

Using XMT to Study Tablet Dissolution (Dr X Jia University of Leeds)

Introduction

X-ray Microtomography (XMT) operates on the same basic principles as X-ray CT scanners found in hospitals, but has a spatial resolution that is typically hundreds or more times higher. X-ray tomograms, (i.e., reconstructed slices through a scanned object) map the relative density distribution. Therefore, if the materials in the scanned object are known, the tomograms can be used to assess where different materials are in the structure. Tomograms can also be stacked to provide the 3D structure. ParticlesCIC is equipped with two XMT systems: SkyScan 1072 and Phoenix v|tomo|x Compact. With a maximum pixel resolution of 4 microns (for SkyScan) or better (less than 1 micron for Phoenix), XMT is an ideal non-destructive means to image microstructural features of materials.

Application

In many cases, simple statistics and visual inspection of the XMT tomograms are sufficient for engineers to make useful inferences or decisions; in other cases, obtaining the structure is only the first step towards predicting structure-related properties of interest. The diagram below (figure 1) illustrates tomogram of a cut-out of a tablet showing distribution of three main components for example.

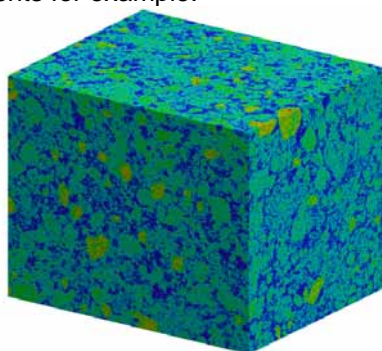


Figure 1: XMT tomogram of a pharmaceutical tablet showing the distribution of three main components

This case study illustrates steps taken to actually predict structure-related properties of tablets and its influence on drug dissolution.

With the advance of 3D structure characterisation techniques such as XMT, real structures of porous

media can now be scanned and reconstructed (Jia et al, 2005). Computer models of particle packing structures such as DigiPac (Jia and Williams, 2001) are also available to generate realistic packing structures. Both XMT and DigiPac give packing structures in digital volumetric format.

Granulation is a widely used method of production for granular products in the pharmaceutical industry. Granules produced in this manner are often agglomerates of finer particles. Their internal structures and distributions of different components affect the observed properties (e.g., dissolution, and mechanical strength) of the agglomerates. XMT is an ideal means to obtain the structural information (figure 2). On the left are the shadow X-ray image and some basic structural statistics along the line indicated in the image on the right, which is a cross-sectional slice through one of the scanned granules. The pseudo colours are used to indicate the relative density of the different regions in the agglomerate.

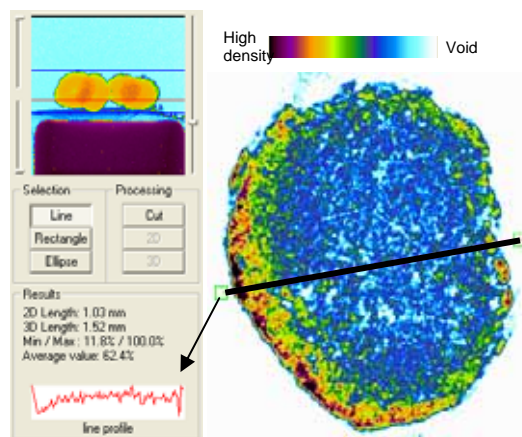


Figure 2: Shadow image and an example of cross-sectional slices of agglomerates

In order to create a software tool for the pharmaceutical industry to predict structure of tablets and its influence on drug dissolution, we must extract flow pathway information from our material. Figure 3 shows a 2D example of simulated flow distribution through a porous structure. Clearly, the majority of the fluid goes through a limited number of pathways and these

pathways can be extracted from the calculated flow pattern.

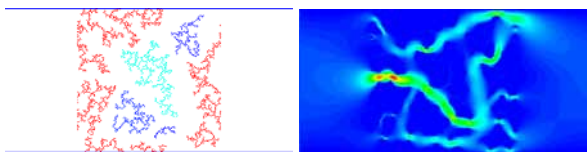
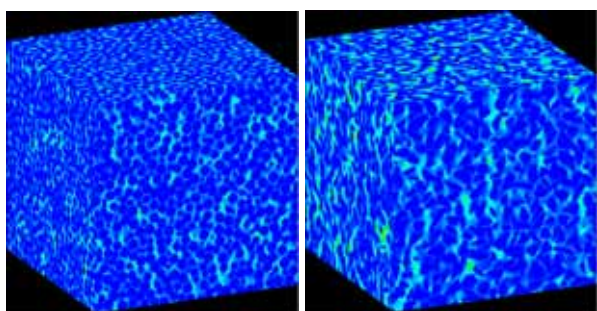


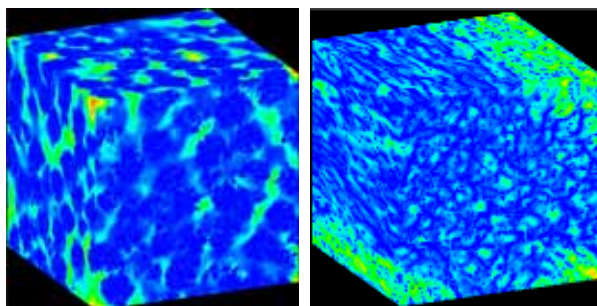
Figure 3: A 2D porous structure and LBM simulated flow distribution through it

Two dimensions may be extended to three, simulations have been performed to show flow pathways for four different packing structures (figure 4):



(a) Equal spheres

(b) Ternary mixture



(c) Random packing porous agglomerate

(d) Real foam

Figure 4: 3D rendering of simulated flow patterns through porous structures. Light areas indicate flow pathways and dark areas solids

The volume of flow active pores as a function of the percentage of the total flow rate is shown in figure 5 for each case. Due to non-uniformity of the flow, the curves bend downward, implying that a **high proportion of flow is carried by a small proportion of the flow active pores**. For

example, it can be seen from Figure 5 that for all cases 50% of the total flow is through only about 25% of the total pore volume.



Figure 5: Flow active pore volume versus its contribution to the total flow rate

Conclusion

XMT is a valuable tool to obtain microstructures non-destructively. As a relatively new technology – lab scale micro-focus XMT scanners only become commercially available 5 years ago and nano-focus scanners less than a year – it has already demonstrated its huge potential in various applications for field engineers and academics alike. Numerical techniques that can make full use of the detailed micro structural information are being developed and practical applications can be expected in the near future.

References

- Jia, X. & Williams, R. A., (2001), A packing algorithm for particles of arbitrary shapes, Powder Technol., 120, pp.175-186.
- Jia, X., Golchert, D. & Williams, R. A., (2005), Some applications of X-ray tomography in powder technology, presented at PSA2005, 21-23 September 2005, Stratford on Avon, UK.

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