Immersive Analysis of Crystallographic Diffraction Data

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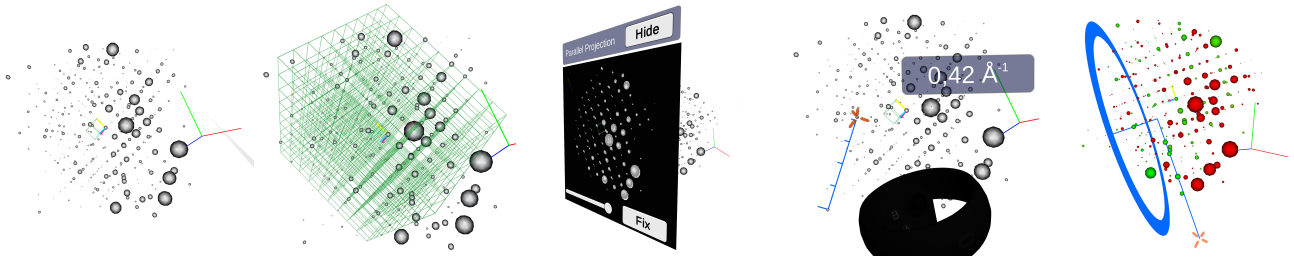

Figure 1: Overview of the immersive analysis of crystallographic diffraction data in reciprocal space. (a) Visualization: Reflections (spheres; size proportional to intensity), unit cell (center; yellow, cyan, magenta), and orthogonal space axis (right; red, green, blue). (b) Reciprocal lattice (green). (c) Orthographic projection to further assist spatial interpretation. (d) Distance measurement. (e) Indexing: Matching a periodic set of diffraction planes to reflections (red: disaligned, green: closely aligned).

ABSTRACT

Single crystal structure determination is the foremost method to determine atomic structures – from minerals to viruses. However, it is a complex process in which errors do not only lead to flawed structures, but may also hinder structure solution entirely. Many of these errors can be recognized by visualizing the measured diffraction data in reciprocal space. Here, we present an immersive tool to support such an analysis. We aim to supplement this traditionally 2D desktop-based investigation of 3D diffraction data with the strengths of immersive visualization, especially depth perception and spatially tracked input devices.

CCS CONCEPTS

• **Human-centered computing** → **Visualization systems and tools**; • **Applied computing** → **Life and medical sciences**.

KEYWORDS

crystallography, reciprocal space, atomic structure solution, scientific visualization, immersive visualization

VRST '20, November 1–4, 2020, Virtual Event, Canada

ACM ISBN 978-1-4503-7619-8/20/11.
https://doi.org/10.1145/3385956.3422097

ACM Reference Format:
Andreas Knote, Sebastian von Mammen, YunYun Gao, and Andrea Thorn. 2020. Immersive Analysis of Crystallographic Diffraction Data . In *26th ACM Symposium on Virtual Reality Software and Technology (VRST '20), November 1–4, 2020, Virtual Event, Canada.* ACM, New York, NY, USA, 3 pages. https://doi.org/10.1145/3385956.3422097

1 INTRODUCTION

X-ray crystallography is the foremost method to determine molecular structures. As a crystal is irradiated with X-rays, diffraction patterns captured with a detector can be used to determine the crystal's atomic structure. In these diffraction patterns, points of constructive interference called *spots* or *reflections* correspond to the amplitudes of the Fourier transform of the *electron density* in the crystal lattice. The reflections consequently allow for the determination of the crystallographic structure [9]. The established workflow of structure determination is as follows: X-ray diffraction data are measured with a suitable detector, resulting in 2D *detector images*. Next, the common *unit cell* of the measured crystal is found during *indexing*. The intensity values are then computed by *integrating* over the area of each individual reflection. During *scaling* and *merging*, the data of multiple detector images taken from different angles is combined. In order to calculate the *electron density map*, *phases* have to be determined for each measured amplitude. Eventually, an atomic model is built and iteratively refined to both interpret and improve the electron density. Highly-efficient automated procedures are used in structure determination. At the same time, they potentially reduce the users' exposure to the raw data. This leads to a great number of issues during measurement and processing

being overlooked, hampering structure solution. Yet, many of these problems manifest as geometric artefacts in *reciprocal space*, where they are easy to recognize by the human eye. Given the geometry of the experimental setup, reciprocal space data can be calculated from the measured detector images early in the processing workflow. Reflections of a sound crystal should form a lattice with a spacing that is related to the crystals' ordered structure. However, if subsets of the reflections form different patterns or "additional lattices", this can point to a second crystal having been in the X-ray beam during measurement, twinning, or a split crystal. Deviations from a perfect lattice can also indicate modulated lattices, misalignment, wrongly assumed crystal rotation direction, diffraction anisotropy, or the contamination with ice in cryo-crystallography. Reciprocal lattice viewers, such as RLATT [1], dials.reciprocal_lattice_viewer [13], and XRayView [11] have proven extremely valuable for experts, yet have not been widely adopted. We consider this to be the case in part due to inadequacies of 2D display and input methods when interacting with 3D content. Virtual reality (VR) devices provide immersive spatial visualization and interaction, have become mainstream, and continue to experience steady progress. As data analysis in reciprocal space is a *spatial* problem, VR is a promising approach.

We present a tool for the immersive, interactive exploration of diffraction data in reciprocal space. The application enables users to quickly identify problems of the crystalline sample, measurement or post-processing, which can hamper automatic state-of-the-art data processing and the subsequent structure solution.

2 RELATED WORK

In [6], Goddard et al. present a comprehensive overview of the challenges and benefits of VR for scientific visualization. Many molecular and protein visualizations in VR exist, e.g. ChimeraX [5], ProteinVR [2], Nanome [8], as well as frameworks for VR [12] and augmented reality (AR) [3]. Yet, none of these offer a visualization of data in reciprocal space. VR applications specifically for crystallography exist for teaching and outreach [4, 14], but in contrast to our work, they do not aim to directly integrate with the data processing workflow. Especially, our application explores methods for the indexing of data using immersive spatial interaction.

3 METHODOLOGY

We approached the design and development of the application as follows: First, the interactive systems engineering team was introduced to structure determination by the crystallographers. Access to literature (e.g. [9]), example data sets and common software (e.g [1, 13]) used for data analysis was provided to allow the engineers to familiarize themselves with crystallography and to provide basic *in-situ* validation. Subsequently, a first minimal immersive visualization prototype was developed and, together with a suitable hardware setup, provided to the domain experts for continuous feedback. Feedback and discussion sessions among the group then continued during testing and development. The following basic requirements regarding visualization, ergonomics, and infrastructure were inferred: (R1) Use of a hard-/software platform apt for typical crystallography laboratory environments and budgets. (R2) No need for extensive training. (R3) Support of input data in common crystallographic formats. (R4) Visual information displayed includes position of the reflection centroids, associated intensity values, reciprocal coordinate system. (R5) Filtering of the visualized data points based on intensity values. (R6) Visual inspection of the data set from arbitrary perspectives. In addition, the following open requirement was identified to advance the usefulness of the tool during data analysis: (R7) Virtual support tools for the assessment of lattice uniformity and the identification of pathologies. The outlined requirements guided an iterative design and development process that was pursued in tight cooperation between the groups. In addition to regular internal testing, a small informal session with crystallographers ($N = 5$) of different levels of experience was performed. No breaking issues were exposed, and positive feedback confirmed the general approach.

4 RESULTING SYSTEM DESIGN

Based on the requirements analysis, the Oculus Quest stand-alone headset (R1, R2) was selected for its easy setup and competitive pricing, yet alternatives, e.g. the Vive Focus, exist. The tool supports data in the commonly used formats P4P [1] and SPOT.XDS [7] (R3). It allows to visualize X-ray reflection data in reciprocal space (Fig. 1a, R4). The user can navigate the data and filter based on intensity values (R5, R6). Visualization of unit cell data and the reciprocal crystal lattice is provided (Fig. 1b, R7). It is possible to add an orthographic projection screen that makes deviations from ordered structures more obvious while providing spatial interaction (Fig. 1c, R7). Distances can be measured (Fig. 1d, R7), and manual indexing can be performed to validate diffraction lattices (Fig. 1e, R7) and determine the crystals' unit cell.

5 DISCUSSION & OUTLOOK

We created an immersive tool for the support of structure determination in crystallography. It accepts diffraction data sets in common file formats and allows users to perform manual indexing. Virtual tools support the identification of issues during measurement and post-processing and make relevant spatial phenomena more accessible. During informal testing, the tool was well received, and the immersive spatial visualization and interaction appealed to the participants. To further embed it into the structure solution workflow, exporting the indexing solution is required, and compatibility with e.g. data exchange formats for established crystallography tools, such as DIALS [13] or HKL2000 [10] is desirable. This would also allow the inclusion of from electron and neutron data, in addition to X-ray data. Despite the benefits of spatial visualization using VR, ergonomic challenges regarding the visualization of large amounts of pointillistic data need to be addressed more rigorously, such as flickering in order to improve spatial perception and reduce eye strain. Formal user studies on the application as well as the integration in the workflow will follow. Although we focused on VR in this work, we would like to extend our research to augmented reality devices. We aim to integrate the strengths of spatial visualization with the established, highly efficient 2D workflows to advance laboratory work all over the world.

ACKNOWLEDGMENTS

This work has partially been funded by the German Federal Ministry of Education and Research Grant Nr.: 05K19WWA / AUSPEX.

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