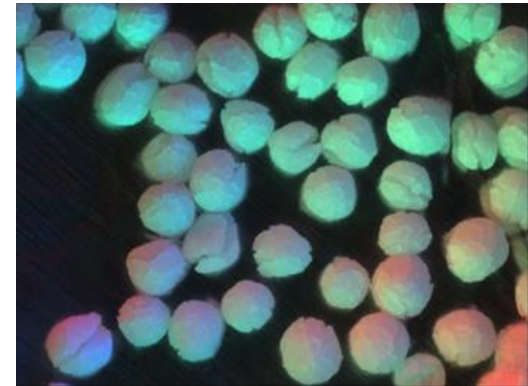
a   b   c

RGB images of Cellets® 700 exposed to 12 M solution of HCl for **(a) 0** mins **(b)**10min and **(c)** 30min

General overview of Image analysis algorithm

ParticlePro®
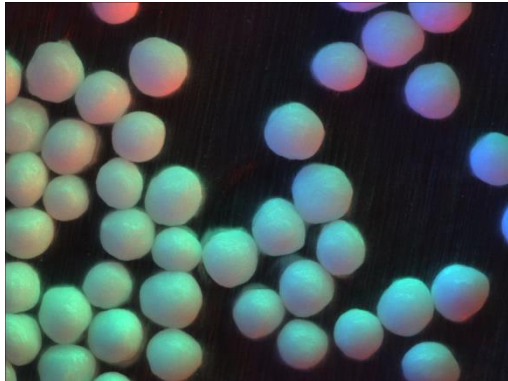
RGB Image

Binary image
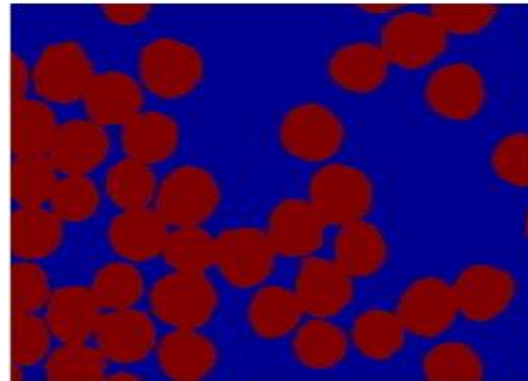
Watershed algorithm applied

Border Cellets® removed
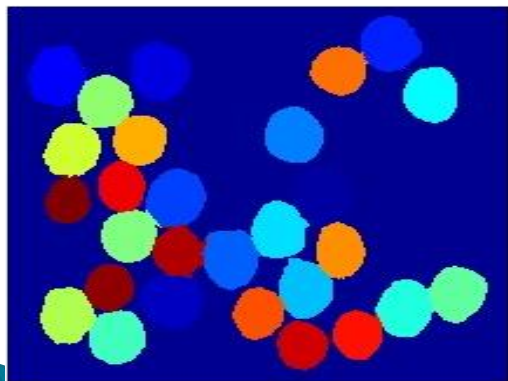
Centers & diameter calculated
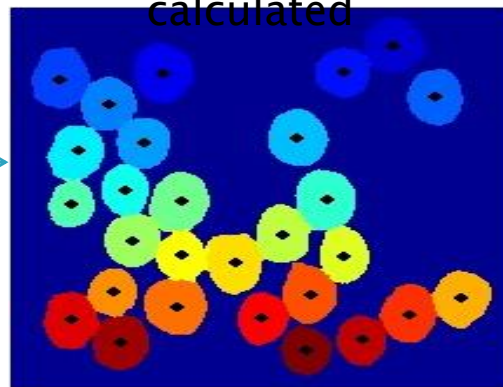
Selecting surfaces
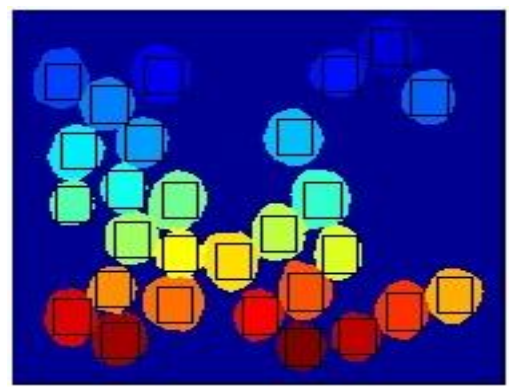
Estimated diameter vs Nominal diameter under static conditions
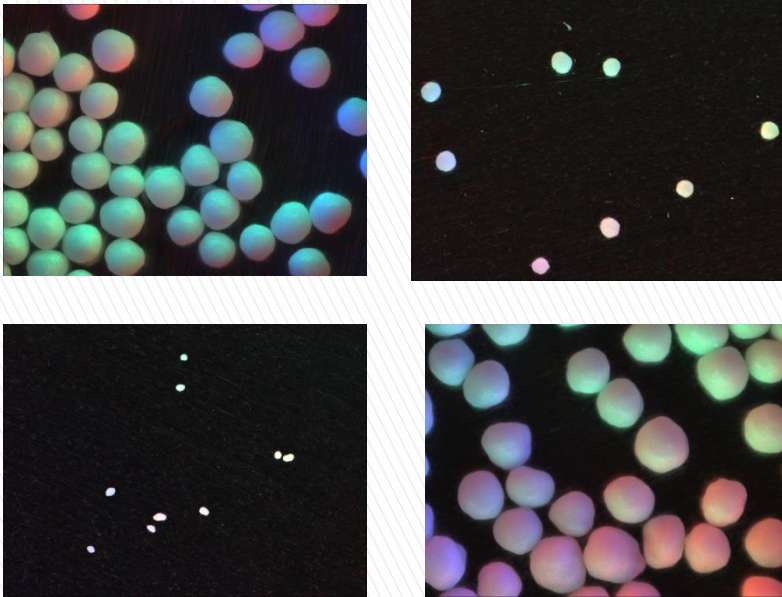
Different size Cellets® RGB images

$y = 1.0109x - 80.081$

$R^2 = 0.9801$

Diameter Estimate(μm)

Nominal cellets value μm
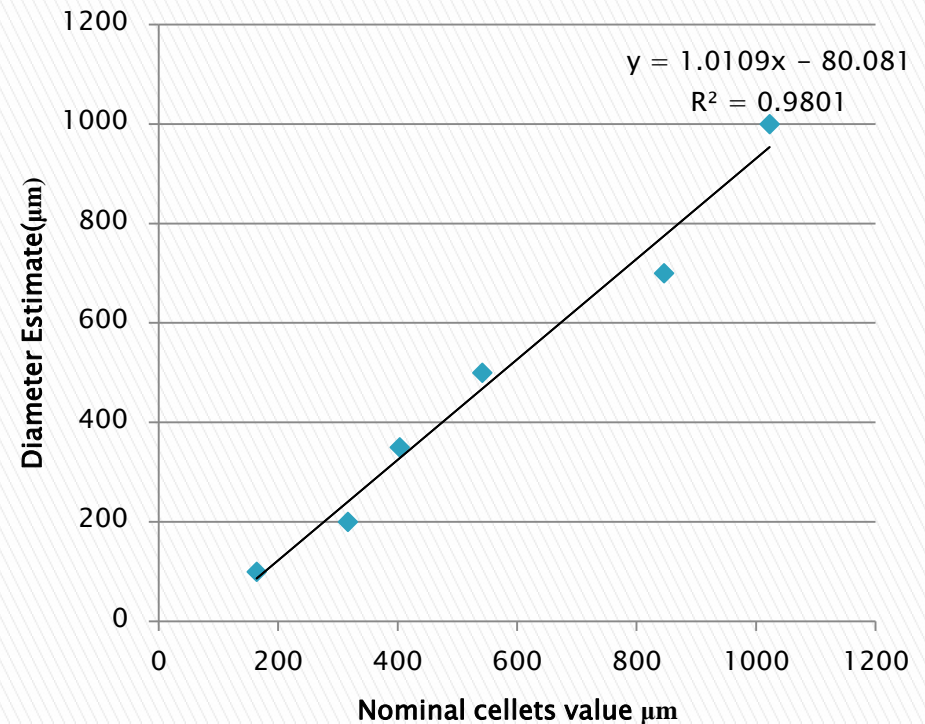
Statistical Analysis for Surface texture

- First order statistics: Estimate the properties of individual pixel values independently of their location; Standard deviation, Histogram…

- Second and higher order statistics: Estimate properties of two or more pixel occurring at specific locations; **Co-occurrence matrix, Autocorrelation function**, **Variograms**

Surface texture using Co-occurrence matrix correlation property

ParticlePro

▸ Co-occurrence matrix is counting how often pixel with value i is adjacent to a pixel with value j

Two colors 6x6 pixel image

0	1	0	0	1	0
1	1	0	1	1	0
0	1	0	0	1	0
1	1	0	1	1	0
0	1	0	0	1	0
1	1	0	1	1	0
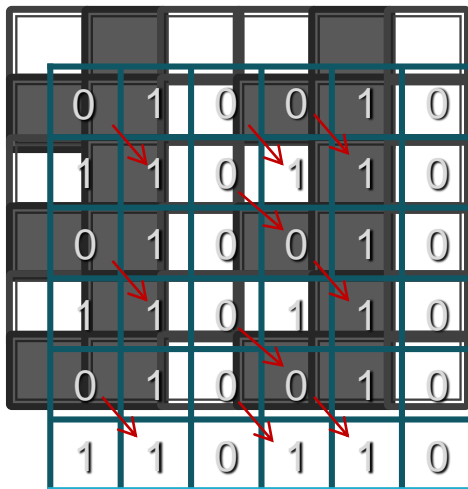
One step -45° direction

i
j
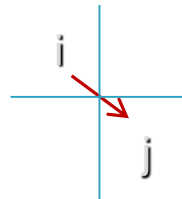
Co-occurrence matrix for one distance step

	0	1
0	2	9
1	4	10

$$Correlation = \frac{\sum_{i=1}^{n} \sum_{j=1}^{n} i \cdot j P_\delta(i,j) - \mu_y \mu_x}{\sigma_y \sigma_x}$$

ParticlePro

Autocorrelation function

- Autocorrelation function could assess the amount of periodicity as well as finess/Coarseness

$$\rho(k) = \frac{\sum_{t=1}^{n-k}(x_t - \bar{x})(x_{t+k} - \bar{x})}{n}$$

Autocorrelation

Periodic texture

fine texture

Coarse texture

Distance
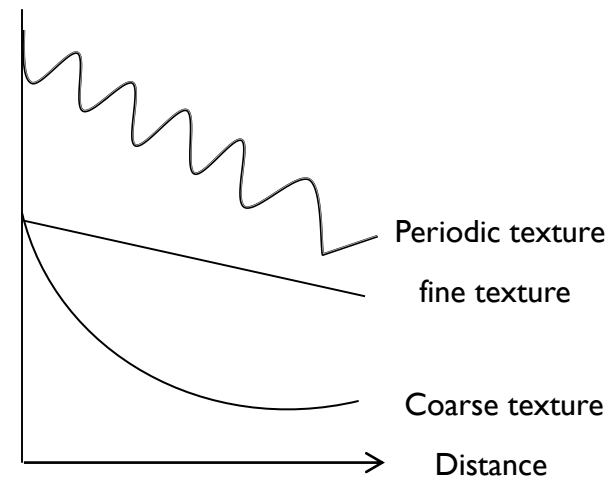
Variogram Model

- Surface texture is indicated by the variogram at the origin, rough texture will have high slop at the origin while smoother surface will have low gradient at the origin

$$\gamma = \frac{1}{2N(h)}\sum_{i=1}^{N(h)}(z_i - z_{i+h})^2$$

Rough texture ——————

Smooth texture ——————

sill $= 1.0$

$\gamma(h)$

nugget $= 0.2$

range h $= 5$

h
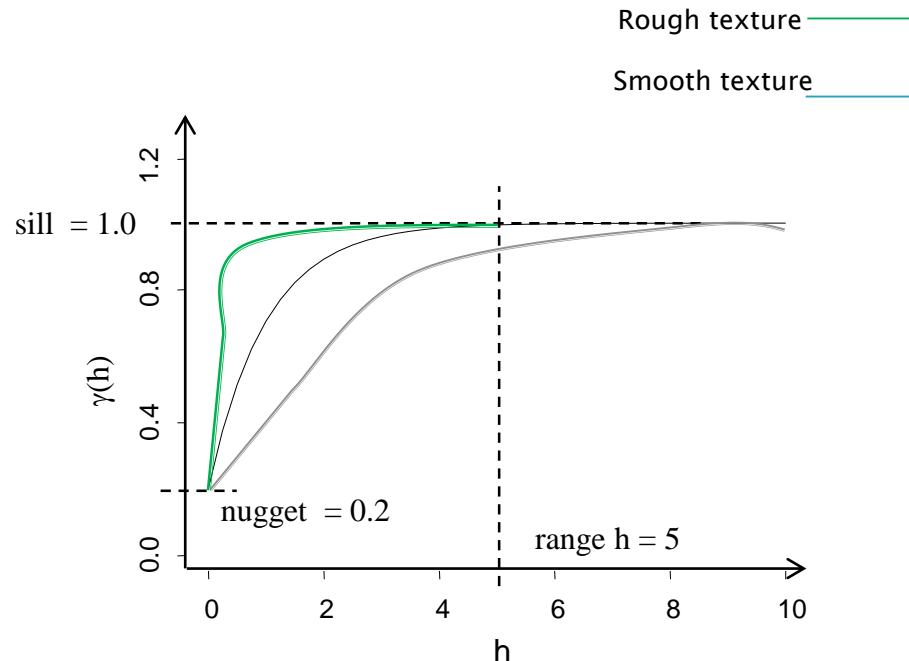
Co-occurrence matrix correlation property of gray-scale image under static conditions
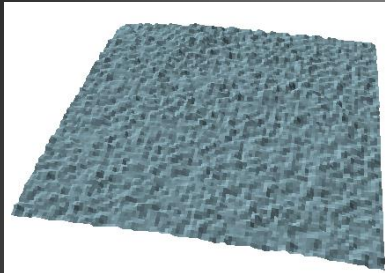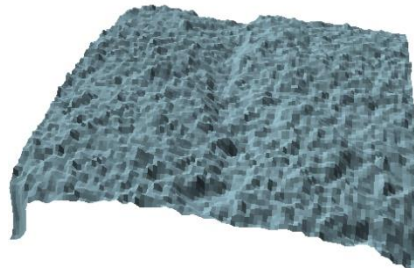

Roughest at 0 min
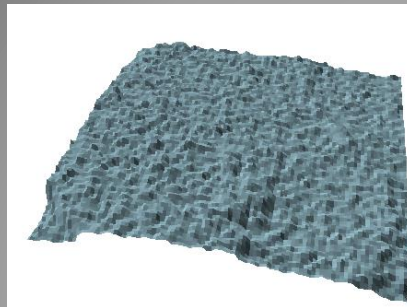
Roughest at 10 min
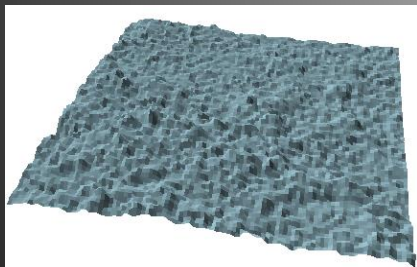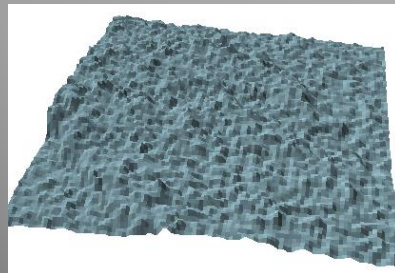
Roughest at 20 min

Roughest at 30 min

Median of haralick correlation for each image

Legend:
- 0 min
- 10 min
- 20 min
- 30 min

Y-axis: Harralick Correlation

X-axis: Distance
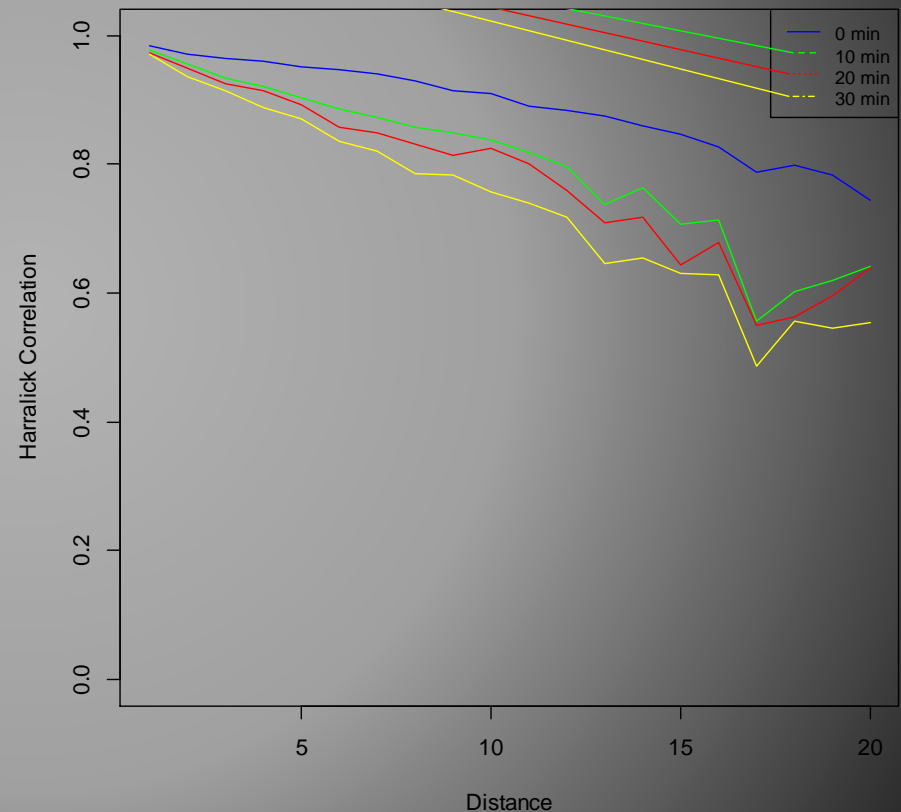
Auto-correlation function of gray-scale image under static condition
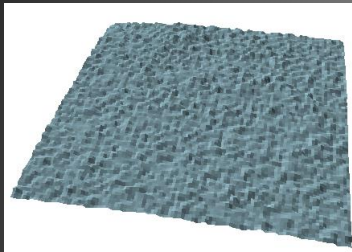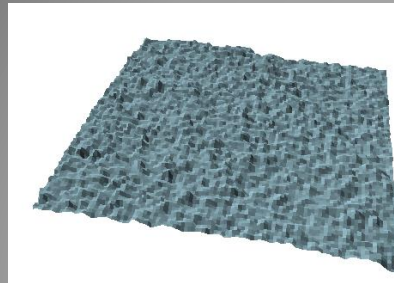
Roughest at 0 min
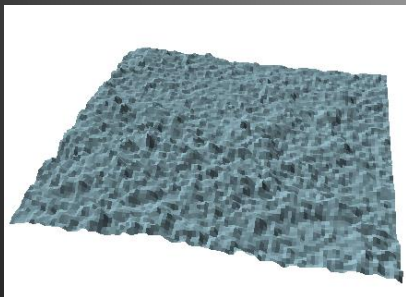
Roughest at 10 min
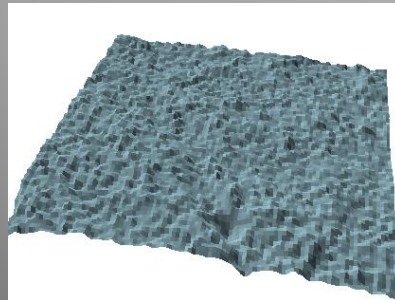
Roughest at 20 min

Roughest at 30 min

Median of auto correlation for each image

Legend:
- 0 min
- 10 min
- 20 min
- 30 min

Y-axis: Auto Correlation function

X-axis: Distance
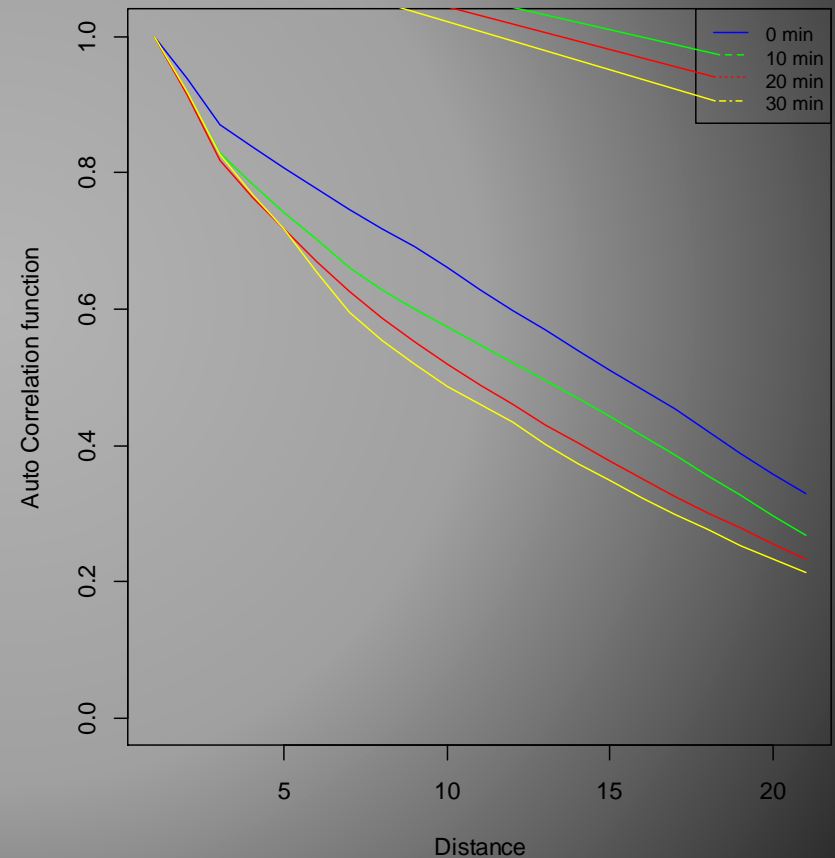
Variogram of gray-scale image under static condition
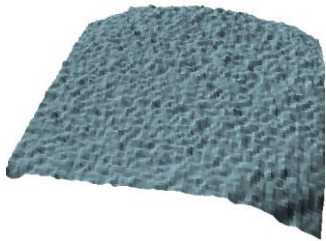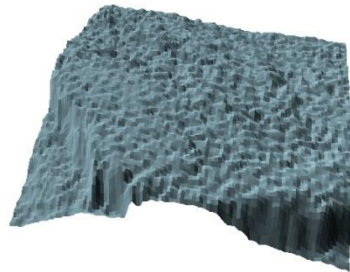
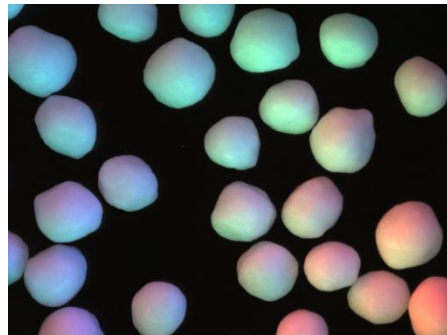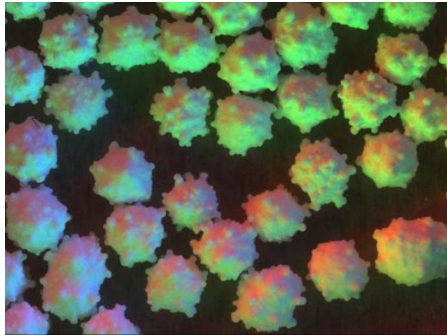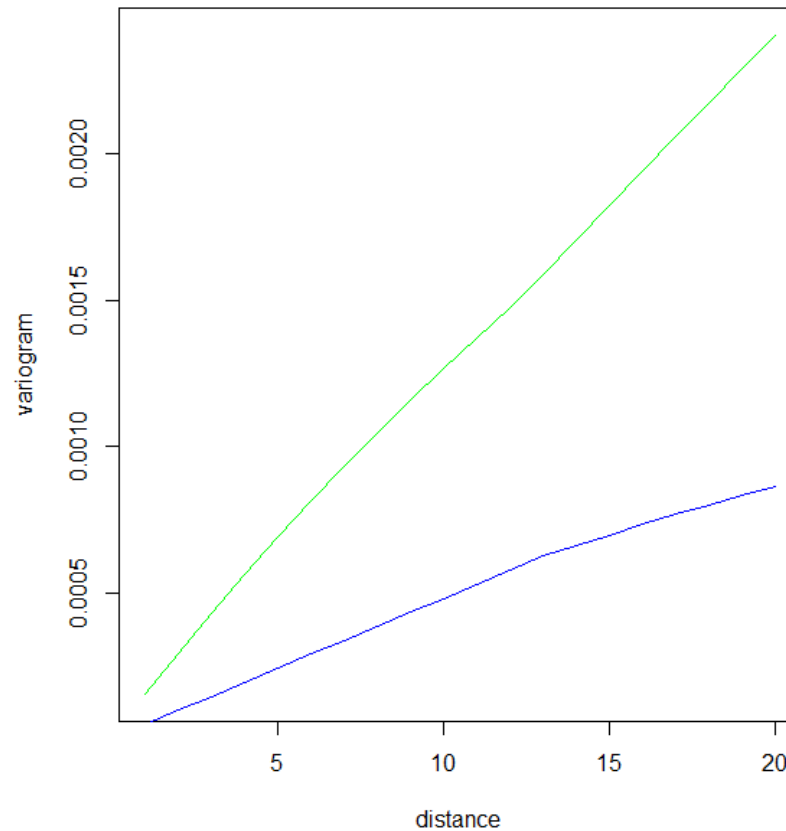Roughest at 0 min
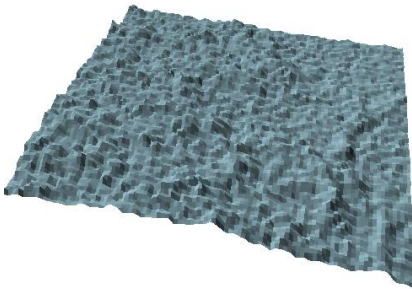
Roughest at 10 min

Roughest at 20

Roughest at 30 min

Median variogram for the four images
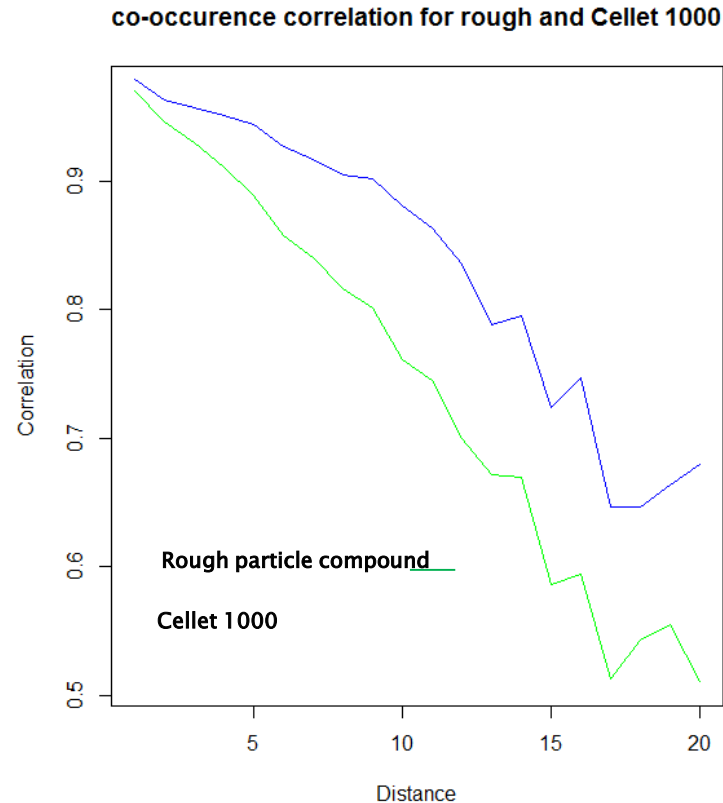
Legend:
- 0 min
- 10 min
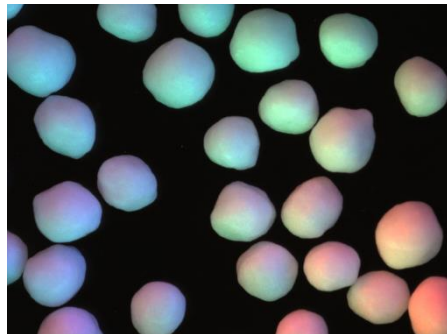- 20 min
- 30 min

Y-axis: Variogram
X-axis: Lag
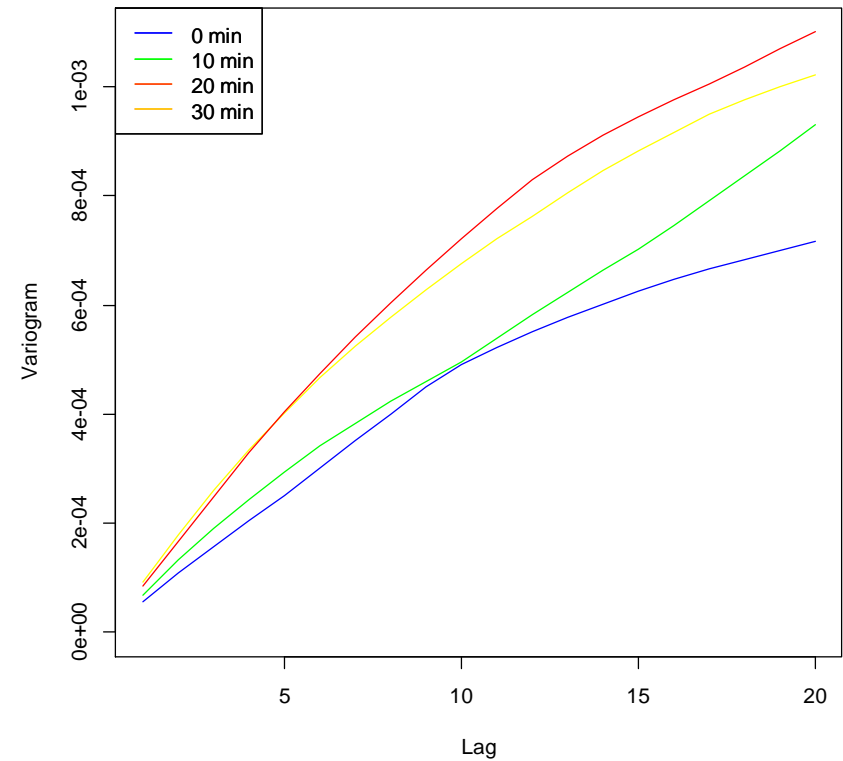
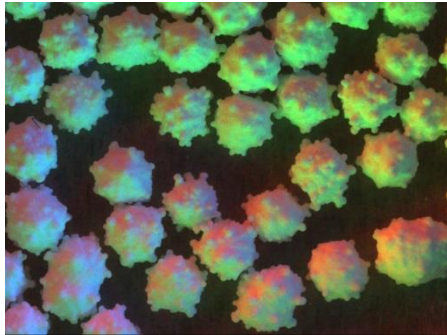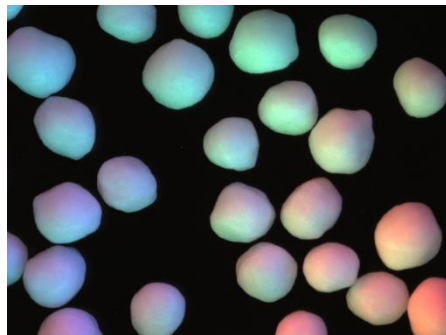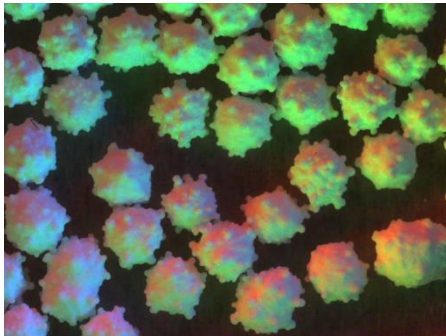# Variogram of particles from a pharmaceutical compound
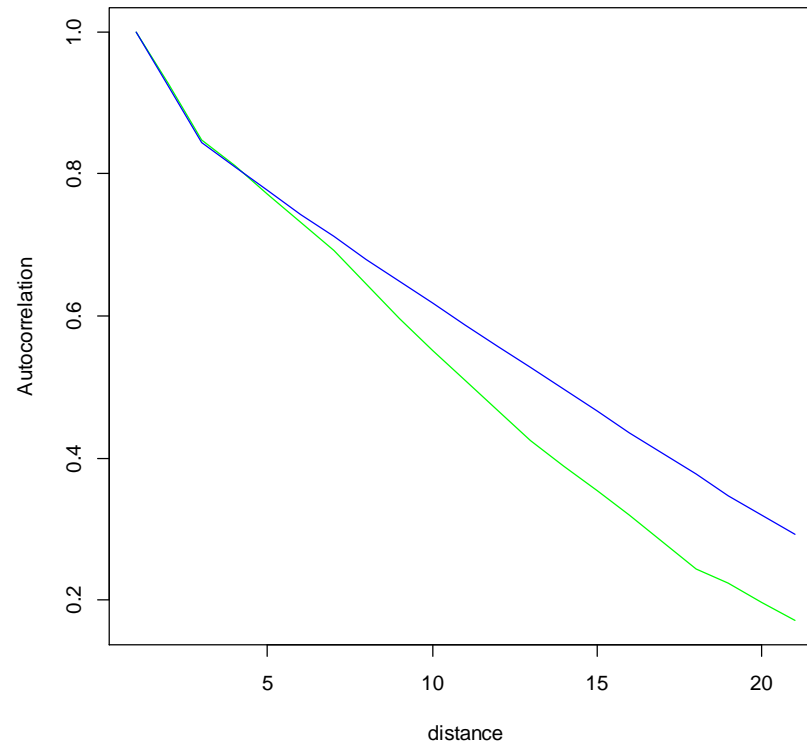

median variogram of rough cellet and Cellet 1000

Co-occurrence correlation property of pharmaceutical compound µm and Cellets 1000 µm

co-occurence correlation for rough and Cellet 1000

Rough particle compound

Cellet 1000

Autocorrelation of phamaceutical compound and 1000 µm

Summary

- Image analysis algorithm was able to estimate particle size under static conditions

- Particle surface texture could be calculated using RGB images

- The autocorrelation function was the fastest in computation time while variogram model was the slowest

Next Step

▸ The surface texture algorithm will be applied on moving particles RGB images using Eyecon

▸ Near Infra red probes will be used simultaneously with Eyecon® to determine the chemical content and the moisture level of the powder
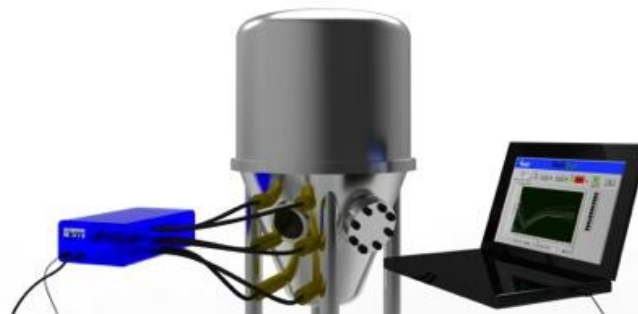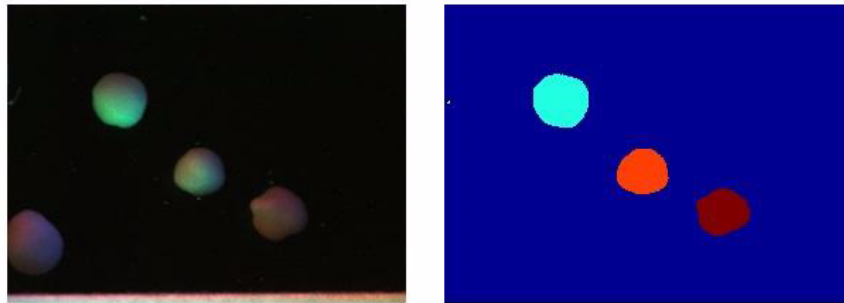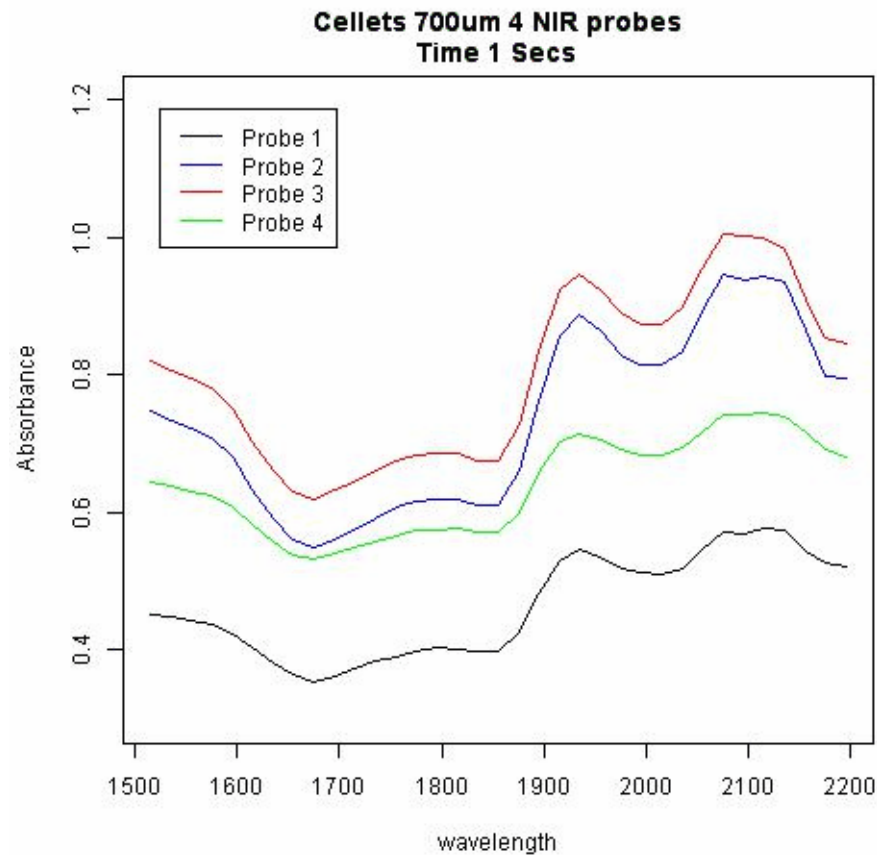
Image analysis for moving particles

cellets 1000

Determination of chemical characteristics

Cellets 700um 4 NIR probes
Time 1 Secs

Acknowledgement

D.M. Togashi, L. Alvarez-Jubete,
C. Sullivan, P.J. Cullen