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Editorial

State-of-the Art Research in Biomolecular Crystals

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This special issue, State-of-the Art Investigations on Biomolecular Crystals, is focused on strategies to procure suitable crystals for high-resolution X-ray crystallographic investigations [1,2] from experimental methods related to the use of different biomolecules for applications in biomedical sciences or bioinorganic chemistry [3]. The structure of these biomolecules, performed by X-ray diffraction, even using synchrotron radiation, combines different applications of peptides, proteins, and DNAs crystals in medicine, biology and in materials science. These techniques, employing the use of synchrotron facilities, will mold a new kind of future protein crystallographers trained in using novel software with big data recorded. Additionally, the tools for manipulating micro or nanocrystals are completely new and will also be included in this special issue.

X-rays, electron, and neutron diffraction techniques have been the most ubiquitously used strategies to obtain the structural elucidation of biomolecules and biomacromolecular complexes. Recently, with the development of synchrotron facilities, we necessitate smaller sizes of crystals progressing from microns to picometers. Exposing biological cryo-protected crystals to the X-ray intensity in a shorter time, combined with the use of highly efficient photon detectors, diminishes radiation damage. However, the use of small angle X-ray scattering techniques (SAXS) has developed into an extremely popular method for obtaining the structural envelope in solution for any biological macromolecule, where the structure is arduous to be solved due to the necessity of crystals [1,3]. Nuclear magnetic resonance (NMR) was also extremely popular in the 90s (of the previous century) for obtaining protein structures in solution, although with a limitation in the molecular weight (MW). This limitation weight occurred because the larger the MW, the lower the possibility to procure the structure at very high resolution (the one-dimensional or two-dimensional NMR spectra are much more multifactorial with regards interpretation) [4]. X-ray crystallography is nowadays not only the principal method, but it also the most puissant method, for obtaining three-dimensional structures of macromolecules at a very high resolution, independently of their molecular weight. Particularly, in the classical crystallographic approach, X-ray diffraction necessitates high-quality single crystals for high resolution. We must take into consideration that possessing beautiful crystals does not necessarily signify that we will procure high-resolution structures in merely a few steps. Occasionally, ugly-shaped crystals, which are internally well structured, produce the appropriate X-ray patterns to solve the three-dimensional structure at excellent resolution. Currently, the existence of other methods to obtain the three-dimensional structure of any biological macromolecule from the investigations on nucleation up to the crystal growth have make it plausible to labor in the direct space, such as the case with cryo-electron microscopy (cryo-EM) or reciprocal space when using the classic X-ray crystallographic approaches [5]. The other possibility will be the use of linear synchrotrons of the fourth generation such as the XFEL, where the data collection does not strictly necessitate any type of high-quality or large crystals but, rather, highly pure proteins, nucleic acids or macromolecular complexes in solution are needed. We can employ even a few microliters of a viscous dispersion of micro and nanocrystals for injection bypassing through the pulses of high energy to obtain the three-dimensional structure of any biomolecule before it is destroyed [6,7].

Citation: Moreno, A. State-of-the Art Research in Biomolecular Crystals. *Crystals* **2023**, *13*, 58. https://doi.org/10.3390/cryst13010058

Received: 16 December 2022
Revised: 16 December 2022
Accepted: 23 December 2022
Published: 29 December 2022

Besides these techniques for obtaining the three-dimensional structure of a variety of proteins, nucleic acids or polysaccharides, as well as their complexes, there is a want of physicochemical mechanisms in crystal formation and protein–protein interactions (based on pH, temperature, or ionic strength). The significance of the crystal quality [8–10], the presence of impurities [11], the insights into the crystallization process from protein nucleation phenomena, crystallization, and crystal growth peculiarities are important topics for review [12]. The existence of polymorphs is another research topic that deserves to be investigated in detail for crystals of biological macromolecules [13]. The use of specific crystallization agents or organic polymers, such as poly-ethylene glycols (400–20,000 MW) and their interaction with proteins, will be discussed in one of the contributions associated with this special issue. The measurements of the crystal growth rate, either on Earth or in microgravity, have recently shown interesting information in terms of crystal quality and mechanisms of crystal growth [14].

The main intention of the the state-of-the art in biomolecular crystals was to present a collection of papers where diverse applications of crystals were investigated. The first group is dedicated to biomedical applications for Parkinson's disease [15,16]; the second group is concerned with the application of crystals for basic research, combining organic (DNA) and inorganic crystals (silica carbonate biomorphs of Ba^{2+}) [17]; theoretical models using PEGs for protein crystallization [18] and the importance of polymorphs are also considered [19]. The third group deals with crystal fracture breakage [20], cross-linked enzyme crystals [21], stabilization of DNA-Protein co-crystals [22], biotechnological approaches using the amidase process [23] and binding of covalent inhibitors, and reversible ligands and substrates [24].

We hope that this collection of papers for this special issue will inspire a plethora of publications regarding these trending topics soon.

Funding: The author is thankful to DGAPA-UNAM for the financial support (grant number IN207922), which, to some extent, has facilitated him towards being guest editor of this Special Issue.

Acknowledgments: The author acknowledges the support from DGAPA-UNAM, project IN207922, for the support regarding the crystallization and structural investigations on human transferrins mentioned in this work and for using SAXS methods. Additionally, the author thanks MDPI editor for their help and professional support concerning the design and completion of this special issue.

Conflicts of Interest: The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

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