Pair Distribution Functions of Amorphous Organic Thin Films from Synchrotron X-Ray Scattering in Transmission Mode

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ABSTRACT

Using high-brilliance, high-energy synchrotron x-ray radiation, we measured for the first time the total scattering of thin organic glass films deposited on a strongly scattering inorganic substrate in the transmission mode. The organic thin film was composed of the weakly scattering pharmaceutical substance indomethacin in the amorphous state. The film was 130 micron thick atop a borosilicate glass substrate of equal thickness. The atomic pair distribution function derived from the thin-film measurement is in excellent agreement with that from bulk measurements. This ability to measure the total scattering of amorphous organic thin films in transmission will enable accurate structural studies for a wide range of materials *in situ*.

The lack of long-range order in liquids and glasses makes their structural characterization more difficult than for crystalline materials. The determination of atomic pair-distribution function (PDF) from total scattering has long been an important tool for characterizing amorphous materials and a foundation for developing their structural models (Narten *et al.*, 1984, Benmore *et al.*, 2011). The accurate determination of PDFs requires a Fourier transform of the "total" scattering function, i.e., the scattering function that covers a sufficiently wide range of the momentum transfer, typically measured with high-energy X-ray available from a synchrotron source in the transmission geometry.

Amorphous organic thin films are essential for many advanced technologies. Organic Light Emitting Diodes (OLED), for example, consist of multiple layers formed by sequential physical vapor deposition. Determining the structure of these thin-film materials is required for optimizing their properties and performance. These thin-film materials, however, present great difficulties for the determination of their PDF because in the transmission geometry, scattering of the substrate typically dominates the total signal. This has limited x-ray scattering studies to the reflection mode (Dawson *et al.*, 2012), while for transmission measurements, the samples would have to be scraped off the substrate and accumulated before measurement, running the risk of destroying the original structure.

A solution to the problem of thin-film characterization is to take advantage of highly penetrating X-ray beams available at third-generation synchrotron facilities. To this end, Jensen *et al.* reported the first measurement for a strongly scattering $FeSb_3$ film 360 nm thick deposited on a 170 µm-thick borosilicate glass substrate [Jensen *et al.,* 2015]. Here in this short communication, we extend this technique to weakly scattering organic glass films. We report the first thin-film PDF measurement on the pharmaceutical substance indomethacin (IMC) in the amorphous state. The structure function and the PDFs extracted from thin-film measurement are in excellent agreement with those from bulk measurements. IMC is arguably the best studied amorphous pharmaceutical and an often-used model for molecular glasses (Bate *et al.*, 2006, Xiang *et al.,* 2013, Yuan *et al.,* 2015). The new capability developed here has the potential to advance structural characterization of similar organic materials.

A thin-film IMC sample was prepared by melting a crystalline powder (Alfa Aesar, Lot #: M19C065; gamma polymorph) between two silicate coverslips (Figure 1). The distance between the coverslips was controlled with spacers (small pieces of the same coverslip) to be 130 microns. The assembly was cooled by contact with an aluminum block at room temperature to produce a glass film of IMC. The top coverslip was removed prior to synchrotron X-ray experiment. The edges of the coverslip was taped to a custom made aluminum frame with a square opening (2 cm × 2 cm), which was then loaded to a goniometer head. In this work, the X-ray struck the film sample perpendicularly from the side of the coverslip. The X-ray that penetrated through the substrate was scattered by the IMC film and the scattered signal was detected by a 2D detector. If necessary, the film can be rotated about an axis perpendicular to the X-ray, as shown with the two-headed arrow, to interrogate potential anisotropies. For conventional bulk PDF measurements, crystalline or amorphous IMC was loaded into kapton capillary tubes with 0.0435"OD and 0.0395"ID (Cole-Parmer, EW-95820-09).

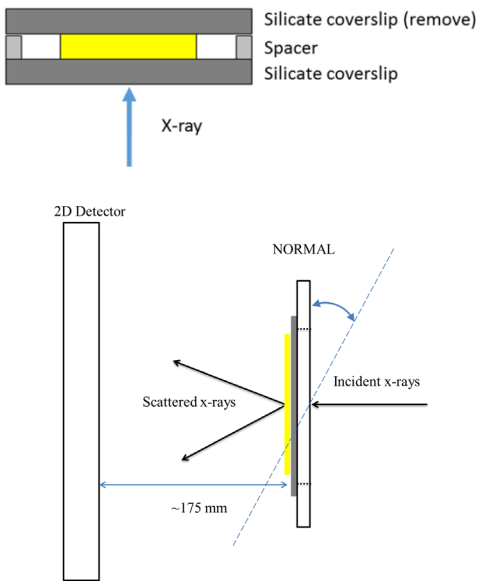

Figure 1: (a) Preparation of an IMC thin film. (b) Experimental setup for thin film X-ray scattering measurement in transmission. The sample can be rotated if necessary.

Synchrotron X-ray total scattering experiments were conducted on beamline 11-ID-B at the Advanced Photon Source (APS) at Argonne National Laboratory. All measurements were performed at room temperature. The rapid acquisition pair distribution function (RaPDF) technique (Chupas *et al.,* 2003) was used with an X-ray energy of 58.705 keV (λ = 0.2112 Å). A Perkin Elmer amorphous Si 2D image plate detector (2048 × 2048 pixels and 200 × 200 µm pixel size) was mounted orthogonal to the beam path with a sample-to-detector distance of ~175 mm. The raw 2D data were azimuthally integrated and converted to 1D intensity versus 2θ using FIT2D (Hammersley *et al.*, 1996). PDFgetX3 (Juhas *et al.*, 2013) was used to correct and

normalize the diffraction data and then Fourier transform them to obtain the PDF, $G(r)$. A value for Q_{max} of 22.5 Å^{-1} was used for all samples.

Figure 2a shows the representative data. Although the silicate substrate dominates the scattering pattern, signal from the organic thin film can be accurately detected. The sample signal amounts to ~11% of the total photon counts at maximum intensity. Subtracting the background from the total signal yielded the signal from the sample film (Figure 2b). Notice the excellent agreement between different runs, all with 10 min collection time, and between the results corresponding to different collection times (10 and 30 min). These results are indistinguishable at the scale displayed, indicating the robustness and feasibility of thin-film X-ray scattering measurements in transmission.

The raw diffraction intensities were corrected to remove background, Compton scattering and self scattering and obtain a coherent scattering intensity $I_c(Q)$ (Q is momentum transfer defined as $Q = 4\pi \sin\theta/\lambda$). A structure function S(Q) can be calculated via Equation 1

$$S(Q) = 1 + \frac{I_c(Q) - \langle f(Q)^2 \rangle}{\langle f(Q) \rangle^2} \quad (1)$$

Where <f(Q)> is the sum of the X-ray scattering form factors of all atoms in IMC weighted by their concentrations and <f(Q)²> is the sum of the X-ray scattering form factors squared of all atoms in IMC weighted by their concentrations. A reduced structure function F(Q), is further calculated via Equation 2.

$$F(Q) = Q[S(Q) - 1] \quad (2)$$

The PDF is obtained by a Fourier sine transform of F(Q) via Equation 3:

$$G_{exp}(r) = {}^{2}/_{\pi} \int_{Q_{min}}^{Q_{max}} F(Q) \sin Qr \, dQ \quad (3)$$

Experimental F(Q)s are shown in Figure 3. Notice the excellent agreement between the F(Q) obtained from the thin-film sample and the bulk sample (measured in Kapton tube using the same experimental setup). The bulk F(Q) has lower signal-to-noise ratio in the high Q range (>20 Å^{-1}), a result of both thicker sample in the beam path and lower scattering by the Kapton tube. Nevertheless, thin film samples still offered a large useable Q range up to 22.5 Å^{-1} for PDF calculations (see below).

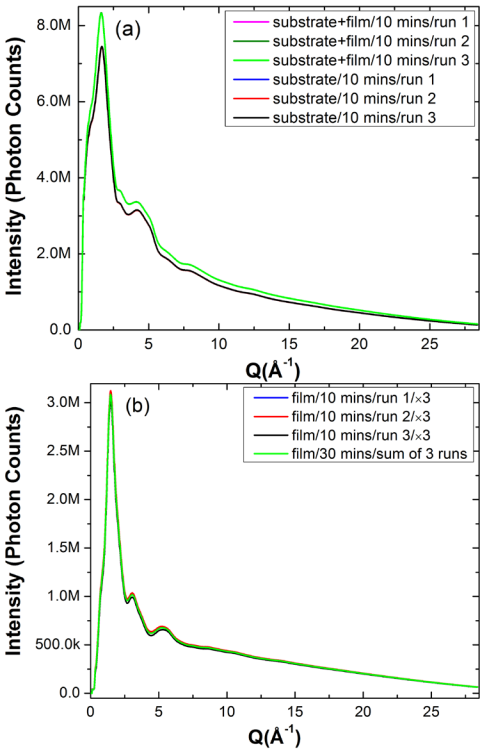

Figure 2. (a) Raw diffraction intensities for the thin film sample including the substrate and the substrate itself. (b) Diffraction intensities of thin film only from four independent measurements. The 10 min runs were scaled to compare with the 30 min run.

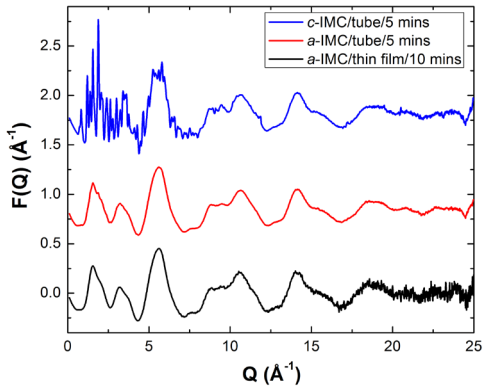

Figure 3. F(Q) of amorphous IMC obtained from thin-film and bulk measurements. For reference, the F(Q) of crystalline IMC (gamma polymorph) is also shown.

The F(Q) of amorphous IMC differs significantly from that of crystalline IMC (γ polymorph), as expected. The latter features sharp Bragg peaks at low Q. Notice, however, the agreement between the F(Q) functions of the crystalline and amorphous samples above Q~7 Å^{-1}. Given that this region is dominated by intramolecular correlations, the agreement indicates that indomethacin has similar molecular conformations in the crystalline and amorphous states.

Figure 4 shows the PDF of amorphous IMC calculated from the thin-film F(Q). This calculation used a Q_{min} of 0.1 Å^{-1} and Q_{max} of 22.5 Å^{-1}, see Equation 3. We find that the PDF computed from the F(Q) of the thin-film sample has an excellent agreement with that from the F(Q) of the bulk sample, also shown in Figure 4. To quantify the similarity between both *a*-IMC PDFs, a Pearson product-moment correlation is often used where a value of 1 implies a complete correlation while -1 an anti-correlation. A Pearson correlation coefficient of 0.9937 is calculated for both curves from 0 to 80 Å. This agreement, again, validates the thin-film method for determining the PDF.

Figure 4 also includes the PDF of crystalline IMC. The oscillations persist up to ~80 Å, demonstrating the Q-resolution limit at current PDF experimental setting. The amorphous PDF signals, on the other hand, vanish at a much smaller

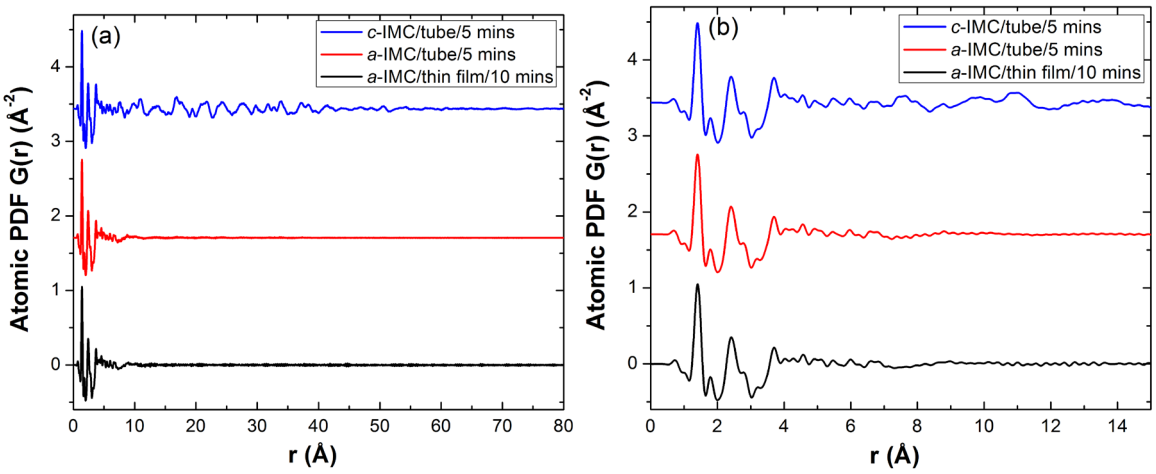

Figure 4. PDFs of crystalline and amorphous IMC plotted in a *r*-range up to 80 Å (a) and 20 Å (b). The measured crystalline PDF is also plotted as a reference.

radial distance (~12 Å). It is evident that the amorphous and crystalline structures have very similar PDFs at short distances (< 3.5 Å), as expected from their similar F(Q) functions at high Q values. This agreement indicates that the molecular structures in crystalline and amorphous IMC are similar.

In summary, this work has demonstrated that by taking advantage of the high-brilliance, high-energy synchrotron x-ray radiation, it is possible to measure the total scattering of a thin organic glass film supported on a strongly scattering substrate in the transmission mode and thus determine its atomic pair-distribution function. For an indomethacin (IMC) film 130 micron thick on a borosilicate glass substrate of equal thickness, a ten minute measurement time is sufficient. The thin-film PDF is in excellent agreement with the PDF obtained for a bulk sample. With minimal optimization of the current procedure and longer integration, we expect that total-scattering measurements are possible in the transmission mode for supported weakly scattering organic thin films that are sub-micrometer thick. This ability will enable structural studies of a wide range of organic materials prepared as supported films, including ultra-stable organic glasses by physical vapor deposition (Swallen *et al.,* 2007).

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DISCLOSURE

AbbVie and University of Wisconsin-Madison jointly participated in study design, research, data collection, analysis and interpretation of data, writing, reviewing, and approving the publication. Rattavut Teerakapibal is a graduate student at University of Wisconsin-Madison; Lian Yu is a professor at University of Wisconsin-Madison. They have no additional conflicts of interest to report. Chenyang Shi and Geoff G. Z. Zhang are employees of AbbVie and may own AbbVie stock.

REFERENCES

Narten, A. H. & Habenschuss A. (1984). *J. Chem. Phys*. **80(7)**, 3387-3391.

Benmore, C. J. &Weber, J. K. R. (2011). *Phys. Rev. X*. **1**, 011004-(1-7).

Dawson, K., Kopff, L. A., Zhu, L., McMahon, R. J., Yu, L., Richert, R. & Ediger, M. D. (2012). *J. Chem. Phys*. **136**, 094505 (1-11).

Jensen, K. M. Ø., Blichfeld A. B., Bauers S. R., Wood S. R., Dooryhée E., Johnson D.C., Iversen B. B. & Billinge S. J. L. (2015). *IUCrJ*. **2**, 481-489.

Bates S., Zografi G., Engers D., Morris K., Crowley K. & Newman A. (2006). *Pharm. Res.* **23**, 2333-2349.

Xiang, T. X. &Anderson, (2013). *Mol. Pharm*. **10 (1)**, 102–114.

Yuan X., Xiang T., Anderson B. D. & Munson E. (2015). *Mol. Pharm.* **12**, 4518-4528.

Chupas, P. J., Qiu, X. Y., Hanson, J. C., Lee, P. L., Grey, C. P. & Billinge, S. J. L. (2003). *J. Appl. Cryst.* **36**, 1342-1347.

Hammersley, A. P., Svensson, S. O., Hanfland, M., Fitch, A. N. & Hausermann, D. (1996). *High Pressure Res.* **14**, 235-248.
Juhas, P., Davis, T., Farrow, C. L. & Billinge, S. J. L. (2013). *J. Appl. Cryst.* **46**, 560–566.
Swallen, S., Kearns, K., Mapes, M., McMahon, R., Kim, S., Ediger, M., Yu, L., Wu, T. & Satija, S. (2007). *Science*, **315**, 353 – 356.