INDUSTRIAL PILOT PROJECT

Probing dynamic processes in freeze-drying of probiotic lactobacilli using in-situ neutron scattering and imaging

THE INDUSTRIAL CHALLENGE

Freeze-drying is an important process in many industries, particularly in life sciences, where dry products are necessary to obtain a long product shelf life. Sensitive biological structures such as probiotic bacteria can be preserved in a dry porous material obtained by freeze-drying. For BioGaia, it is essential to understand where water is located for both the material and the bacteria. It is also important to understand how the bacteria are influenced by drying and rehydration in order to improve product uniformity and shelf life.

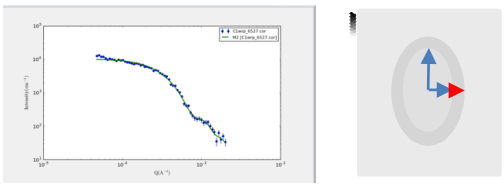

Figure 1. Modelling of the USANS data results in a core-shell structure, inidicating a thick hydrated shell around the water-filled center (cell).

WHY USING A LARGE SCALE FACILITY

While laboratory based Karl-Fischer titration can determine trace amounts of water in a sample, it gives no information on where in the sample the water is located. Neutrons are likely to be advantageous as they can identify where specific components occur in samples, such as the presence and location of water. Neutrons can measure the shape of objects and distinguish if objects, for example, have a core that is different from its shell. Neutrons can penetrate deep into samples and through the walls of containers suitable for freeze-drying. This suggests that ultra-small angle neutron scattering technique (USANS) in combination with imaging could give some useful answers.

HOW THE WORK WAS DONE

Due to the scheduled upgrade of ISIS Neutron and Muon Source, England, and the pandemic both test imaging measurements at ISIS and USANS measurements at the NIST Center for Neutron Research, USA, had to be performed remotely. Samples were prepared in deuterated and normal lyoprotectant and sent dry to both UK and USA for further preparation by the instrument scientist. Dr Winfried Kockelmann at ISIS and Dr Susana Teixeira at NIST are acknowledged for their skilful contributions to the performance of the experiments.

The team consisted of freeze-drying specialist from BioGaia, and the experts in neutron scattering techniques Dr Maja Hellsing (RISE) and Prof. Adrian Rennie at Uppsala University.

THE RESULTS AND EXPECTED IMPACT

The imaging measurements performed provided an overall image of water location in the freeze-dried cake, while the USANS measurements explored the size and shape of objects as well as determining any core-shell structure.

The next step will be to design and make a purpose-built sample environment for both scattering and imaging instruments where one can do controlled drying under vacuum and simultaneously measure loss of mass.

Discussions with instrument-responsible personnel at neutron scattering facilities have proven very fruitful in finding suggestions for design of future experiments.

"We believe that the use of neutron-based techniques is the next step for gaining an even deeper understanding of our processes" / ***Sebastian Håkansson, Director Process R&D, BioGaia AB***

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