

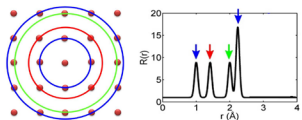


Advanced X-ray Characterizations for Medicine Manufacturing Products and Processes

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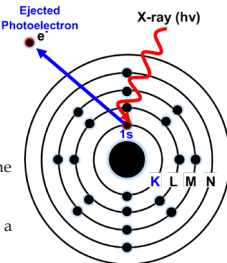
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X-ray Pair Distribution Function (XPDF)



- The PDF is the probability of finding an atom at any distance r from another atom. It is obtained by Fourier-transforming the total X-ray scattering pattern $S(Q)$.
- Provides local structure information, hence powerful for non-crystalline materials (amorphous, melts, solutions)
- Synchrotron radiation is required.

X-ray Photoelectron Spectroscopy (XPS)

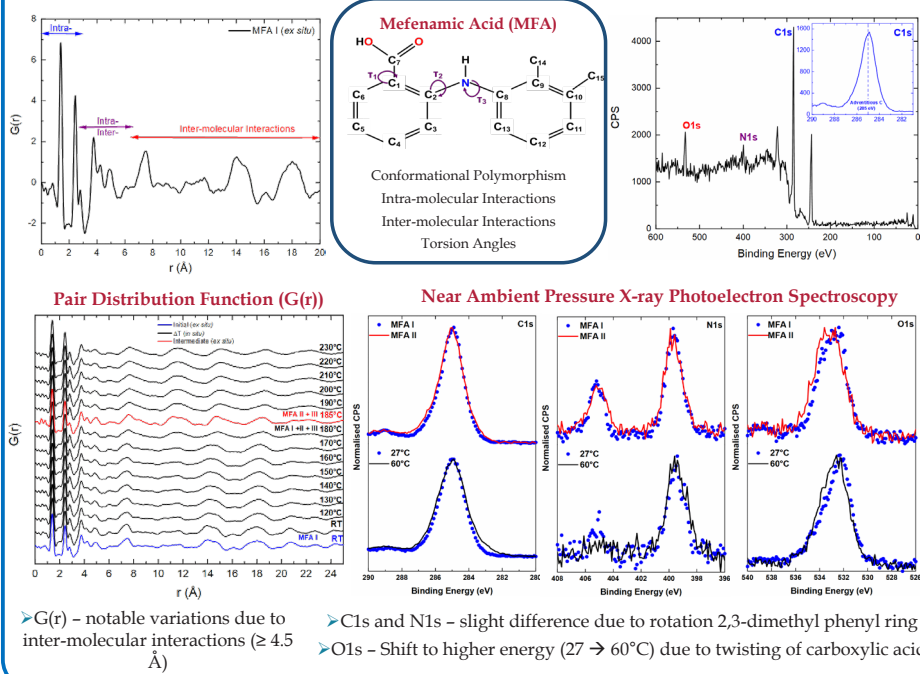


- Powerful Technique for analyzing local chemical interactions and surface chemistry.
- Determines elemental composition as well as the chemical and electronic state of the atoms within a material quantitatively.
- Both synchrotron and laboratory instruments.
- Conventional XPS restricted to ultra-high vacuum. Latest instruments operate near-ambient pressure

X-ray Phase Contrast Imaging (XPCI)

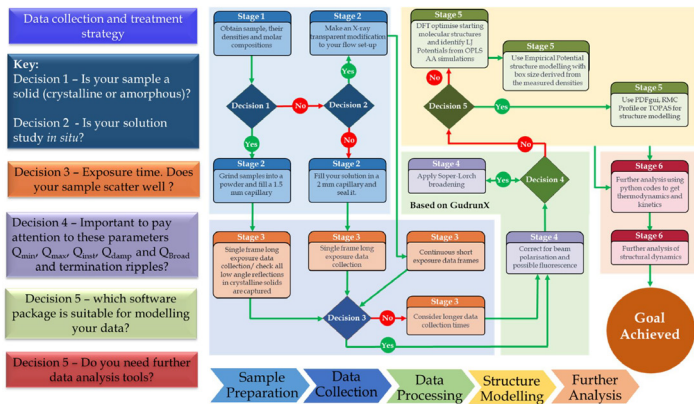
- Time-resolved XPCI can be applied to visualize several crystallization processes in real time
- Capable of visualising the sequence of events taking place in the mixing zone of an anti-solvent flow crystalliser.
- XPCI have been applied to reveal even more detail, as we extended this work to imaging filtration processes and extrusion products.
- Synchrotron radiation is required.

Conformational polymorphism established by XPDF and NAP XPS



- $G(r)$ - notable variations due to inter-molecular interactions ($\geq 4.5 \text{ \AA}$)
- C1s and N1s - slight difference due to rotation 2,3-dimethyl phenyl ring
- O1s - Shift to higher energy (27 \rightarrow 60°C) due to twisting of carboxylic acid

XPDF WORKFLOW



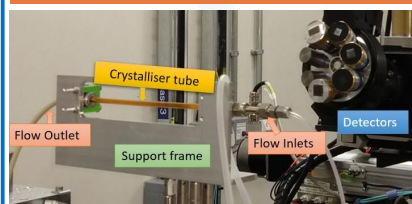
❖ XPS and XPCI workflows are being developed

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Collaborations in CMAC

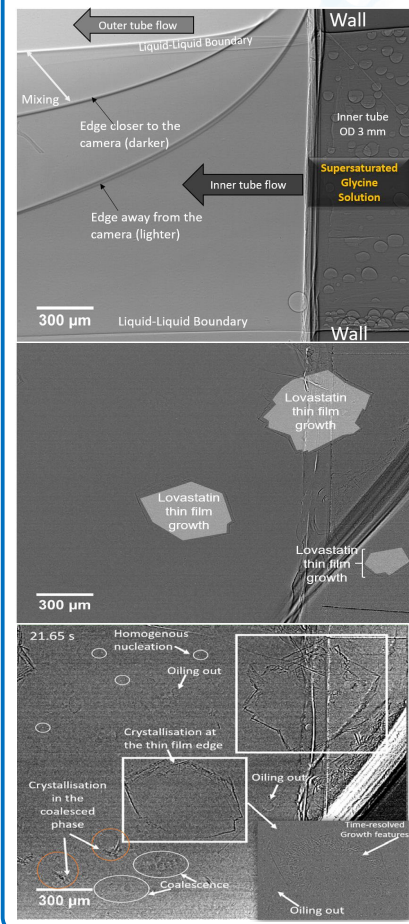
1. Continuous anti-solvent crystallisation (J Sefcik / J McGinty)
2. Twin screw extrudates (J Robertson / A Florence / G Halbert / E Prasad)
3. Powder particle compaction, breakage formulation (J Robertson / CM Torrecillas / E Bordo)
4. Filtration & Washing (C Price / S Ottoboni)

2D XPCI In-situ of Anti-solvent Crystallisation of Lovastatin



Schematic of the setup

Real time images of crystallisation



Acknowledgements

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