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Nanoscale and Microscale Research Centre

nmRC CASE STUDY

VISUALISING PROTEIN AND SURFACTANT DISTRIBUTION IN PLGA MICROSPHERES

nmRC_CS_02

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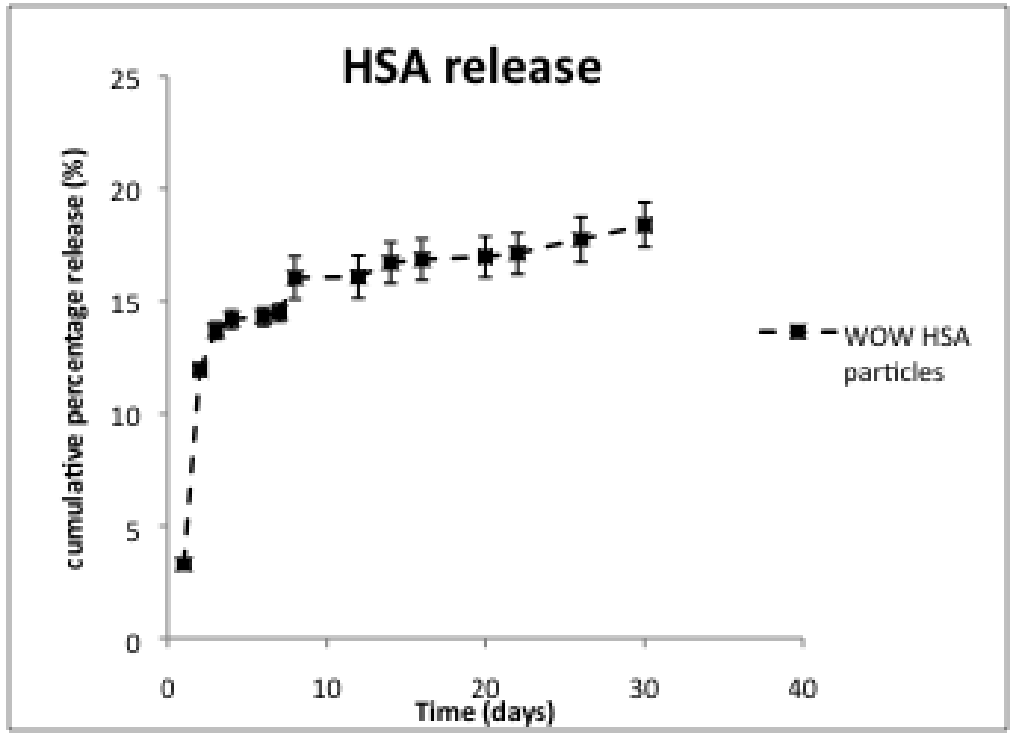
Visualizing Protein and Surfactant Distribution in PLGA Microspheres

A Materials Characterisation Case Study

MICROSPHERES FOR DRUG DELIVERY

- Polymers are often used in order to maintain controlled release of drug.
- Water-in-oil-in-water (w/o/w) fabricated PLGA microspheres containing lysozyme stabilised by PVA surfactant were analysed using a suite of materials characterisation techniques to investigate a 2 stage release profile observed from a similar system.

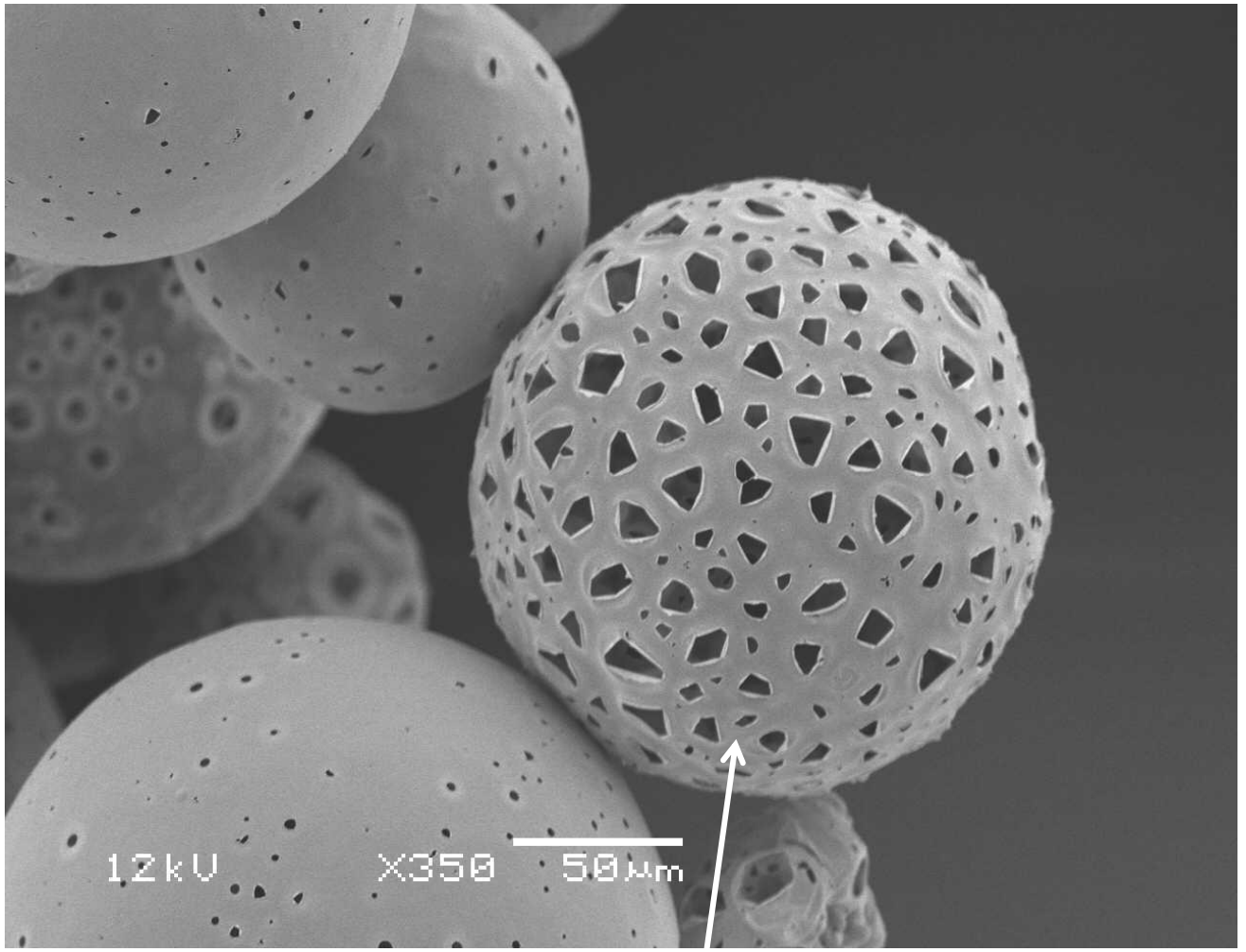


SURFACE CHARACTERISATION

What Influences the release profile?

What is the morphology of the particles?

How consistent is the size and structure?



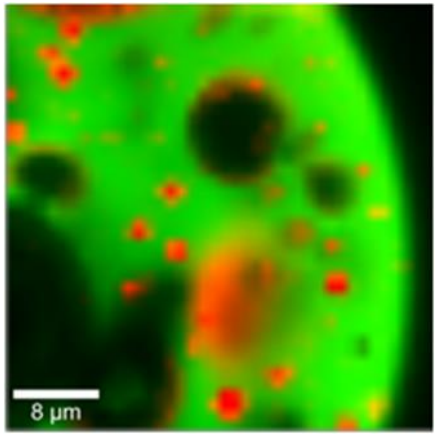
Where is the protein component?

How is the surfactant distributed?

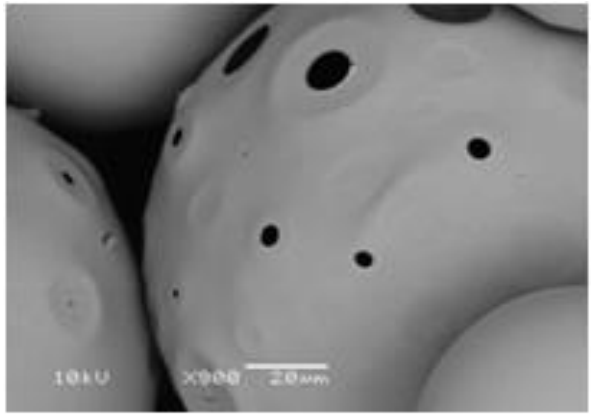
SURFACE CHARACTERISATION METHODS

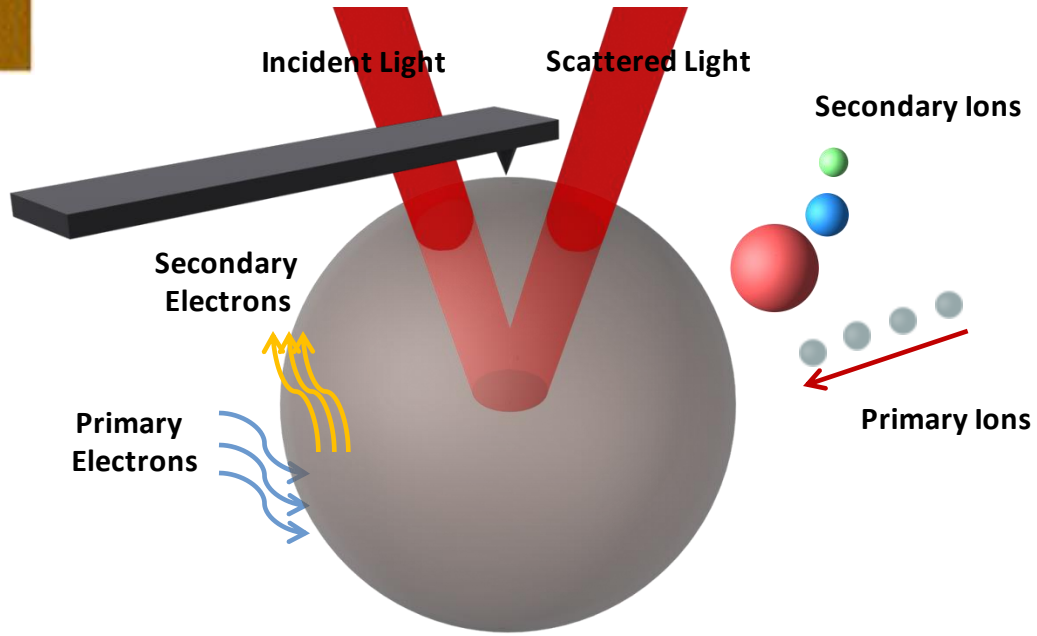
Atomic Force Microscopy (AFM)

Confocal Raman Spectroscopy

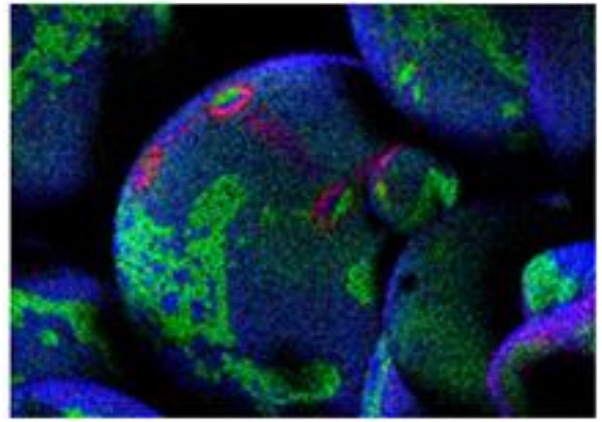


Scanning Electron Microscopy (SEM)



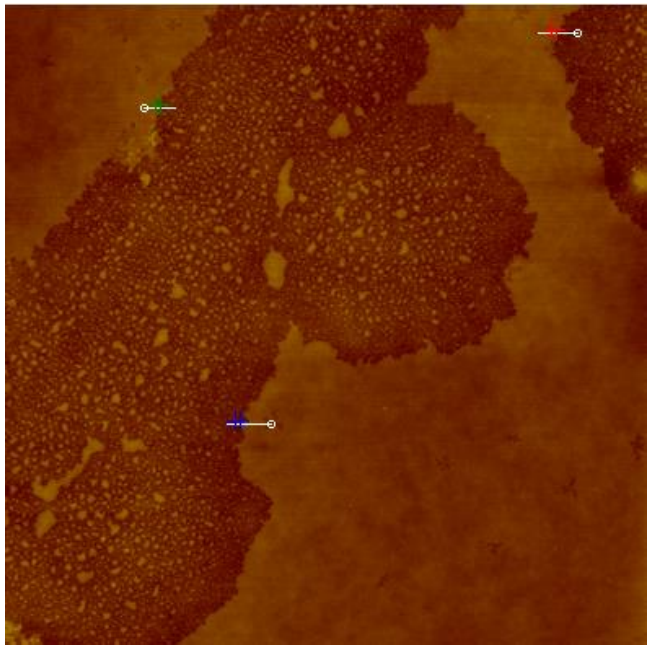


Time-of-Flight Secondary Ion Mass Spectrometry (ToF-SIMS)



AFM ANALYSIS

Pre-Sputtering



Post-Sputtering

- AFM imaging shows a surface layer of material measuring approximately 5nm in thickness.
- After sputtering in the ToF-SIMS this layer is gone, confirming it to be the surfactant.

MULTIVARIATE DATA ANALYSIS

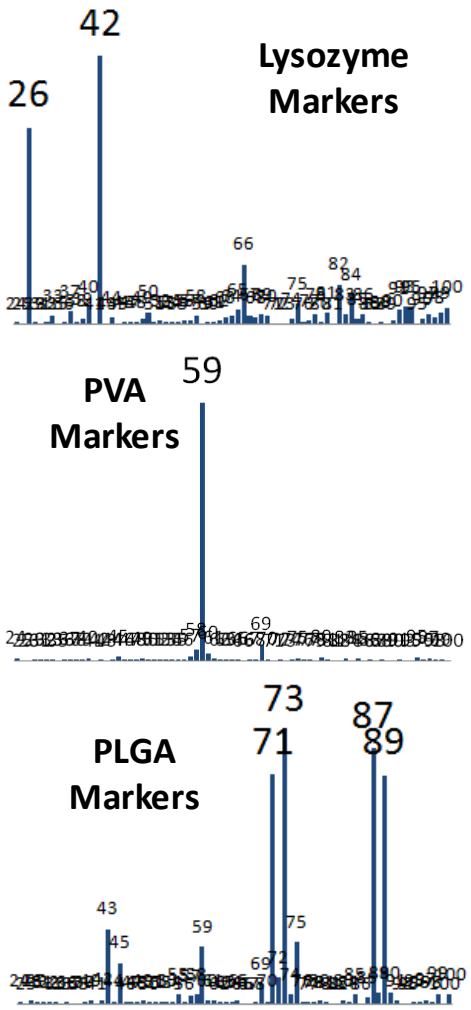
- Multivariate data analysis is a technique useful in reducing the dimensionality of hyperspectral data to simplify its analysis.

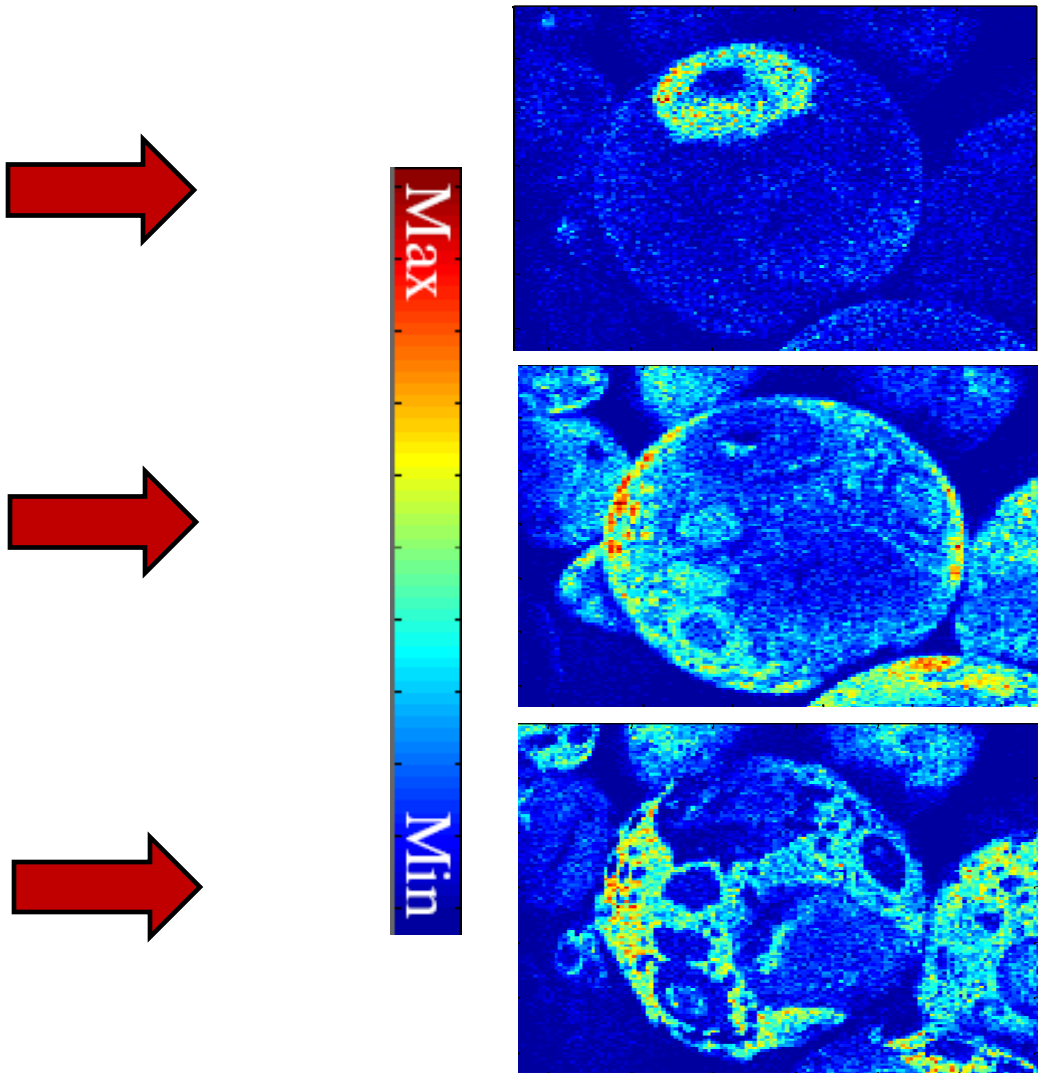
- Multivariate Curve Resolution (MCR), a type of multivariate data analysis, was applied to the microsphere **ToF-SIMS** chemical data to help identify the pure components in the multicomponent system.

- This analysis was undertaken in addition to testing reference samples of the individual components.

COMPONENT IDENTIFICATION

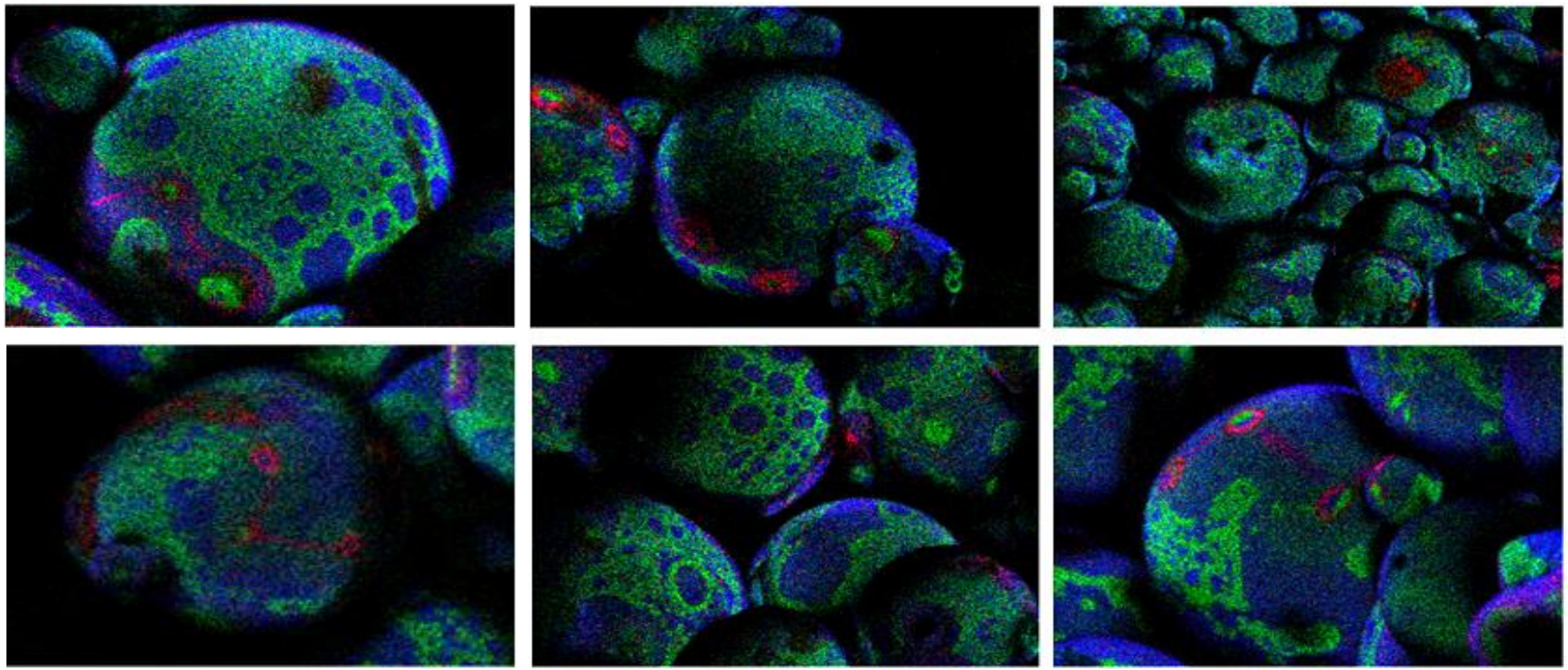
Component Distributions (by MCR)





ToF-SIMS SURFACE CHEMICAL IMAGING

Green – PLGA
Blue – PVA
Red – Lysozyme



- ToF-SIMS mapping shows a discontinuous PVA surfactant layer.
- Insufficient stabilisation of the microspheres leads to presence of surface pores.
- Majority of lysozyme observed surrounding these pores – Leading to a **burst** release.
- Secondarily localised to pore walls – Leading to **slower** release.

CONFOCAL RAMAN SPECTROSCOPY

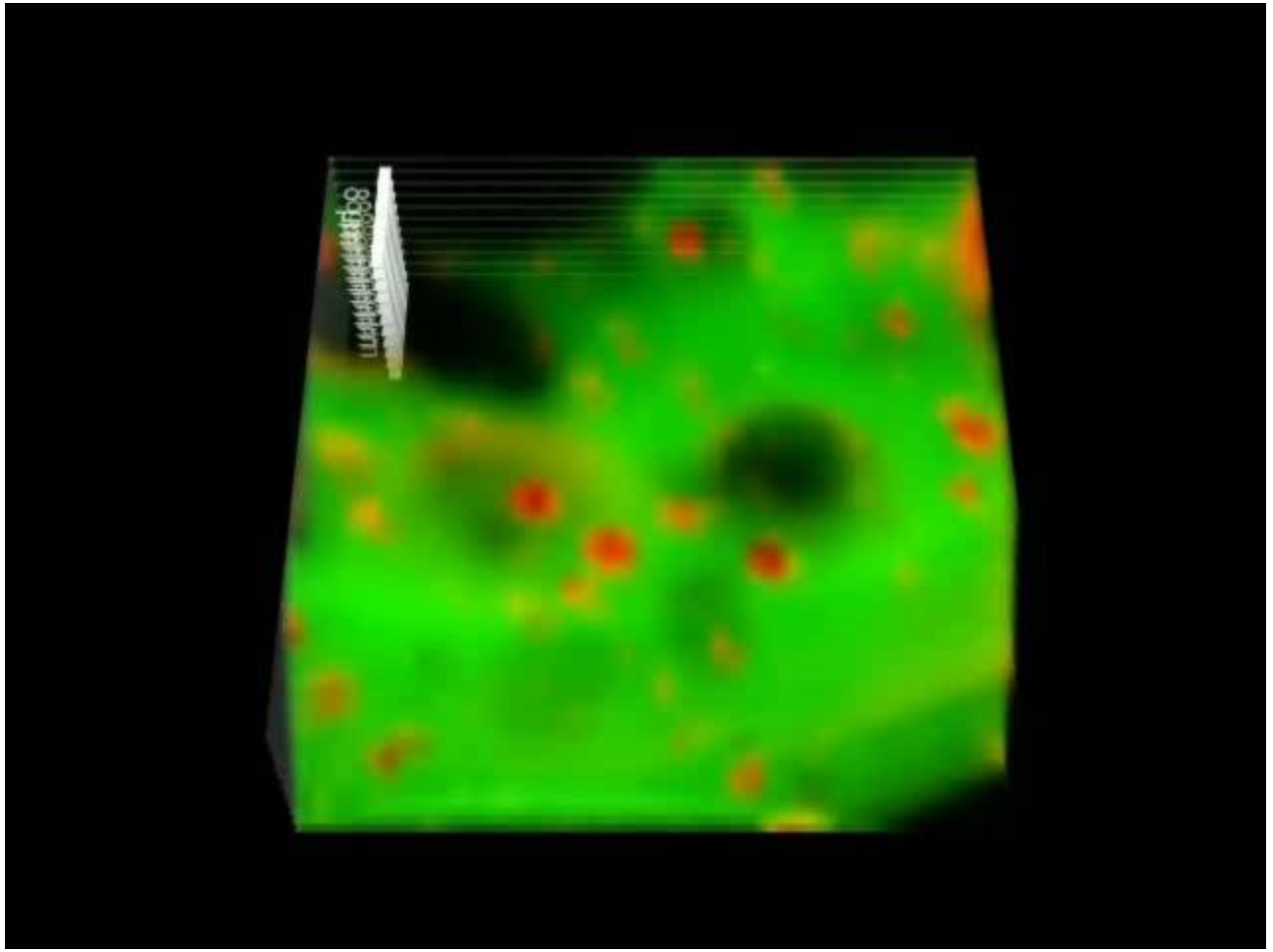
3D Localisation of Components

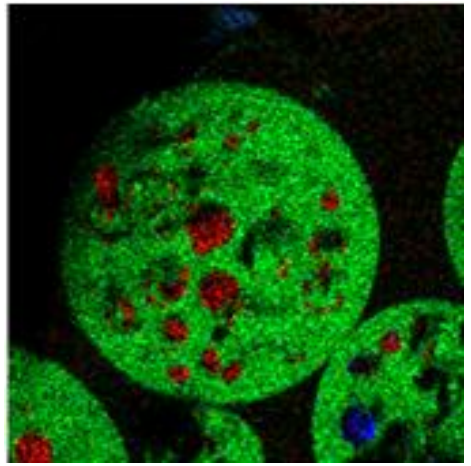
Green – PLGA

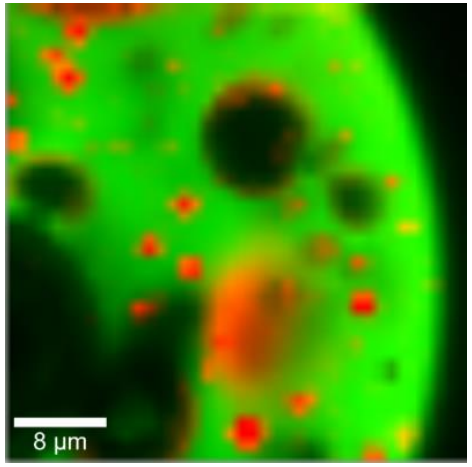
Red – Lysozyme

Video

Click to play



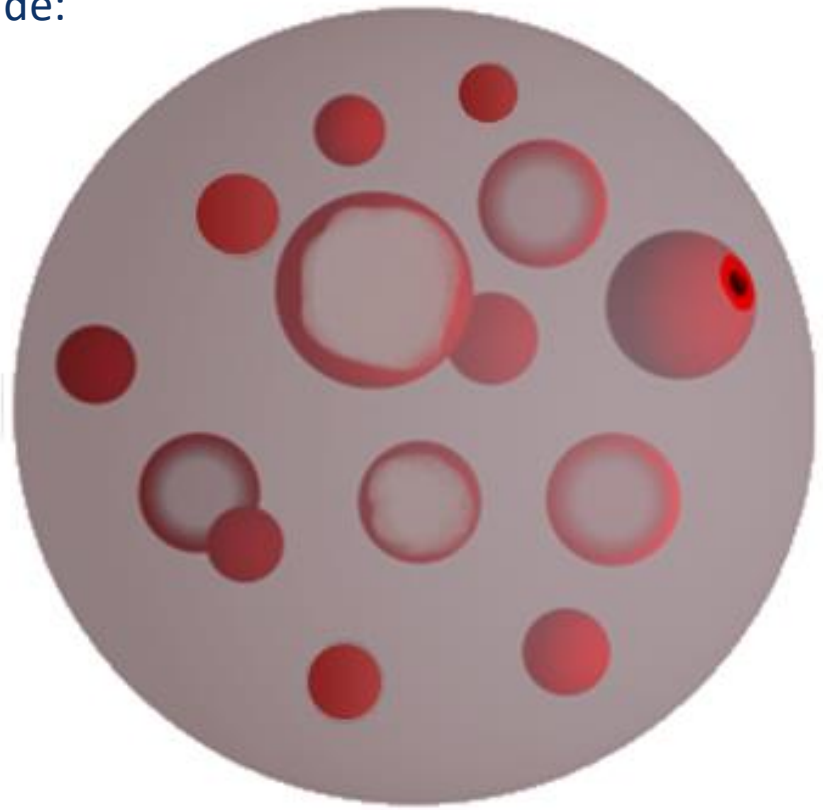




Note: Video disabled in pdf version

CONCLUSIONS

- The bulk analysis of the microspheres by confocal Raman spectroscopy clearly outlines the composition of the microspheres
- The combination of characterisation techniques employed on these microspheres allows for a schematic for the distribution of components to be made:



CONCLUSIONS

- Combinations of materials characterisation techniques can generate a wealth of complementary information critical to the understanding sample behaviours that is not available to one technique alone.
- ToF-SIMS and Raman spectroscopy were successfully used to describe the surface and 3D chemical distribution of the surfactant and protein components of a micro particulate formulation.
- AFM and SEM were used in conjunction with ToF-SIMS to confirm the existance of a 4.5 nm thick overlayer of surfactant (not just a surface feature of PLGA).
- In combination this information together helped explain the development of a 2 phase release profile.

REFERENCES & ACKNOWLEDGEMENTS

For more details on the work showcased in this case study see the following publication:

A.Rafati et al. Chemical and spatial analysis of protein loaded PLGA microspheres for drug delivery applications. Journal of Controlled Release. 162 (2012) 321-329

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ADDITIONAL INFORMATION

- We hope the information provided in this case study is of interest.
- If you wish to get in touch with us to discuss any of the information provided, raise a query/concern or provide feedback then please use any of the methods listed below:

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