Commission on Small-angle Scattering

CURRENT HIGHLIGHTS AND FUTURE TRENDS IN SMALL-ANGLE SCATTERING

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Abstract

This paper presents a short topical review highlighting some of the current advances in small-angle X-ray and neutron scattering (SAXS and SANS) studies. These advances encompass studies in biological small-angle scattering (bioSAS), porous materials, alloys, soft matter, magnetically ordered phenomena studied using magnetic SANS techniques, as well as SAXS, and surface structure studies using grazing-incidence small-angle X-ray scattering (GI-SAXS), as well as surface-sensitive SANS methods. Some important future trends are also identified where relevant.

Introduction

Small-angle scattering (SAS) was born in the 1950s when Guinier and others developed laboratory-based small-angle X-ray scattering (SAXS) methods to characterize material microstructures. This is of course based on the scattering intensity profile, as a function of scattering angle, being related to a material's internal microstructure via an inverse Fourier sine transform [1]. From the mid-1960s onwards, and particularly after the development of cold-neutron facilities in the 1970s [2], long-wavelength small-angle neutron scattering (SANS) instruments became available at neutron research reactors. From the late 1980s, SANS instruments were also developed at major pulsed neutron sources [3] using both short-wavelength and long-wavelength neutrons. Meanwhile, from the 1980s, powerful SAXS instruments were developed at the major X-ray synchrotron facilities [4]. In parallel with conventional geometry SAS instruments, both SAXS and SANS have benefitted from the development of Bonse-Hart [5,6] ultrasmall-angle X-ray and neutron scattering (USAXS and USANS) instrumentation to extend the microstructure characterization into the micrometer-scale regime. Indeed, at the major X-ray and neutron facilities, SAXS and SANS now provide microstructure characterization routinely over length scales from below one nanometer to several micrometers. Although traditional SAS measurements employ a transmission geometry for microstructure characterization representative of the bulk sample, reflection geometry measurements have also been developed and grazing-incidence SAXS (GI-SAXS), in particular, [7] has become a standard method for surface and near-surface characterization. Especially over the last 25 years, SAXS and SANS have become indispensable characterization tools relevant to research issues in materials, chemistry and biology, as well as providing critical microstructural information complementing other crystallographic investigations based on powder diffraction and X-ray or neutron scattering. Over that time SAS-related publications in the literature have increased dramatically by five times or more, and this trend has been reflected both in participation in the triennial International Conferences on Small-Angle Scattering, and in the number of SAS-related microsymposia and talks presented at the triennial Congresses of the International Union of Crystallography (IUCr).

Recent years have seen two important and continuing trends in SAS development. Firstly, increased fluxes and innovative instrument designs at the major X-ray and neutron facilities [8,9] have resulted in much faster data collection times, permitting real-time studies of material processes with time-resolution not previously considered possible. Secondly, in common with other crystallographic methods, the combination of SAS measurements with other measurements such as wide-angle X-ray scattering (WAXS), X-ray or neutron diffraction (XRD, ND), or even X-ray or neutron imaging, in rapid measurement sequence, has enabled materials microstructure characterization to start to be supplanted by materials process characterization [10]. Increasingly, SAS is being used as an integral part of real-time materials process or materials phenomena characterization, such as may be relevant to catalysed chemical reactions, nanoparticle formation or dissolution, degradation or precipitation phenomena in alloys, etc. As well as requiring the integrated application of multiple measurement methods, both crystallographic and non-crystallographic, such efforts also place strong demands on the development of increasingly sophisticated structural and microstructural models capable of predicting the diffraction and scattering data obtained in such studies. This trend has extended to biological applications of SAS (bioSAS), and to surface science, where bioSAS solution scattering methods are increasingly being used to provide macromolecular structural envelope information to accompany protein crystallography data destined for the worldwide Protein Data Bank (wwPDB) [11].

In the sections that follow, we highlight important developments in SAXS and SANS within the past 5 years or so, and try to anticipate where future trends are leading. Specifically, we cover studies in biological small-angle scattering (bioSAS), porous materials, alloys, soft matter, magnetically ordered phenomena studied using magnetic SANS techniques, and surface structure studies using GI-SAXS.

Biological small-angle scattering (bioSAS)

The increasingly ambitious and extensive application of bioSAS methods to support protein crystallography in particular, and to macromolecular research in biology, in general, continues without any slowing of pace. The ***complementarity of SAS with other structural biology approaches and methods*** remains a significant present and future focus. For example [12], the conformational plasticity of disordered protein molecules hampers application of more traditional structural methods. In this connection, the low-resolution of bioSAS can be compensated for with computational tools and interpretation of bioSAS data can be supported with complementary structural information. In such studies it is critical that interpretative SAS models are developed and made readily available. There needs to be a mix of capabilities [13]: to model atomic structures based on SAXS profiles, to compute a SAXS profile of a given atomistic model, to compute (and fit) the SAXS profile of docked pairs of rigid protein structures, as well as to treat other more complex situations.

Consideration of the dynamics and non-equilibrium conditions for biological systems, leads to an extension of the above theme into ***solution scattering and combined techniques for complex biological systems, including component dynamics***. In this connection, it is important to focus on clarifying aspects such as the equilibrium between association and dissociation of multiple biomacromolecules, as well as the dynamics within each biomacromolecule. Clarification of the solution structure and its modu -lation in proteins and protein complexes is crucially important for understanding the dynamical ordering that exists in macromolecular systems [14]. Recent progress in sample preparation, instrumentation and software is opening up a new era for bioSAS in this area, and the potential of molecular dynamics (MD) simulations to elucidate the dynamics of complex biological systems, in combination with time-dependent bioSAS data, is emerging as an important trend for the future [15].

Staying in the general area of solution scattering, another current important focus lies in: ***bioSAS: membrane proteins, disordered and partly disordered systems***. In principle, bioSANS provides the advantage of H_2O/D_2O contrast variation to identify components within the protein complex while bioSAXS provides excellent signal-to-noise ratio and fast counting times. Used together with techniques such as size-exclusion chromatography to avoid aggregation and degradation issues, much progress has been made, for example, in investigating complex samples of membrane proteins embedded in nanodisk particles consisting of both phospholipid and protein components [16]. Important methods that complement bioSAS in this area include cryo-electron microscopy (cryoEM), emerging free-electron laser (FEL) capabilities, and general advances in serial crystallography. In this way, many new insights are now being gained into challenging biological problems associated with membrane proteins and partially disordered biological systems.

Departing somewhat from the above themes, another major focus for biology comprises ***hierarchical biological materials***. Biological systems have evolved complex and interdependent structures that are organised over many length scales, and small angle scattering is an important tool to understand how molecules at each of these length scales interact. The implications of being able to predict and control these assemblies reach into studies of pathology, origins of life, and the development of advanced biomaterials. Playing to one of the strengths of modern SAXS and SANS instruments at major facilities whereby data are obtained across many length-scales rapidly and almost simultaneously, real-time *in situ* studies are now feasible for important self-assembly processes. These include, for example, studies of hierarchical self-assembly processes for cyclic peptide proteins assembling into nanotubes, and characterization of the evolution of their gelation properties [17].

Data and model validation, as well as data archiving, comprise an area of major concern to the bioSAS research community, in part, as already mentioned, due to the increasing relevance of bioSAS results to the wwPDB [11]. More generally, there is significant current interest in ***advances in data and model validation in bioSAS: impacts on data and metadata recording and data archiving***. Certainly, for bioSAS to contribute maximally to the field, it is essential to ensure open access to the information required for evaluation of the quality of SAS samples and data, as well as the validity of bioSAS-based structural models. It is also essential to develop software that takes into account the hydration layer around solvated biological molecules during *ab initio* restorations of low-resolution molecular envelopes from both bioSAXS and bioSANS data [18]. Major international discussion and workshops will continue to be needed to address this issue over coming years.

Small-angle scattering for materials science, chemistry and industrial applications

While much overlap now exists between biological and non-biological applications of SAXS and SANS, many areas of bio- and non-bio-application remain significantly different partly, perhaps, because the complex microstructure elements in bioSAS remain, for the most part, monodispersed. For non-biological SAS, by contrast, there is almost always some significant dispersity in the shape and size of the scattering features. Partly due to this polydispersity, ambiguities can occur regarding the interpretation of SAS data from multi-component systems, thus requiring an integrated approach combining SAS with other methods. One such area of current focus can be summed up as: ***evolution of phase morphology and distribution upon phase interactions and crystallization: integrative and time-resolved observations with SANS, SAXS/WAXS, TEM, electron diffraction, and optical spectroscopes***. In this connection, possible interactions among coexistent phases and corresponding impacts on the evolution of the phase morphology, distribution, and size, need to be considered. While barely understood currently, these could provide important new insights on ordering behaviours. The ability to evolve desired phase distributions and morphologies would help resolve bottlenecks for complex materials applications in many fields, but most specifically perhaps in the area of polymer and soft-matter physics [19, 20].

In the area of materials science and hard materials, a major current interest is to combine ***small- and wide-angle scattering for industrial materials far from equilibrium***. For example [21], rapidly growing applications of 3D printing (additive manufacturing) and similar near-net-shape manufacturing methods result in complex microstructures far from equilibrium. This raises challenges in their optimization for application – be it in the as-built condition or after required post-processing steps have been completed. Many microstructures are metastable and follow unpredictable paths during post-processing, severely limiting application of computer models as the preferred method of optimization. In this connection, SAXS, SANS and diffraction studies of these complex materials, ideally in combination, can deliver critically important, quantitative data. We recognize that hard X-ray FELs will play an increasingly important role in this area due to their rapid data collection rates and fast time resolution properties [22].

Both SAXS and SANS have steadily expanded into commercial applications in a range of industries (as already apparent in some of the areas presented above). However, in recent years, a more focussed interest has developed regarding ***integrative small- and wide-angle scattering for customized commercial and medical products***. This can involve a detailed in-depth commercial (even proprietary) collaboration, harnessing SAXS, SANS, diffraction and non-crystallographic methods, among industrial companies, universities and publicly funded major (X-ray or neutron) facilities. Such studies that are published in the open literature [23] indicate tightly coordinated measurements using the various multiple measurement techniques, as well as modelling and theory, to achieve a focussed (and complete) result.

Magnetic phenomena have always been an area of interest for both SAS and other diffraction-based studies. Specifically, ***advances in magnetism enabled by small-angle scattering*** have been striking in the last few years – especially with regard to ferrofluids, spin texture and skyrmions. For example [24], SANS measurements on a bulk single crystal can reveal a pronounced effect of the magnetic history and cooling rates on the magnetic phase diagram. While SANS methods tend to dominate this area, there is also an ongoing role for fast time-resolution SAXS measurements relevant to ferroelastic and ferroelectric device applications [25]. Such SAS studies will continue to increase in the coming years with anticipated major advances in the devices that will be made possible.

Surface science and GI-SAXS

GI-SAXS methods, using a surface-scattering geometry rather than a bulk-sample transmission geometry, have been of continuing interest for many years. A recent highlight has been in the use of ***integrative methodologies for novel thin film structures*** analyses. There is currently a major interest in creative strategies for the development and encompassing characterization of novel thin film structures. This combines structural and application-relevant aspects, and includes, e.g., complementary *in situ* and real-time characterization during deposition and processing (e.g. by surface-sensitive x-ray, neutron, or electron scattering and spectroscopy methods), and efficient screening approaches for large material libraries. Current thin film structures of interest include those relevant to both biological (e.g., drug-eluting substrates) [26] and non-biological applications (e.g., deposition of nanoscale metallic films) [27]. For many studies of thin film structures, GI-SAXS or surface-sensitive SANS must be combined with reflectivity and surface diffraction measurements to build a complete picture, but new design routes can then be opened up for tailoring nanoscale devices.

Concluding remarks

In this short topical review we have highlighted some of the most interesting current advances in SAS studies, and pointed to some future trends that are becoming apparent. All of the highlighted areas deserve major international dissemination and discussion at the present time to stimulate and enhance future developments. If there is one area that deserves singling out as representing the state-of-the-art it is probably that focussing on “evolution of phase morphology and distribution upon phase interactions and crystallization: integrative and time-resolved observations with SANS, SAXS/WAXS, TEM, electron diffraction, … and other methods”. Aspects of almost all other areas described are brought together here, with distinguished researchers providing world-class research leadership in an exciting field [19, 20, 28].

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