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Peer Review File

Equivariant Diffusion Solution for Inorganic Crystal Structure Determination from Powder X-ray Diffraction Data

Corresponding Author: Professor Yizhou Zhu

Parts of this Peer Review File have been redacted as indicated to remove third-party material.

This file contains all reviewer reports in order by version, followed by all author rebuttals in order by version.

Version 0:

Reviewer comments:

Reviewer #1

(Remarks to the Author)
This manuscript presents a data-driven approach to the structure prediction problem in extended solids. Neural networks trained on known crystal structures are a promising tool for structure prediction of polycrystalline solids without expensive ab initio or semi-empirical calculations. Yu et al describe XRDSol, an equivariant diffusion model that allows rapid crystal structure prediction taking only elemental composition and an observed PXRD pattern as inputs. Authors test their model on both observed and predicted PXRD patterns corresponding to known crystal structures with >80% success rate of reproducing the solved structure. Further, authors predict structures for crystals that have been called into question and show that XRDSol predictions fall in line with more recent experiments.
Generally, XRDSol is shown to effectively reproduce manually solved crystal structures, however the presented work does not demonstrate the effectiveness of XRDSol at predicting structures for crystals that are difficult or impossible to solve. The manuscript also does not provide an appropriate comparison of the presented work to relevant works in machine-learning based crystal structure prediction that do aim to predict much more complicated structures. For these reasons, we recommend that the current manuscript should only be accepted following major revisions that both expand the scope of the approach and better delineate its limitations.
Because manual solving allows each step to be checked and justified, there is an additional level of rigor to manually solved structures that should not be readily sacrificed when new utility is not gained by a structure prediction algorithm. We believe that the utility of this approach should lie in predicting structures of unsolvable or unusually difficult to solve phases. Thus, it remains unclear how the authors envision their approach being used, as the manuscript, by focusing inherently on solved structures, provides limited improvements to structure solution methods that are actively being made more readily implementable by improvements in crystallographic data analysis software (such that a student of crystallography should be equipped to tackle these types of structures).
To clarify this point, it would be helpful if the authors explicitly stated the constraints of the training set employed, such as limits on the symmetry and number of atoms in the unit (for example, it does not seem like this tool is appropriate for molecular crystals or proteins), and ensure that the language used throughout the manuscript is consistent with the specific challenges being tackled (c.f. comments on the bottom of page 4, ln 86-87, describing DFT based approaches with the statement that “the information on the number and type of atoms within the determined unit cell is also usually known” describing their approach on page 6, ln 121-123). Can the authors also clarify what inputs are required? How does the stated need for knowing the “periodic lattice” differ from knowing the space group?
How did the authors choose the examples focused on in the manuscript? They are mainly well-described as ionic materials that are chemically limited, with some notable exceptions (the HoGeAg is particularly intriguing). For example, does predicted magnetic order (or other symmetry breaking phenomena) influence the efficacy of this structure solution approach? More generally, the examples shown raise questions regarding bias towards solving specific types of structures. We suggest the application of XRDSol to a more chemically diverse set of materials. Particularly, we believe that predicting structures of high energy or low symmetry materials would provide a more robust test of XRDSol and we suggest that authors verify that XRDSol does not have an implicit bias towards any space groups, substructures, structure types.
An additional challenge to XRDSol that would demonstrate the effectiveness of the model is the ability to explicitly predict structures that present particularly thorny crystallographic challenges, such as (in)commensurate order, patterns that arise from mixtures of components, or patterns collected on poor quality samples with limited resolution. The authors’ testing on Sr0.5Ca0.5TiO2N and Eu0.5Dy0.5TiO3 provides a starting point for modelling substitutional disorder (see comment on

substitutional and positional disorder), however the model seems limited in that it does not explicitly predict random placement of Sr/Ca and Eu/Dy at otherwise chemically equivalent positions, which may be indicated by multiple closely related solutions that differ simply by atom identity at equivalent sites. Rather, XRDSol predicts a larger unit cell with the empirical formulas $SrCaTiO_4N_2$ and $EuDyTi_2O_6$. Can the authors comment on this distinction? Extending XRDSol to consider long range order and demonstrating that solutions are accurate for a larger variety of materials would warrant its use for structure prediction over manual solving methods and allow this work to stand among other machine learning based structure prediction algorithms.
We further highlight the importance of appropriate comparison to existing works. Authors claim to have “demonstrated that conditional equivariant generative model(s) can tackle the ab initio structure determination problem and provide high-quality structure models for inorganic crystalline materials” (ln 28-30). While XRDSol does provide structures with minimal input, neural networks are not ab initio methods. Rather, XRDSol is a data-driven model that “implicitly learns crystallographic knowledge” (ln 387-388). We believe that comparison to ab-initio and manual structure determination methods is inappropriate considering the existence of other machine-learning based structure prediction methods.
We encourage the authors to continue to develop XRDSol. We are particularly encouraged by the highly accessible computational cost of XRDSol in comparison to other structure prediction approaches. We also believe that machine learning structure prediction is a promising area of development given the ability of a machine learning model to go beyond what can be done by manual human analysis. We provide the following comments as additional notes for the reference of the authors who we hope to see present a more robust demonstration of their structure prediction algorithm in future works. ---
Authors refer to how in a PXRD experiment “the three-dimensional atomic spatial information is compressed into one-dimensional spectra” (ln 50-51). The result of a PXRD experiment is a pattern not a spectrum. Similarly, the use of Rcos as a metric is not standard, and this variable should be defined in the manuscript.

Authors claim that XRDSol can provide a crystal structure in an average time of 0.6 seconds (ln 103). We suggest a comment on the distribution of run times for XRDSol or a figure demonstrating this distribution. A demonstration of consistent fast structure generation provides confidence in the computational cost of XRDSol that is a point of strength for this work. ---
Authors claim that XRDSol performs well in systems with chemical disorder (ln 113). While this claim is based on the predicted structures of $Sr_{0.5}Ca_{0.5}TiO_2N$ and $Eu_{0.5}Dy_{0.5}TiO_3$, we suggest clarifying that the model performs in crystals with substitutional disorder as opposed to positional disorder within the unit cell. Additionally, we believe that the future development of XRDSol should include a more robust treatment of disordered structures. The standard representation of disorder is not multiple unit cells each with one possible microstate of the disordered crystal, but rather a single unit cell that has a specified variation at a certain position that corresponds to the relevant disorder. A model that generates multiple unit cells containing different microstates of a disordered position does not accurately depict the symmetry of the crystal and does not address either the dynamics or the site-to-site variation of the material
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Authors attribute uncharacteristically low Rcos values for $NaSrPO_4$ to low phase impurity and a highly textured sample (ln 355-356). Further, authors attribute the absence of predicted peaks in the MnO_2 observed pattern to Rietveld refinement failure (ln 364-365). We suggest providing a reference that justifies these statements in the relevant system or a chemically similar system.

(Remarks on code availability)

Reviewer #2

(Remarks to the Author)
I co-reviewed this manuscript with one of the reviewers who provided the listed reports. This is part of the Nature Communications initiative to facilitate training in peer review and to provide appropriate recognition for Early Career Researchers who co-review manuscripts.

(Remarks on code availability)

Reviewer #3

(Remarks to the Author)
The authors
- developed a conditioned diffusion model based on an equivariant graph neural net
- trained it on MP20 (~45k structures with simulated data, 9k held out for testing) and ICDD20 (~1000 structures with experimental data).
- conditioned it on simulated x-ray powder diffraction data
- the model is able to predict atomic structures given a powder diffraction pattern.

To summarize my assessment of this manuscript:
- the paper started very slowly, reading a little bit the way I would expect a computer scientist explaining materials science to a materials scientist. However, later it got much better with quite detailed descriptions of structures from different materials classes. I strongly recommend to get rid of most of the introduction and get right to the point.

- This work is quite similar to a related paper on arxiv: arXiv:2406-10796. It is nature policy that papers in preprint servers cannot be used to assert precedent, so the existence of the arxiv paper should not affect whether the current manuscript is accepted. However, it would seem appropriate to cite that paper (and possibly place the current work in context of that work).

- The problem the current authors tackled was, given a known unit cell and composition, what are the fractional coordinates of the atoms in the unit cell. This is justified on the basis that the indexing of the diffraction pattern to get the unit cell information is straightforward. This is not completely unreasonable, but in many interesting cases it is actually not super straightforward to get the unit cell for powder patterns, especially when the unit cell is larger (not considered in this work). This is a limitation of the broader applicability of the current work.

- This is a significantly simplifying assumption because it results in the Bragg peaks being in the right positions and the model simply changes the intensities of the peaks when it atoms around. It gives a subjective impression that the model is working better than it is because the Bragg peaks are all in the right locations, but close inspection of the figures shows that even "successful" solutions have the intensities that don't match. It is not so clear that a crystallographer would be satisfied with these structure solutions. This is expanded on a bit below.

- These authors did a decent job of assessing the outcomes of their studies. In common with most studies in this domain they faced the challenge of determining some way of assessing whether a structure was successfully solved or not. They used standard methods (Rcos of the initial and final diffraction pattern) and similarity tools. I wasn't able to find the MaxDist measure so not sure how it works (I looked in the reference that was cited and it doesn't seem to appear in that paper, or I couldn't find it anyway). This should be addressed.
In general, the structure solution field needs better measures of when structures are successfully solved. The problem with this is that there is disagreement even among crystallographers about the exact definition.

For example, an Rcos of 0.899 sounds pretty good (almost 90% good!), but a crystallographer looking at the powder patterns in figure S7 of the supplementary would be pretty surprised with how bad it is. Clearly wrong. Even the Rcos of 0.974 in figure S2 has a bunch of problems. These could possibly be fixed by a final Rietveld refinement step, which was not done by these authors, but this would normally be part of a minimal requirement from a crystallographer.

- I did like that the authors computed the formation energies using DFT and compared to the complex hull. It was very reassuring that the model was able to find on hte whole low energy solutions, and indeed some solutions that had lower formation energy than the reported ones. This gives good confidence that the diffusion model is learning structures that are energetically stable (it was trained on stable structures).

- They tested against experimental data with solved structures from ICDD and the model performed well in most cases. This is good.

- They also used it to propose structure solutions from some experimental patterns that didn't have structure solutions proposed in the ICDD and the models performed well. It wasn't completely clear the inputs in this case. Was the stoichiometry known and input? And the number of formula units in the unit cell? This needs to be placed more prominently.

Some comments on the validity and areas for improvement are:

- if the model architecture was built from or inspired by or reused architecture from the literature I encourage the authors to mention this in the methods section where the model is described. I would be a bit surprised if it were not built off an existing one or ones because this structure is quite similar to CDVAE for example (ref 12 in the current manuscript). It is ok to admit where the inspiration came from and what was reused. It gives correct credit to prior workers. This needs to be fixed before publication.

- is it possible to show one or more schematics of the model architecture in a figure? this can be very helpful

- In the description of the model the L vector is described but I had to think hard to figure out it was the lattice vectors. Makes sense in hindsight (L) but please add a few words so that all the letters are fully defined in the place where they appear.

- The work would benefit from better baselining. It was baselined against some non ML approaches that use evolutionary algorithms, For example, and the trained model was much faster (not a huge surprise). But can it be benchmarked against other ML models and simple models such as nearest neighbor models or something like that?

(Remarks on code availability)
sorry, I don't have time to do that.

Reviewer #4

(Remarks to the Author)
Strength:
- The writing is good and easy to follow.
- This work is both interesting and novel. Unlike previous methods focused on accurate 3D reconstruction, this study

explores the use of a diffusion model to approximate spatial structures.
- The adoption of a graph model to represent the spatial structure of XRD is intuitive and naturally lends itself to being extended and learned by the diffusion model.
- Compared with numeric methods (e.g., the DFT), the diffusion-based method is efficient with a significant speedup of at least 10,000x. The estimation accuracy under both the simulation and observation environment is also acceptable for further study of the crystal.

Weakness&Questions:
(1) Some algorithm details are not clear.
(a) How is the graph initialized? Is any prior knowledge required? If not, could incorporating prior knowledge, such as partial spatial structures, improve prediction accuracy?
(b) How is the number of diffusion steps determined? Is it consistent across all crystals, or does it vary? Would increasing the number of steps consistently enhance performance?
(c) What is the detailed structure of the model used for the denoising process?
(2) The diffusion process involves inherent randomness. What is the statistical significance of the reported results, considering this randomness?
(3) Figure 2(b) shows examples with relatively low estimation accuracy. What distinguishes these "bad" examples from others? Do they share specific characteristics, such as belonging to a similar group? While the paper effectively highlights the success of using the diffusion model for accurate XRD predictions in most cases, it would be helpful to provide a more detailed analysis of these failed examples.
(4) Does the number of cells affect estimation accuracy? Do different space groups exhibit similar accuracy trends?
(5) Is there any way to use DFT or something else to further refine the structure?
(6) It would be beneficial to include more details about the diffusion model to enhance clarity for the materials science community.

(Remarks on code availability)
The code is open-source with all data available, with good instructions to reproduce the results.

Reviewer #5

(Remarks to the Author)
I co-reviewed this manuscript with one of the reviewers who provided the listed reports. This is part of the Nature Communications initiative to facilitate training in peer review and to provide appropriate recognition for Early Career Researchers who co-review manuscripts.

(Remarks on code availability)
The code is clean and organized. The instructions are clean to install the software. The data is also available.

Version 1:

Reviewer comments:

Reviewer #1

(Remarks to the Author)
This revised manuscript details a particularly fast ML informed tool for predicting atomic positions given a PXRD pattern and unit cell data. As was noted by multiple reviewers, this paper exists in a somewhat strange intermediate space between computer science and chemistry. From a chemistry perspective, it is not written in a way to convince the field that this would be useful, although the point made about autonomous materials discovery and the particularly time efficient nature of this tool is a compelling one that should be centered in the introduction (rather than a general overview to crystallography). Although I find the manuscript improved upon revision in terms of clarity and better defining the tool developed, by not significantly revising the manuscript to address the source of reviewer comments, it still seems like a computational tool was developed first and a chemical problem was searched for second. It remains unclear what chemical problem is actually being solved, and the question remains how the authors envision it will be used? Can the authors include a demonstration/provide an example of how it can be implemented completely autonomously? Or how the process of correcting a database would be performed (it is not stated how the potentially incorrect ICSD structures were identified, or can an entire database be screened at once?). I find this issue embodied by the lack of chemical analysis presented in the discussion section, which is too speculative in ways that are not specific enough to bridge the disconnect.

(Remarks on code availability)

Reviewer #2

(Remarks to the Author)
I co-reviewed this manuscript with one of the reviewers who provided the listed reports. This is part of the Nature

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(Remarks on code availability)

Reviewer #3

(Remarks to the Author)
The authors have worked hard to address my comments, but I still feel that they fall somewhat short. I am not sure if they have a professional crystallographer among the authors, but tha paper still lacks insights that I would expect from such a person, and since the paper is really about developing a tool for crystallographers to do their crystallography, this is a significant shortcoming. A reading of the comments of the other referees and the author responses doesn't do anything to allay this impression. With that said, the paper is greatly improved from the original version.

I focus primarily on responses to my comments.

I appreciate their efforts to place their work in context of the PXRDNet paper that was mentioned. This is mostly handled well, though I note that the version that has now appeared in print does have a post-validation step which invalidates one of their comments in the rebuttal.

In Response 3 the authors attempt a justification of the reason for mismatched Bragg peak intensities in some of their solutions. They mention experimental things such as temperature and absorption effects. However, these cannot explain the differences in relative Bragg peak intensities that are a characteristic of atoms being in incorrect positions that I was referring to in my original comment, and so they have not successfully addressed my comment, unfortunately and this issue still remains. They did work hard to incorporate a Rietveld post-processing step, at least on one representative sample. As one might expect, it did result in an improvement of metrics like Rwp. However, they did not select one of the patterns that had problematic relative peak intensities. It is therefore not quite clear whether this would have corrected the problematic cases that showed success by the MaxDist (thanks for fixing the description of this in the manuscript) measure, but which were almost certainly not actually correct in some key way based on a visual assessment of the diffraction pattern.
I also find their rebuttal on the basis that their data are from simulated data so the Rietveld will give a lower Rwp, with a citation to a paper in Powder Diffraction journal, to be a bit lazy and to be an attempt to evade the question rather than address it head on as a serious scientist would seek to do.
All in all, these responses reinforce an impression that the crystallography expertise in the group is lacking.
The authors have worked hard on this work and it deserves better.
In summary, the authors did not address the key point of my original objection in comment #5 with any of their responses.

Further, on the point of the use of structureMatcher/MaxDist to assess structures: This metric has not been validated in any meaningful way by the crystallographic community, and whilst it is widely used by the ML community, this is an issue that needs to be urgently addressed. this is not the fault of the current authors, and they are following practices used by others in this regard, but with respect to the specific scientific claims of the paper, this measure is so flawed as to make them highly dubious. Increasing the crystallographic domain knowledge in the team would, again, greatly help.

I appreciate the efforts of the authors to increase the clarity of the presentation. Also, they report at making a better effort of acknowledging the inspiration for their work (e.g., CDVAE) in the methods section, but I still find this inadequate. I would rather expect to see it high up in the paper (e.g., the Introduction) and with a bit more fanfare. There is no harm in a full bodied celebration of the work of others. It does not diminish in any way the developments made by the authors. Perhaps they feel pressure to publish in a high profile journal, and they feel they need to try and make their work stand out to accomplish that. But this is bad for science in general, and counter-productive for the authors as it makes it harder for others to cite their work if it doesn't do a fair job of explaining how it fits in to the broader community.

I thank the authors for their efforts at better benchmarking. Just a note that I am more interested in benchmarking prediction performance, in part as a way to understand how the model is working, where it is getting information from, and so on, and less interested in computation time. It is clear that a trained ML model will work in production much quicker than any regression method, but getting an answer is of greater interest in structure solution rather than wall-clock time in most applications and so understanding the performance is more important than how quickly it gets there. Overall, given the challenges of not really having good success metrics in general, the benchmarking work that the authors have done is abut as good as we can hope for.

Some small points.

In one response the authors mention that better performance can be obtained by incorporating "'domain knowledge (e.g., space group information)". This an incorrect use of the term 'domain knowledge' which refers to the general knowledge of a domain expert rather than incorporating additional information in a particular input. I sugget to just delete mention of domain knowledge at that point.

In a later comment they also mention 'peak distinction'. Do they mean 'peak extinction here'? Again, bolstering their crystallography domain expertise might help this paper.

In methods they describe how they run the model 25 times with different random seeds and pick the best solution. This is fine, it is fairly standard practice, but then they call it 'Top-1', but I find this a bit misleading. I think more normally this would be called 'Top-25'. Clearly you measure the model performance with the best model of your sample and report that performance, but I think of 'top-1' as how well the model performs at a guess of one sample, Top-10 when you let it guess 10 times and take the best one, and so on. So I would think that what the authors are doing is better described as Top-25. They justify very nicely why they do that, so it is no criticism of the approach, just the naming.

They call their approach ``end-to-end'' on pag 3 but requiring knowledge of the lattice parameters suggests that this is more mid-to-end than end-to-end. I recommend simply to remove this statement. It doesn't add much.

(Remarks on code availability)

Reviewer #4

(Remarks to the Author)
I appreciate the authors' detailed responses. My main concerns, including the graph initialization, diffusion step selection & potential randomness, and failure case analysis, have been well addressed.

To further improve clarity, I suggest the authors consider simplifying the presentation of the diffusion model in the final revision. Including a clear formulation of the forward and reverse steps, perhaps via a concise pseudo-code for one noising and denoising step, would help a lot.

(Remarks on code availability)
The code is clear and runnable with good instructions to reproduce the results.

Reviewer #5

(Remarks to the Author)
I co-reviewed this manuscript with one of the reviewers who provided the listed reports. This is part of the Nature Communications initiative to facilitate training in peer review and to provide appropriate recognition for Early Career Researchers who co-review manuscripts.

(Remarks on code availability)
The code is runnable with clear instructions.

Version 2:

Reviewer comments:

Reviewer #1

(Remarks to the Author)
This manuscript presents a fast machine-learning model for predicting structures in a polycrystalline sample from powder x-ray diffraction data. This is a promising application of machine learning within the expanding interface between chemistry and computer science, highlighting the need for input by both machine-learning experts and experienced crystallographers. I believe that this work has substantially improved from the initial manuscript in its presentation of the effectiveness and shortcoming of XRDSol.

The crux of my critique against this paper that remains unaddressed is that I disagree with the author's statement regarding "solving" structures from powder x-ray diffraction data: "determining atomic coordinates is the most crucial and challenging step." Such a statement reflects a lack of understanding of how a Rietveld refinement works, in terms of refining against models (rarely are candidate structures generated from scratch), and reveals a core weakness of the manuscript. Instead, most of the high energy structures highlighted in the manuscript could likely be easily corrected by inspection, once identified as a high energy structure. There may be utility in this approach if the algorithm could solve entirely new structure types (ones without models for refining against), but given the chemical constraints of the examples presented, this seems to be outside the scope of the tool developed. Instead, I maintain that the utility of the approach is overstated, and while it lays a good groundwork, it is disingenuous for the authors to claim that it significantly improves on other approaches because it requires less input when not all input is created equal. Instead, the authors state XRDSol requires stoichiometry and "periodic lattice" as inputs, although I do not think the latter is a standard crystallography term (maybe unit cell is meant instead?). This information may indeed prove quite difficult to obtain depending on the quality of a diffraction pattern or sample purity, something that is not adequately considered throughout the manuscript.

Accordingly, the authors failed to satisfactorily address my prior comments concerning how this model could be implemented for materials discovery. Indeed, the success rate of ~1-3% on correcting database entries speaks to the fact that the authors have developed a tool with limited ability to fix outstanding challenges in crystallography. I reiterate the suggestion of the reviewers that for further work on PXRD-informed structure prediction they collaborate with an experienced

crystallographer to provide additional perspective on the problems that they aim to solve.

Lastly, the manuscript contains some typos (ex: On lines 206-208, the authors repeat the phrase “All these structure analysis were performed with pymatgen”). I suggest the authors perform one more review of the prose in their manuscript.

(Remarks on code availability)

Reviewer #2

(Remarks to the Author)
I co-reviewed this manuscript with one of the reviewers who provided the listed reports. This is part of the Nature Communications initiative to facilitate training in peer review and to provide appropriate recognition for Early Career Researchers who co-review manuscripts.

(Remarks on code availability)

Reviewer #3

(Remarks to the Author)

(Remarks on code availability)

Responses to Reviewers

(*Black italic: Reviewer's comments*; Black type: Our response; Blue type: Key revisions)

Responses to Reviewer #1:

Comments #0: *This manuscript presents a data-driven approach to the structure prediction problem in extended solids. Neural networks trained on known crystal structures are a promising tool for structure prediction of polycrystalline solids without expensive ab initio or semi-empirical calculations. Yu et al describe XRDSol, an equivariant diffusion model that allows rapid crystal structure prediction taking only elemental composition and an observed PXRD pattern as inputs. Authors test their model on both observed and predicted PXRD patterns corresponding to known crystal structures with >80% success rate of reproducing the solved structure. Further, authors predict structures for crystals that have been called into question and show that XRDSol predictions fall in line with more recent experiments. Generally, XRDSol is shown to effectively reproduce manually solved crystal structures, however the presented work does not demonstrate the effectiveness of XRDSol at predicting structures for crystals that are difficult or impossible to solve. The manuscript also does not provide an appropriate comparison of the presented work to relevant works in machine-learning based crystal structure prediction that do aim to predict much more complicated structures. For these reasons, we recommend that the current manuscript should only be accepted following major revisions that both expand the scope of the approach and better delineate its limitations.*

Response #0: We truly appreciate your thorough evaluation and valuable comments of our work. We have addressed your concerns point by point below.

Comments #1: *Because manual solving allows each step to be checked and justified, there is an additional level of rigor to manually solved structures that should not be readily sacrificed when new utility is not gained by a structure prediction algorithm. We believe that the utility of this approach should lie in predicting structures of unsolvable or unusually difficult to solve phases. Thus, it remains unclear how the authors envision their approach being used, as the manuscript, by focusing inherently on solved structures, provides limited improvements to structure solution methods that are actively being made more readily implementable by improvements in crystallographic data analysis software (such that a student of crystallography should be equipped to tackle these types of structures).*

Response #1: Thanks for your valuable comments. We fully agree that an automated solution algorithm should not compromise the rigor and accuracy of the crystal structure solution results. This is why we implemented multi-level validation tests to verify the reliability of our approach. We agree that manual structure solving provides a level of rigor since the crystallographer can check each step. At this stage, XRDSol is designed to complement rather than replace manual approaches. Particularly, our approach does not target PXRD patterns that are difficult or even impossible for human experts to solve. Since XRDSol has demonstrated a decent (>80%) success rate and rapid solution time, we envision three practical application scenarios for XRDSol:

(1) Integration into autonomous materials discovery platforms

Autonomous materials discovery has become a major focus in materials science recently. These platforms typically employ fully automated, high-throughput synthesis-characterization-experimentation workflows. In such closed-loop systems, rapid and automated structural characterization of large numbers of synthesized samples forms an essential component. Our algorithm is particularly well-suited for these applications due to its minimal human intervention requirements, rapid processing capability, high accuracy, and standardized outputs that enable seamless system integration. These characteristics make our approach ideal for maintaining the uninterrupted flow required in autonomous materials discovery workflows.

(2) Maintenance and quality control of large-scale structural databases

As illustrated in our manuscript, even state-of-the-art inorganic materials structural databases (e.g., ICSD, ICDD) contain entries with incomplete or incorrect structural information. XRDSol provides a systematic solution for addressing these limitations, by enabling the initial screening of suspicious entries, identifying potential errors in existing records, supplementing missing structural parameters, and offering cross-validation for ambiguous cases. This combination of accuracy and efficiency makes our method particularly valuable for large-scale database maintenance and quality control.

(3) Assistant for manual PXRD analysis

While human experts generally possess more domain-specific knowledge and experience than XRDSol, our tool can serve as a valuable assistant for manual PXRD analysis. Specifically, in manual PXRD analysis, XRDSol can serve as an efficient first-step tool to provide preliminary structural models that experts can either verify directly or use as optimized starting points for Rietveld refinement. This complementary approach enables researchers to concentrate their specialized expertise on the critical tasks of validation and refinement while maintaining rigorous

standards of accuracy.

In addition, although beyond the current capability of XRDSol, we also hope to build algorithms that can handle more difficult cases (or what you called "*unsolvable or unusually difficult phases*"). However, there are two practical difficulties: First, when human experts deal with these cases, they often need to consider more factors, such as thermal vibration, possible twinning, preferred orientation, etc., and our current model is not yet compatible with these complex multiple factors. Second, and more importantly, for these complex cases, even human experts can make controversial judgments. Since ground truth is usually not available for these cases, we lack effective means to verify the reliability of automated algorithms. Therefore, our current algorithm does not target these extremely difficult cases.

Action #1: We appreciate your valuable comments regarding the potential applications of XRDSol. We have explicitly elaborated on three key application scenarios in the revised manuscript as follows:

(Discussion in the revised Manuscript)

"We envision three practical application scenarios for XRDSol: integration into autonomous materials discovery platforms, quality control of large-scale structural databases for inorganic materials, and AI-assistant for manual PXRD analysis."

Comments #2: *To clarify this point, it would be helpful if the authors explicitly stated the constraints of the training set employed, such as limits on the symmetry and number of atoms in the unit (for example, it does not seem like this tool is appropriate for molecular crystals or proteins), and ensure that the language used throughout the manuscript is consistent with the specific challenges being tackled (c.f. comments on the bottom of page 4, ln 86-87, describing DFT based approaches with the statement that "the information on the number and type of atoms within the determined unit cell is also usually known" describing their approach on page 6, ln 121-123). Can the authors also clarify what inputs are required? How does the stated need for knowing the "periodic lattice" differ from knowing the space group?*

Response #2: Thanks for the comments.

(1) Constraints of training set:

Our model XRDSol was trained on the MP-20 dataset, which is a relatively commonly used benchmark dataset for machine learning approaches in the inorganic material community (Tian Xie

et, al. Crystal Diffusion Variational Autoencoder for Periodic Material Generation, *ICLR*, 2022). The MP-20 dataset consists of inorganic crystal structures with up to 20 atoms per unit cell, most of which are thermodynamically stable based on first principle calculations. This dataset can be openly accessed from the Materials Project database.

For symmetry, the training structures include different space groups with different symmetry. We did not screen or filter any data in this dataset. As described by Tian Xie *et, al.* (*ICLR*, 2022), MP-20 is a realistic dataset that includes most experimentally known inorganic materials. Therefore, it inherently exhibits an imbalance among different space groups, as some space groups are more common or rare in experimentally observed inorganic crystal structures. The generated structures can also be naturally influenced by the underlying distribution of different symmetries of the training data.

In addition, XRDSol was designed for inorganic crystal structures. It is not appropriate for molecular crystals or proteins.

Action #2: To better reflect the scope of our work, we have clarified that XRDSol is specifically designed for inorganic crystals by updating the manuscript title as follows:

(Title in the revised Manuscript)

"Equivariant Diffusion Solution for Inorganic Crystal Structure Determination from Powder X-ray Diffraction Data"

(2) Consistency in language:

We understand the concern about consistent language in the manuscript. Below is a clarification of our intended meaning:

- **Line 86-87**: The statement "*Besides, they require predetermined space group information, which may be unavailable or unreliable*" means that space group information is usually known, but there are cases where it is unavailable or incorrect. This claim is supported by our statistical analysis of the ICDD database: among the ICDD entries without reported crystal structures, 25.8 % entries (5348 out of a total 20741) lack space group information. Additionally, previous studies have also reported cases of incorrect space group assignments (*Angewandte Chemie International Edition*, 2021, 60, 17452-17454; *Zeitschrift für anorganische und allgemeine Chemie,* 2018, 644, 1721-1726).

- **Line 121-123**: The statement "*the information on the number and type of atoms within the*

determined unit cell is also usually known" refers to the atom type, number of atoms, and lattice parameters (*a*, *b*, *c*, *α*, */3*, and *γ*). The lattice parameters are usually available. This claim is also supported by our statistical analysis of the ICDD database: among the ICDD entries without reported crystal structures, only 0.0002% entries (4 out of a total 20741) lack lattice information.

The key difference is that the first statement refers to the uncertainty in the space group, while the second statement talks about lattice parameters. These ideas do not contradict each other.

(3) Clarification of inputs:

The inputs for solving the crystal structures used in this work include **the target PXRD patterns, lattice parameters**, **number and type of atoms**. The lattice parameters refer to the unit cell parameters (*a*, *b*, *c*, *α*, */3*, and *γ*). The lattice parameters define the periodic translation symmetry of the crystal, which differ from the space group. In contrast, space groups provide other symmetry information, such as reflection, rotation, and mirror symmetries. Our XRDSol uses lattice parameters and does not rely on prior knowledge of the space group.

Comments #3: *How did the authors choose the examples focused on in the manuscript? They are mainly well-described as ionic materials that are chemically limited, with some notable exceptions (the HoGeAg is particularly intriguing). For example, does predicted magnetic order (or other symmetry breaking phenomena) influence the efficacy of this structure solution approach? More generally, the examples shown raise questions regarding bias towards solving specific types of structures. We suggest the application of XRDSol to a more chemically diverse set of materials. Particularly, we believe that predicting structures of high energy or low symmetry materials would provide a more robust test of XRDSol and we suggest that authors verify that XRDSol does not have an implicit bias towards any space groups, substructures, structure types.*

Response #3: Thanks for the comments. Regarding examples that we focused on (Fig. 3 and Fig. 4), our selection was guided by a principle: we focused on cases where we could be most confident that XRDSol had achieved a correct solution. By "correct" we refer to either cases where XRDSol provided a more reasonable structural solution compared to existing entries in the ICSD, or cases where the ICSD or ICDD entry originally lacked complete or partial atomic position information that our method was able to successfully determine.

Since both ICSD and ICDD are state-of-the-art databases for inorganic crystalline materials, we exercised extreme caution when correcting or completing these entries. A few approaches we adopted include manual inspection, literature review, and first-principles calculations.

(1) Prediction of magnetic order and symmetry breaking:

XRDSol is not trained to solve magnetic order at the current stage. Since our model is trained on structures in MP-20 datasets, few of which contain magnetic order information, it is not capable of predicting magnetic order.

As a future research direction, one possible approach to predict magnetic order is to combine the candidate crystal structure solutions proposed by XRDSol with different magnetic ordering calculation based on density functional theory (DFT). As demonstrated in a previous study (*npj Computational Materials*, 2019, 5, 64), it is possible to construct a high throughput workflow to evaluate the possible ground state magnetic ordering.

Note that correctly evaluating the ground state magnetic ordering with DFT calculation is a non-trivial task, as the authors in the reference remarked: "*The workflow successfully predicts the experimental ground state in over 60% of the materials benchmarked.*" In addition, it is computationally expensive, as it requires multiple DFT calculations with different proposed magnetic ordering for each candidate crystal structure. Therefore, we have not implemented magnetic ordering prediction in our model yet.

(2) Chemical and structural diversity of chosen examples.

The chosen examples in our manuscript mainly come from existing entries in ICSD and ICDD databases.

From the ICSD database, we corrected 39 incorrect crystal structures (6 in Fig. 3a while 33 in SI) and completed 3 structures lacking H atoms (Fig. 3b). These 39 materials exhibit chemical and structural diversity. Chemically, we have included 20 metallic compounds, 19 ionic or covalent compounds. Structurally, we have included half-Heusler, perovskite etc. To ensure representativeness, we highlighted 6 examples across the three types of materials, including 3 metallic compounds (HoAgGe, NbSnRh, and HoSbPd), 1 ionic compound ($SrPbF_6$), and 2 covalent compounds (NbP and $CsIO_3$).

From the ICDD, we solved 912 entries with XRD patterns but no available atomic position information. We focused on entries that lack full atomic positions but no chemical or structural bias was introduced in the selection process. As for the examples chosen in Fig. 4, we aimed to highlight

different types of materials, such as materials containing light elements (2 examples in Fig. 4d: structures containing H and Li), natural minerals (2 examples in Fig. 4e: both oxides as oxides dominate natural minerals), and substitutional disorder lattice sites (1 example in Fig. 4f). Chemically, we have included oxides, fluorides, and oxynitrides.

(3) Solving crystal structures with high-energy

Thank you for your suggestion. To the best of our understanding, high-energy inorganic crystalline materials may refer to materials that are less thermodynamically stable, such as materials synthesized under non-ambient conditions. Our model XRDSol was trained using the MP-20 dataset, which is sourced from the ICSD database. This dataset only includes crystal structures with relatively good thermodynamic stability (energy above hull below 0.08 eV/atom). These limits ensure that the structures in the dataset are stable under common experimental conditions. Because of this, XRDSol was only trained on low-energy structures. Since most high-energy materials are outside the MP-20 training dataset, XRDSol is currently not specifically designed to handle them effectively.

Another obstacle is: to test the performance of XRDSol on high-energy materials, we lack such a reliable dataset that contains high-energy materials with available ground truth crystal structure information. One way we could think of is to assemble another dataset from the Materials Project that specifically focuses on materials with poor thermodynamic stability (high energy above hull). However, based on the analysis from a previous study (*Science Advances*, 2016, e1600225), approximately 20% highest-energy metastable compounds from the ICSD are considered as spurious entries. Based on their manual inspection, many of these high-energy entries could either correspond to defected structures, which form unphysical bulk crystals when repeated by DFT periodic boundary conditions, or correspond to unobserved hypothetical, computationally-constructed structures. Therefore, even if we could perform such a validation test, it may still not correctly reflect the performance of XRDSol on real-world high-energy materials.

Nevertheless, we agree with the reviewer that testing the ability (or limit) of XRDSol on high-energy materials is interesting and also important for the future development of our algorithm. In the future, one potential solution is to collect more high-energy crystal structures and train a generative model specifically for these cases.

(4) Solving crystal structures with low symmetry

To address concerns about potential bias on certain symmetry or space groups, we re-examined

XRDSol's performance on the MP-20 benchmark dataset. This dataset contains 9046 diverse structures, including structures with low symmetry and structures from various space groups.

(a) Structures from different crystal systems:

We first evaluated XRDSol's performance across different crystal systems, which exhibit different degrees of symmetry. For example, the cubic system has the highest symmetry with multiple high-order rotation axes and the triclinic system has the lowest symmetry. As shown in Fig. S3, i.e., Fig. R1-1, the success rate varies across the seven crystal systems with different symmetries (cubic 97.72%, hexagonal 90.33%, trigonal 77.86%, tetragonal 88.02%, orthorhombic 76.32%, monoclinic 68.91%, and triclinic 48.48%). Among these, the cubic crystal system, which has the highest symmetry, shows the best performance. In contrast, the triclinic system exhibits the poorest accuracy. The model's performance decreases as the symmetry decreases. It indicates that structures with higher symmetry are easier to solve accurately, while lower-symmetry structures pose greater challenges.

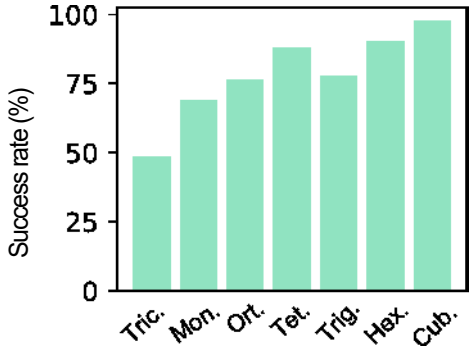

Fig. R1-1 Success rate across the 7 crystal systems, including triclinic, monoclinic, orthorhombic, tetragonal, trigonal, hexagonal, and cubic.

(b) Structures from various space groups:

We further analyzed model accuracy across different space groups. In this work, we excluded those space groups with 10 or fewer samples in the MP-20 test dataset, as they would lack statistical significance. As shown in Fig. S4, i.e., Fig. R1-2, the accuracy varies across different space groups. Generally, space groups with higher symmetry tend to exhibit higher estimation accuracy. Specifically, 26 space groups achieved an accuracy of 100%, and 41 space groups had accuracy greater than 90%. However, there are 6 space groups with accuracy lower than 50%,

namely space groups 2, 19, 46, 51, 55, and 156. This suggests that symmetry plays a significant role in the model's ability to predict crystal structures accurately.

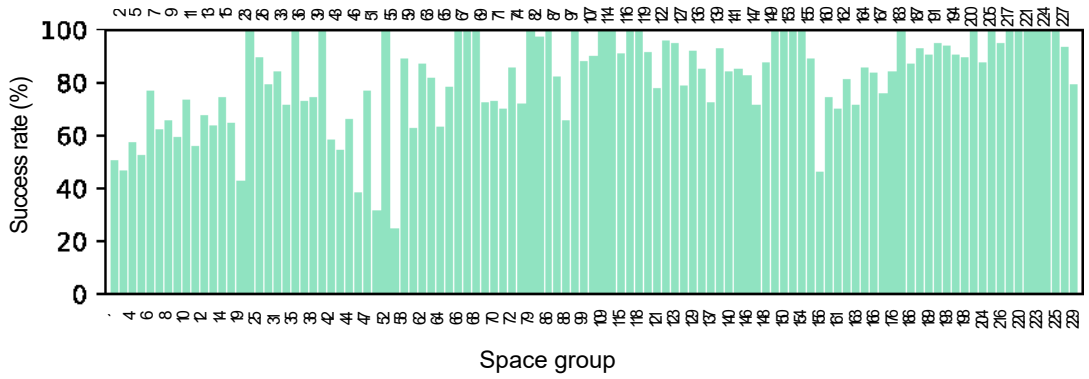

Fig. R1-2 Success rate across the 107 space groups.

An intuitive explanation of the better accuracy on high symmetry structures is that, although symmetry information is not provided as input for our model, a high symmetry structure intrinsically contains fewer unique Wyckoff sites and lower degrees of freedom, which implicitly assists our model in identifying the correct crystal structure solutions.

Action #3: We thank the reviewer for raising this important point about potential bias in different structure types. We have now included a detailed analysis of structure symmetry in the revised Supporting Information. Moreover, we have included future direction for low-symmetry in the revised manuscript.

(Paragraph 1 of Page 5 in the revised Supporting Information)

"To investigate the potential bias on certain symmetry or space groups, we evaluated XRDSol's performance on the MP-20 benchmark test dataset. This dataset contains 9046 diverse structures, including structures with low-symmetry and structures from various space groups. We first evaluated XRDSol's performance across different crystal systems, which exhibit different degrees of symmetry. For example, the cubic system has the highest symmetry with multiple high-order rotation axes and the triclinic system has the lowest symmetry. As shown in Fig. S3, the success rate varies across the seven crystal systems with different symmetries (cubic 97.72%, hexagonal 90.33%, trigonal 77.86%, tetragonal 88.02%, orthorhombic 76.32%, monoclinic 68.91%, and triclinic 48.48%). Among these, the cubic crystal system, which has the highest symmetry, shows the best performance. In contrast, the triclinic system exhibits the poorest accuracy. The model's

performance decreases as the symmetry decreases. It indicates that structures with higher symmetry are easier to solve accurately, while lower-symmetry structures pose greater challenges. We further analyzed model accuracy across different space groups. In this work, we exclude those space groups with 10 or fewer samples in the MP-20 test dataset, as they would lack statistical significance. As shown in Fig. S4, the accuracy varies across different space groups. Generally, space groups with higher symmetry tend to exhibit higher estimation accuracy. Specifically, 26 space groups achieved an accuracy of 100%, and 41 space groups had accuracy greater than 90%. However, there are 6 space groups with accuracy lower than 50%, namely space groups 2, 19, 46, 51, 55, and 156. This suggests that symmetry plays a significant role in the model's ability to predict crystal structures accurately."

(Paragraph 2 of Page 19 in the revised Manuscript)

"In the future, we will focus on overcoming the current limitations in handling large-unit-cell crystals and low-symmetry systems."

Comments #4: *An additional challenge to XRDSol that would demonstrate the effectiveness of the model is the ability to explicitly predict structures that present particularly thorny crystallographic challenges, such as (in)commensurate order, patterns that arise from mixtures of components, or patterns collected on poor quality samples with limited resolution. The authors' testing on Sr0.5Ca0.5TiO2N and Eu0.5Dy0.5TiO3 provides a starting point for modelling substitutional disorder (see comment on substitutional and positional disorder), however the model seems limited in that it does not explicitly predict random placement of Sr/Ca and Eu/Dy at otherwise chemically equivalent positions, which may be indicated by multiple closely related solutions that differ simply by atom identity at equivalent sites. Rather, XRDSol predicts a larger unit cell with the empirical formulas SrCaTiO4N2 and EuDyTi2O6. Can the authors comment on this distinction? Extending XRDSol to consider long range order and demonstrating that solutions are accurate for a larger variety of materials would warrant its use for structure prediction over manual solving methods and allow this work to stand among other machine learning based structure prediction algorithms.*

Response #4: Thanks for the insightful comments. As you pointed out, we agree with the importance of addressing complex crystallographic challenges such as (in)commensurate order, patterns that arise from mixtures of components, or patterns collected on poor-quality samples with limited resolution. We agree that improving the XRDSol's ability to solve these challenging cases would make it more useful. However, we also recognize that these issues represent significant

challenges. As a team dedicated to developing automated algorithmic frameworks for materials structural characterization, a common dilemma for us lies in balancing a model's fitting capacity with the risk of overfitting. Human experts leverage domain-specific expertise and accumulated empirical knowledge to make nuanced judgments when handling such tasks. Integrating these domain-specific knowledge into trainable machine learning architectures and ensuring reliable model outputs remain an inherently complex endeavor.

For the handling of substitutional disorder, our current XRDSol model cannot directly propose a structure solution containing sites with partial occupancy, as the reviewer correctly pointed out. The primary cause of this limitation comes from the constraints we imposed on the model. Specifically, XRDSol's training dataset (MP-20) exclusively comprises fully ordered structures, while atomic species and occupancies remain fixed during the denoising process. Consequently, XRDSol cannot directly propose crystal structures containing partial occupancy sites.

Despite this limitation, we showcase these two examples in the manuscript for two key reasons. First, even though our model was never exposed to partially disordered structures during training, it can still propose a structural model closest to the ground truth under certain constraints, demonstrating non-trivial extrapolation capability beyond its training domain. Second, we demonstrate that XRDSol's extrapolation ability enables it to generate physically reasonable starting models for disordered structures, which is an essential first step for the following refinement. Therefore, it can effectively assist (rather than fully replace) researchers in interpreting PXRD patterns of disordered structures.

In the future, we plan to lift the constraints on atomic species in the structural model, allowing XRDSol to propose structures with substitutional or positional disorder. Practically, this would require the model to be retrained on datasets containing partially disordered structures, which is probably beyond the scope of the current work. Nevertheless, we acknowledge that enabling the model to handle structures with disordering represents a critical direction for future improvement. We will add these features to XRDSol to handle a wider variety of materials in the future. We appreciate your feedback and will continue to improve XRDSol to address these challenges.

Comments #5: *We further highlight the importance of appropriate comparison to existing works. Authors claim to have "demonstrated that conditional equivariant generative model(s) can tackle the ab initio structure determination problem and provide high-quality structure models for inorganic crystalline materials" (ln 28-30). While XRDSol does provide structures with minimal input, neural networks are not ab initio methods. Rather, XRDSol is a data-driven model that*

"implicitly learns crystallographic knowledge" (ln 387-388). We believe that comparison to ab-initio and manual structure determination methods is inappropriate considering the existence of other machine-learning based structure prediction methods.

Response #5: Thank you for the comments. We agree that comparing our data-driven model to other machine-learning (ML) based structure prediction methods is more appropriate. We compared our XRDSol to two recent ML models for crystal structure solutions: CrystalNet (*npj Computational Materials*, 2024, 10, 209) and Crystalyze&StructSnap (*Journal of the American Chemical Society*, 2024, 146, 44, 30340–30348). CrystalNet uses PXRD patterns and chemical composition information as inputs. It achieves a success rate of 93.4% on simulated PXRD data of 737 test set, but only for cubic (500 samples) and trigonal (237 samples) crystal systems. Its inference time is under a minute per structure. Crystalyze&StructSnap is another ML model based on the CDVAE framework. It was tested on 1280 samples from the MP-20 test set (out of 9046 total samples) and achieved a success rate of 66.6%. While the paper of Crystalyze&StructSnap does not provide exact inference times and source code, it is inferred to be on the order of seconds to minutes based on the CDVAE framework. In comparison, our model achieves a success rate of 82.3% on the full MP-20 test dataset (9046 samples) with an inference time of 0.6 seconds per structure. This represents a scale advantage over the two approaches: CrystalNet (737 samples) and Crystalyze&StructSnap (1280 samples). While the results of these models vary depending on the datasets, our XRDSol model shows at least competitive performance in terms of success rate and speed. Moreover, our XRDSol has no crystal system restrictions and has solved the largest number of experimental PXRD patterns to date (912 structures, Fig. S11). We appreciate your suggestion to refine our comparison. We have added comparisons to these two ML models in the revised manuscript.

Comments #6: *We encourage the authors to continue to develop XRDSol. We are particularly encouraged by the highly accessible computational cost of XRDSol in comparison to other structure prediction approaches. We also believe that machine learning structure prediction is a promising area of development given the ability of a machine learning model to go beyond what can be done by manual human analysis. We provide the following comments as additional notes for the reference of the authors who we hope to see present a more robust demonstration of their structure prediction algorithm in future works.*

Response #6: Thank you for your encouraging feedback and for noting the computational cost of XRDSol. We appreciate your helpful suggestions for improving XRDSol. For example, XRDSol

can be designed to solve high-energy materials and improve the performance of low-symmetry structures. Furthermore, your comments also helped us identify why some cases are harder to solve. We noticed that the success rate decreases when the unit cell has more atoms or when the symmetry is lower. Your suggestion to look into how different space groups influence results is also very useful. This will guide us to incorporate more crystallography domain knowledge (e.g., space groups) into XRDSol. Thank you again for your suggestions. Your feedback will help us improve the XRDSol in the future.

Comments #7: *Authors refer to how in a PXRD experiment "the three-dimensional atomic spatial information is compressed into one-dimensional spectra" (ln 50-51). The result of a PXRD experiment is a pattern not a spectrum. Similarly, the use of Rcos as a metric is not standard, and this variable should be defined in the manuscript.*

Response #7: Thank you for your valuable comments. We realize that calling the result of a PXRD experiment a "spectrum" is incorrect. It should be called a "pattern". We have corrected this in the revised manuscript. About the term R_{cos}, we understand it is not commonly used and needs to be explained better. In the Method section, we have now added a detailed description of R_{cos}. The R_{cos} is a measure of similarity between the original XRD patterns and reconstructed XRD patterns of related solved crystal structures.

Action #4: The descriptions of R_{cos} have been provided in the revised manuscript as follows:

(Paragraph 1 of Page 23 in the revised Manuscript)

"R_{cos} is based on cosine similarity, which measures the similarity of two vectors (*npj Computational Materials*, 2023, 9, 135). In this work, the two vectors are the original XRD pattern and reconstructed XRD patterns of related solved crystal structures, respectively. The cosine similarity is calculated as the cosine of the angle between the vectors. The value ranges from -1 to 1, where - 1 means completely dissimilar, 1 means completely similar, and 0 means no correlation."

Comments #8: *Authors claim that XRDSol can provide a crystal structure in an average time of 0.6 seconds (ln 103). We suggest a comment on the distribution of run times for XRDSol or a figure demonstrating this distribution. A demonstration of consistent fast structure generation provides confidence in the computational cost of XRDSol that is a point of strength for this work.*

Response #8: Thank you for your critical and valuable comments. We appreciate your suggestion

to provide more details on the distribution of run times for XRDSol to strengthen the confidence in the computational cost of our model. To illustrate the computational efficiency of XRDSol, we conducted a statistical analysis of the distribution of run time across 71 batches using the MP-20 test dataset (9046 samples, batch size = 128). As shown in Fig. S2, i.e., Fig. R1-3, XRDSol takes an average of 0.57 seconds (about 0.6 seconds) to solve each crystal structure from XRD patterns when running on a single NVIDIA V100 GPU. The runtime ranges from 0.48 to 0.67 seconds, with a standard deviation of 0.04 seconds. This detailed distribution of run times underscores the efficiency of XRDSol as a key strength of our work. Thank you again for your insightful suggestion.

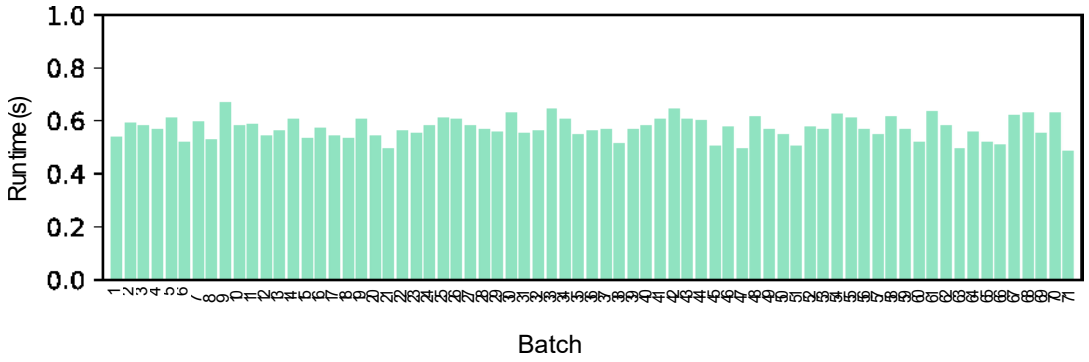

Fig. R1-3 Distribution of run times in 71 batches (MP-20 test dataset (9046 samples), batch size = 128) for XRDSol.

Comments #9: *Authors claim that XRDSol performs well in systems with chemical disorder (ln 113). While this claim is based on the predicted structures of Sr0.5Ca0.5TiO2N and Eu0.5Dy0.5TiO3, we suggest clarifying that the model performs in crystals with substitutional disorder as opposed to positional disorder within the unit cell. Additionally, we believe that the future development of XRDSol should include a more robust treatment of disordered structures. The standard representation of disorder is not multiple unit cells each with one possible microstate of the disordered crystal, but rather a single unit cell that has a specified variation at a certain position that corresponds to the relevant disorder. A model that generates multiple unit cells containing different microstates of a disordered position does not accurately depict the symmetry of the crystal and does not address either the dynamics or the site-to-site variation of the material.*

Response #9: Thank you for your helpful comments about the chemical disorder in XRDSol. We acknowledge our XRDSol currently addresses substitutional disorder rather than positional disorder within the unit cell. To make it clearer, we have revised line 113 to explicitly state that XRDSol performs well in systems with substitutional disorder. We appreciate the Reviewer's

suggestions about the disorder representation, which is essential for the future development of XRDSol. Solving disorder structures from XRD patterns using a generative model remains a challenge and we consider this an important research goal for our future work. Further details on the topic have been provided in **Response #4**.

Comments #10: *Authors attribute uncharacteristically low Rcos values for NaSrPO4 to low phase impurity and a highly textured sample (ln 355-356). Further, authors attribute the absence of predicted peaks in the MnO2 observed pattern to Rietveld refinement failure (ln 364-365). We suggest providing a reference that justifies these statements in the relevant system or a chemically similar system.*

Response #10: Thank you for your comments. In our original manuscript, we cited references for $NaSrPO_4$ and MnO_2 crystal structures. Specifically, for $NaSrPO_4$, we refer to Reference 42 (*Canadian Mineralogist*, 2005, 43, 1521-1526), and for MnO_2, we refer to Reference 43 (*American Mineralogist*, 2004, 89, 969-975) and 44 (*Acta Crystallographica Section B*, 1968, 24, 1233-1236). These references were placed in the section discussing crystal structures rather than specifically in the XRD analysis. To link these references to the XRD analysis, we have added citations above in the section discussing the XRD analysis of the revised manuscript.

Responses to Reviewer #2:

Comments #0: *I co-reviewed this manuscript with one of the reviewers who provided the listed reports. This is part of the Nature Communications initiative to facilitate training in peer review and to provide appropriate recognition for Early Career Researchers who co-review manuscripts.*

Response #0: We thank the Reviewer for the co-reviewed comments.

Responses to Reviewer #3:

Comments #0: *The authors*

- developed a conditioned diffusion model based on an equivariant graph neural net

- trained it on MP20 (~45k structures with simulated data, 9k held out for testing) and ICDD20 (~1000 structures with experimental data).

- conditioned it on simulated x-ray powder diffraction data

- the model is able to predict atomic structures given a powder diffraction pattern.

To summarize my assessment of this manuscript:

- the paper started very slowly, reading a little bit the way I would expect a computer scientist explaining materials science to a materials scientist. However, later it got much better with quite detailed descriptions of structures from different materials classes. I strongly recommend to get rid of most of the introduction and get right to the point.

Response #0: We thank the Reviewer for the comments and assessment of our work. Following the suggestion to be more concise, we have removed certain sections from the introduction in the revised manuscript. This revision allows us to present our key points more directly.

Comments #1: *This work is quite similar to a related paper on arxiv: arXiv:2406-10796. It is nature policy that papers in preprint servers cannot be used to assert precedent, so the existence of the arxiv paper should not affect whether the current manuscript is accepted. However, it would seem appropriate to cite that paper (and possibly place the current work in context of that work).*

Response #1: Thank you for the comments regarding the similarity between our work and the related paper on arXiv (*arXiv:2406-10796*). We agree that the paper on arXiv is relevant to our work. We have now cited the paper (*arXiv:2406-10796*) in the Introduction section of our revised manuscript. Furthermore, we have taken this opportunity to place our work in the context of the paper on arXiv.

Moreover, we have observed that while the PXRDnet model assesses solution correctness based solely on XRD fitting R_{wp}, our experience suggests that this approach can sometimes produce solutions with similar PXRD patterns but different structures, particularly when atoms with similar atomic numbers (Z) are interchanged. This insight has guided our methodology, leading us to incorporate supplementary validation techniques to enhance the reliability of our structure determinations.

Action #1: To acknowledge the related paper on arXiv, the descriptions of their PXRDnet model have been provided in the revised manuscript as follows:

(Paragraph 2 of Page 5 in the revised Manuscript)

"Recently, Lipson *et al*. proposed a generative diffusion model, PXRDnet, to determine the crystal structures from nanocrystalline powder diffraction patterns. This approach addresses the challenge of peak broadening effects due to nanosize crystallites, and solved 200 structures of varying symmetry and complexity from simulated nanocrystalline PXRD patterns."

Comments #2: *The problem the current authors tackled was, given a known unit cell and composition, what are the fractional coordinates of the atoms in the unit cell. This is justified on the basis that the indexing of the diffraction pattern to get the unit cell information is straightforward. This is not completely unreasonable, but in many interesting cases it is actually not super straightforward to get the unit cell for powder patterns, especially when the unit cell is larger (not considered in this work). This is a limitation of the broader applicability of the current work.*

Response #2: Thank you for the insightful comments. We fully agree that in many interesting cases, it is not super straightforward to get the unit cell for powder patterns, especially when the unit cell is larger. To improve the clarity of our discussion, we have revised the corresponding statement in the manuscript as follows:

(Paragraph 2 of Page 6 in the revised Manuscript)

"Solving crystal structures from PXRD patterns typically begins with determining lattice parameters and identifying space group, both of which are relatively straightforward tasks if the pattern has reasonable resolution and especially when the unit cell is not large."

We are currently working on an improved version of XRDSol to infer the unit cell information directly from PXRD patterns, rather than providing them as inputs. As far as we currently know, lifting such constraints makes it more difficult. Regarding the broader applicability of our model XRDSol to larger unit cells, we recognize the current limitations and outline the following three methods for future improvement:

(1) Enhancing unit cell indexing for large structures: Our model XRDSol can be integrated with more advanced indexing algorithms to improve the determination of lattice parameters for large unit cells.

(2) Dataset generation and model training for large crystal structures: Our model XRDSol

was trained on the MP-20 dataset, which is the benchmark dataset for the machine learning approach in the material community. The MP-20 dataset consists of crystal structures with up to 20 atoms per unit cell. As a result, our model is currently constrained to the structures within this atom number range. To extend its applicability, generating a sufficiently large dataset (on the order of tens of thousands) of crystal structures with large unit cells can enable the model to learn and generalize to these more complex cases.

(3) Incorporating domain knowledge in XRD crystallography: Within our current framework, incorporating additional crystallographic domain knowledge (e.g., space group information) can aid in structure determination for larger unit cells. For a given space group, once the special and general Wyckoff positions are identified, the model only needs to predict the general Wyckoff positions. This approach can be particularly beneficial for large crystals, especially those with high symmetry. A very recent work in this direction is WyckoffAUGen (Rees Chang *et, al.* Crystal Generative Modeling with Explicit Autoregressive Conditional Likelihoods and Nontrivial Space Group Stabilizers, *ICLR*, 2025). The WyckoffAUGen integrates hard space group constraints into a generative model, which enables more efficient and physically plausible crystal structure prediction.

Comments #3: *This is a significantly simplifying assumption because it results in the Bragg peaks being in the right positions and the model simply changes the intensities of the peaks when it atoms around. It gives a subjective impression that the model is working better than it is because the Bragg peaks are all in the right locations, but close inspection of the figures shows that even "successful" solutions have the intensities that don't match. It is not so clear that a crystallographer would be satisfied with these structure solutions. This is expanded on a bit below.*

Response #3: Thank you for your insightful comments. We acknowledge that our assumption of fixed lattice constants simplifies the structure determination problem by ensuring Bragg peaks are correctly positioned, with peak intensities adjusted solely through atomic movements (though peak distinction may occur when some atoms occupy special positions).

In the experimental XRD patterns, such as those from the ICDD database, peak intensities are influenced by more than just atom type and positions (as assumed in our approach). Additional variables, including temperature effects, absorption effects, preferred orientation, crystallite size, and instrument settings, also play significant roles. These extra influences may explain why some predicted structures look reasonable but still have intensity mismatches. As the reviewer suggests

in the following comment #5, using Rietveld refinement as a post-processing step can help fine-tune the predicted crystal structures. This can improve how well the simulated XRD patterns of predicted structures match the experimental XRD patterns. We have included the representative refined structure in the comment #5 section below to show these improvements.

While the fixed lattice constant assumption is a simplification, pairing our model with Rietveld refinement offers a practical approach to producing structure solutions that better align with crystallographic standards. We are grateful for your critique, which has helped us refine our methodology and clarify these points.

Comments #4: *These authors did a decent job of assessing the outcomes of their studies. In common with most studies in this domain they faced the challenge of determining some way of assessing whether a structure was successfully solved or not. They used standard methods (Rcos of the initial and final diffraction pattern) and similarity tools. I wasn't able to find the MaxDist measure so not sure how it works (I looked in the reference that was cited and it doesn't seem to appear in that paper, or I couldn't find it anyway). This should be addressed.*

Response #4: We thank the Reviewer's comments on the assessment of our results. Regarding the MaxDist measure, we acknowledge the oversight in providing a clear reference. **MaxDist** refers to the **maximum root-mean-square (RMS) displacement** between two structures (Ground truth structure and reconstructed structure in this work), normalized by the average free length per atom. The maximum root-mean-square (RMS) displacement is the maximum distance between all paired atomic sites between two structures. If the MaxDist falls below a specified site tolerance (stol; stol = 0.5 in this work) (Tian Xie *et, al.* Crystal Diffusion Variational Autoencoder for Periodic Material Generation, *ICLR*, 2022), the two structures are considered as match. Specifically, the MaxDist is calculated by the StructureMatcher class in Pymatgen module (*Computational Materials Science*, 2013, 314-319), where the fit function compares the MaxDist against a specified site tolerance (stol = 0.5). If the MaxDist is less than stol, the fit function returns True, indicating a successful match.

Action #2: The detailed explanation and reference to the MaxDist metric have been provided in the revised manuscript. Specifically, we have expanded the description of the StructureMatcher usage in evaluating the success rate. The revised text now is provided as follows:

(Paragraph 1 of Page 24 in the revised Manuscript)

"Furthermore, we used StructureMatcher in Pymatgen (*Computational Materials Science*, 2013,

314-319) to evaluate the success rate by calculating the maximum root-mean-square displacement (MaxDist) between the structures. The fit function in StructureMatcher compares the normalized MaxDist against the specified site tolerance (stol). If the MaxDist is less than stol (stol = 0.5), the fit function returns True, indicating a successful match."

Comments #5: *In general, the structure solution field needs better measures of when structures are successfully solved. The problem with this is that there is disagreement even among crystallographers about the exact definition. For example, an Rcos of 0.899 sounds pretty good (almost 90% good!), but a crystallographer looking at the powder patterns in figure S7 of the supplementary would be pretty surprised with how bad it is. Clearly wrong. Even the Rcos of 0.974 in figure S2 has a bunch of problems. These could possibly be fixed by a final Rietveld refinement step, which was not done by these authors, but this would normally be part of a minimal requirement from a crystallographer.*

Response #5: Thank you for your insightful comments. We agree that the field of structure solution needs more robust and universally accepted metrics to determine when a structure is successfully solved. Numerical measures like R_{cos} alone, while useful, often do not fully capture the accuracy of a solution. We also agree that Rietveld refinement can help improve the final crystal structures. Fig. S2 (HoGeAg) and Fig. S7 (NbP) highlight the similarity of powder XRD patterns between incorrect ICSD structures and our more plausible structures. Since the XRD patterns come from the simulated XRD pattern based on **incorrect** ICSD crystal structures, we sought to obtain the experimental XRD patterns of the HoGeAg and NbP to enable more meaningful refinement. However, the HoGeAg was originally determined by neutron diffraction rather than XRD, and the XRD data of NbP from the original publication in 1954 consists of low-precision peak intensities which are unsuitable for refinement. Therefore, we did not refine these proposed structures by XRDSol in Fig. S2 and Fig. S7.

To show the benefit of doing Rietveld refinement, we applied Rietveld refinement to an experimental XRD pattern from the ICDD database. We chose Li_2SrGeO_4 (Fig. S13) as an example. The crystal structure of Li_2SrGeO_4 was refined with GSAS-II software (Fig. R2-1b). The refined Li_2SrGeO_4 crystallizes in the space group $P3m1$. The refinement converged with factors: R_{wp} = 14.67%, R_{exp} = 10.05%, and χ^2 = 2.12 (Fig. R2-1b), indicating a good fit quality between the experimental and calculated diffraction patterns. This represents a substantial improvement over the fit quality without Rietveld refinement (Fig. R2-1a). We noticed that the R_{wp} is not sufficiently low. This may be attributed to the fact that the XRD pattern used in the refinement was simulated

from an experimental XRD stick pattern. So the XRD pattern lacks background and noise, which are typically present in the experimental XRD data. The absence of these features leads to higher R_{wp} in the refinement process (*Powder Diffraction*, 2006, 21, 67-70). The refined Li_2SrGeO_4 structure exhibits only minor adjustments in atomic coordinates compared to the Li_2SrGeO_4 proposed by our XRDSol.

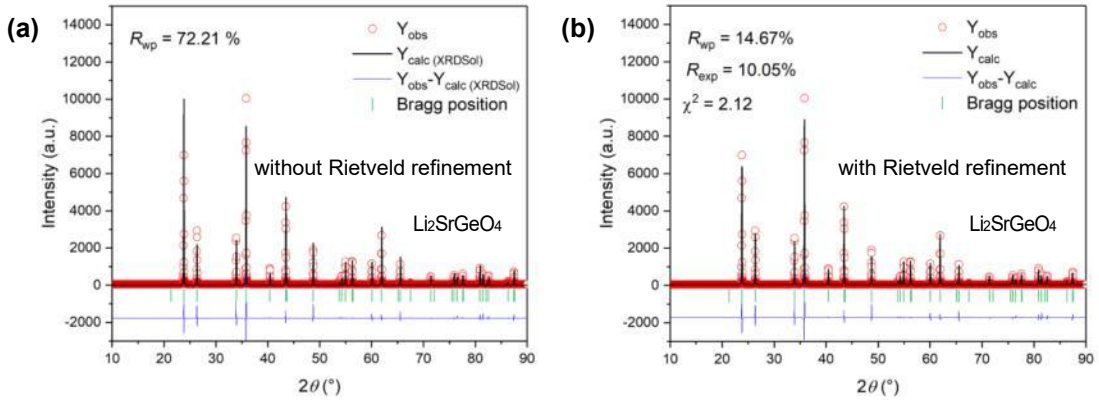

Fig. R2-1 Comparison of observed and calculated XRD patterns for Li_2SrGeO_4, (a) without and (b) with Rietveld refinement.

Comments #6: *I did like that the authors computed the formation energies using DFT and compared to the complex hull. It was very reassuring that the model was able to find on hte whole low energy solutions, and indeed some solutions that had lower formation energy than the reported ones. This gives good confidence that the diffusion model is learning structures that are energetically stable (it was trained on stable structures).*

Response #6: Thank you for the feedback on our DFT calculations and energy above convex hull analysis. We appreciate your recognition of the ability of our model XRDSol to identify low-energy solutions.

Comments #7: *They tested against experimental data with solved structures from ICDD and the model performed well in most cases. This is good.*

Response #7: We thank your positive comment regarding our model's performance against experimental ICDD data.

Comments #8: *They also used it to propose structure solutions from some experimental patterns*

that didn't have structure solutions proposed in the ICDD and the models performed well. It wasn't completely clear the inputs in this case. Was the stoichiometry known and input? And the number of formula units in the unit cell? This needs to be placed more prominently.

Response #8: Thank you for the comments. The experimental XRD patterns in the ICDD database that we used for structure proposals contained known lattice parameters, stoichiometry, and the number of formula units per unit cell. However, the corresponding atomic coordinates are not available. The input for solving the crystal structures used in this work includes **the target PXRD patterns, lattice parameters**, **number and type of atoms**.

Action #3: To ensure clarity and highlight the model's inputs more prominently, the related description has been provided in the revised manuscript:

(Paragraph 2 of Page 15 in the revised Manuscript)

"The input for solving these entries includes known target PXRD patterns, lattice parameters, number and type of atoms."

(Paragraph 2 of Page 22 in the revised Manuscript)

"The target PXRD patterns, lattice parameters, number and type of atoms are already known and used as the inputs of XRDSol."

Some comments on the validity and areas for improvement are:

Comments #9: *if the model architecture was built from or inspired by or reused architecture from the literature I encourage the authors to mention this in the methods section where the model is described. I would be a bit surprised if it were not built off an existing one or ones because this structure is quite similar to CDVAE for example (ref 12 in the current manuscript). It is ok to admit where the inspiration came from and what was reused. It gives correct credit to prior workers. This needs to be fixed before publication.*

Response #9: Thank you for the comments. Our model was inspired by CDVAE (Tian Xie *et, al.* Crystal Diffusion Variational Autoencoder for Periodic Material Generation, *ICLR*, 2022), and its architecture was built upon existing works, including EGNN (*PMLR*, 2021, 139, 9323-9332), CDVAE (Tian Xie *et, al.* Crystal Diffusion Variational Autoencoder for Periodic Material

Generation, *ICLR*, 2022), and DiffCSP (*NeurIPS*, 2024, 36). These works were already cited in the main text of our original manuscript. In the revised manuscript, we have further explicitly mentioned these prior works in the Method section to provide proper credit and clarify the inspiration behind our model design.

Comments #10: *is it possible to show one or more schematics of the model architecture in a figure? this can be very helpful.*

Response #10: Thank you for the comments. We have drawn a figure to illustrate the model architecture (Fig. S22, i.e., Fig. R2-2). The related description was added in the revised manuscript.

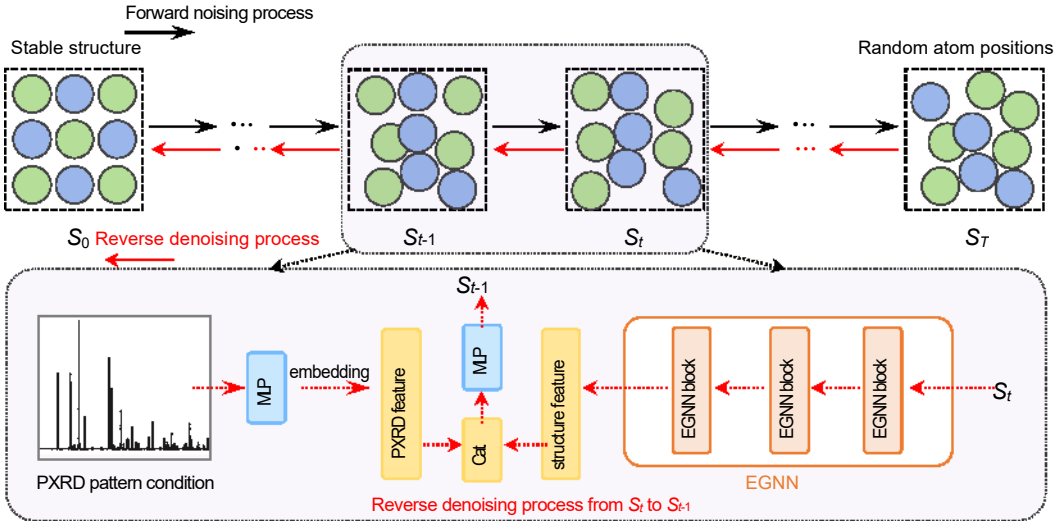

Fig. R2-2 Schematics workflow of the XRDSol.

Comments #11: *In the description of the model the L vector is described but I had to think hard to figure out it was the lattice vectors. Makes sense in hindsight (L) but please add a few words so that all the letters are fully defined in the place where they appear.*

Response #11: Thank you for the comments. We acknowledge that the description of the L matrix in the original manuscript could have been clearer. A more detailed description of L is now provided as follows:

(Method section in the revised Manuscript)

"where ***L*** represents the lattice vectors of a crystal structure in three-dimensional space, and the lattice parameters (a, b, c, α, β, and γ) are used to define the unit cell of the crystal lattice,"

Comments #12: *The work would benefit from better baselining. It was baselined against some non ML approaches that use evolutionary algorithms, For example, and the trained model was much faster (not a huge surprise). But can it be benchmarked against other ML models and simple models such as nearest neighbor models or something like that?*

Response #12: Thank you for the valuable feedback. We appreciate the suggestion to compare our model to other ML approaches. We compared our XRDSol to two recent ML models for crystal structure solutions: CrystalNet (*npj Computational Materials*, 2024, 10, 209) and Crystalyze&StructSnap (*Journal of the American Chemical Society*, 2024, 146, 44, 30340–30348). CrystalNet uses PXRD patterns and chemical composition information as inputs. It achieves a success rate of 93.4% on simulated PXRD data of 737 test set, but only for cubic (500 samples) and trigonal (237 samples) crystal systems. Its inference time is under a minute per structure. Crystalyze&StructSnap is another ML model based on the CDVAE framework. It was tested on 1280 samples from the MP-20 test set (out of 9046 total samples) and achieved a success rate of 66.6%. While the paper of Crystalyze&StructSnap does not provide exact inference times and source code, it is inferred to be on the order of seconds to minutes based on the CDVAE framework. In comparison, our model achieves a success rate of 82.3% on the full MP-20 test dataset (9046 samples) with an inference time of 0.6 seconds per structure. This represents a scale advantage over the two approaches: CrystalNet (737 samples) and Crystalyze&StructSnap (1280 samples). While the results of these models vary depending on the datasets, our XRDSol model shows at least competitive performance in terms of success rate and speed. Moreover, our XRDSol has no crystal system restrictions and has solved the largest number of experimental PXRD patterns to date (912 structures, Fig. S11). We appreciate your suggestion to refine our comparison. We have added comparisons to these two ML models in the revised manuscript.

Responses to Reviewer #4:

Strength:

Comments #0:

- The writing is good and easy to follow.

- This work is both interesting and novel. Unlike previous methods focused on accurate 3D reconstruction, this study explores the use of a diffusion model to approximate spatial structures.

- The adoption of a graph model to represent the spatial structure of XRD is intuitive and naturally lends itself to being extended and learned by the diffusion model.

- Compared with numeric methods (e.g., the DFT), the diffusion-based method is efficient with a significant speedup of at least 10,000x. The estimation accuracy under both the simulation and observation environment is also acceptable for further study of the crystal.

Response #0: We truly appreciate the Reviewer for the comments and thorough evaluation of our work. We have addressed the Reviewer′s questions point by point below.

Weakness&Questions:

Comments #1: *(1) Some algorithm details are not clear.*

(a) How is the graph initialized? Is any prior knowledge required? If not, could incorporating prior knowledge, such as partial spatial structures, improve prediction accuracy?

(b) How is the number of diffusion steps determined? Is it consistent across all crystals, or does it vary? Would increasing the number of steps consistently enhance performance?

(c) What is the detailed structure of the model used for the denoising process?

Response #1: Thank you for the comments.

(a) Graph Initialization and Prior Knowledge

The graph is initialized based on atomic positions and lattice information. Specifically, the edge construction follows a **fully connected graph**, where every atom in the unit cell is connected to every other atom. The edge features are defined as fractional coordinate differences between connected atoms. This method does not require explicit prior knowledge is required beyond the atom types, atom numbers, and lattice parameters. We agree that incorporating prior knowledge (e.g., partial spatial structures) could potentially enhance prediction accuracy. Partial spatial structures could serve as constraints to guide the model′s predictions and provide physical atomic

interactions. To verify this, we conducted a comparative experiment using trigonal crystal system as an example. Two versions were tested. One version used our current XRDSol model without any predefined partial spatial structures. The other version added prior partial spatial structures using Wyckoff site properties. In this setup, atom positions at general Wyckoff sites are unknown, but those at special Wyckoff sites were fixed. Thereby, we added partial spatial constraints. As shown in Fig. R3-1, using partial spatial structures improved accuracy to 90.5%, which is higher than the 77.4% achieved without such constraints. This result supports the reviewer's suggestion and gives us a solid direction for improving our model.

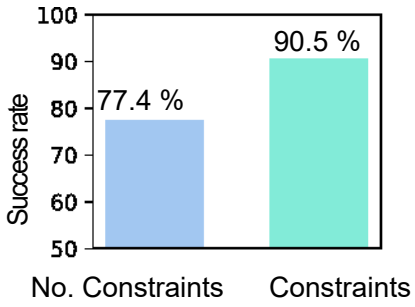

Fig. R3-1 Success rates of trigonal crystal system with or without constraints.

(b) Diffusion steps and their impact on the model's performance

In our model XRDSol, the number of diffusion steps is set to 1000, which is commonly used in the field (*NIPS*, 2020, 33, 6840-6851; *CVPR*, 2022, 10674-10685). The diffusion steps across all crystal structures are consistent. To assess the impact of the number of diffusion steps on the performance, we conducted experiments comparing different diffusion steps, including 500, 750, 1000, and 1250 steps. We investigated the different setups on 5 batches (batch size = 128) in the MP-20 test set. As shown in Fig. R3-2, the performance slightly improves with an increase in diffusion steps. However, further increasing the number of steps leads to a stable performance.

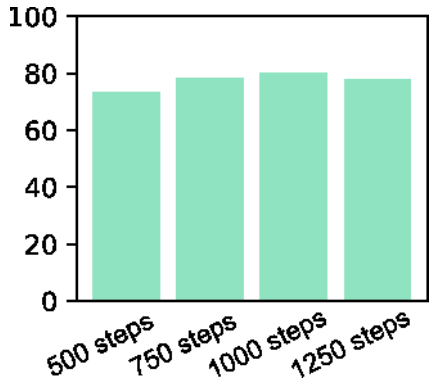

Fig. R3-2 Success rates in different diffusion steps, including 500, 750, 1000, and 1250 steps.

(c) Detailed structure of the denoising process

The detailed structure of the model XRDSol used for the denoising process has been shown in Fig. S22, i.e., Fig.R3-3. The reverse denoising process aims to reconstruct the original structure S_0 from S_T with random atomic coordinates. This is achieved using an equivariant graph neural network ϕ (EGNN) (*PMLR*, 2021, 139, 9323-9332). The EGNN predicts the noise to construct the desired samples. EGNN is a type of Graph Neural Network that satisfies the equivariance constraint. It ensures the reflection, translation, rotation, and mirror symmetries of crystal structures. The network operates on a fully connected graph G, where each node represents an atom with coordinates and features. The EGNN includes 3 EGNN blocks, each composed of equivariant convolutional layers. The noisy structure S_t is passed through the EGNN to extract structure features. And the structure features are concatenated with the PXRD features which are derived from the target PXRD pattern by using a neural network. Next, the concatenated features are fed into a neural network to predict the atomic coordinates of S_{t-1}. This process is repeated for 1000 steps and gradually restores the atomic coordinates from S_T to S_0 with the guidance of target PXRD patterns.

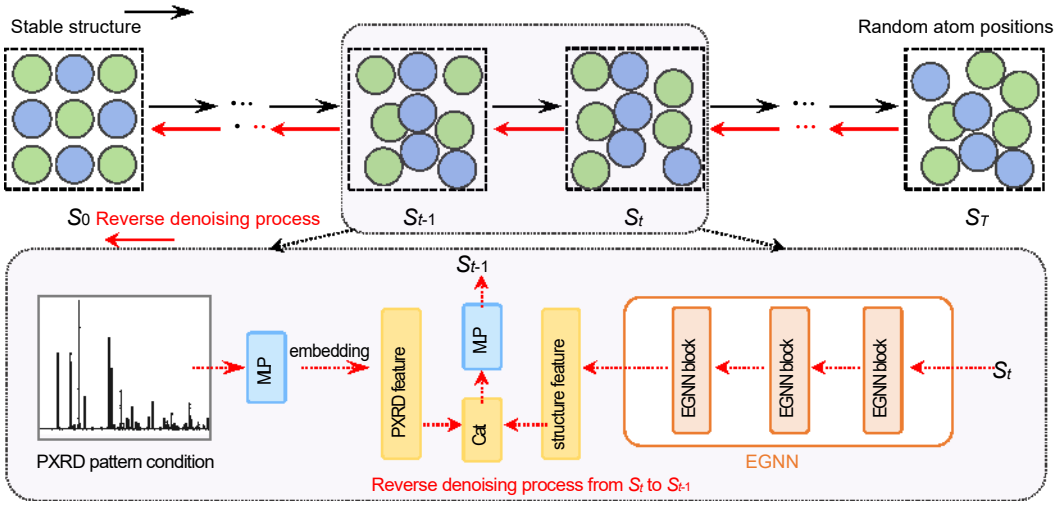

Fig. R3-3 Schematics workflow of XRDSol.

Comments #2: *The diffusion process involves inherent randomness. What is the statistical significance of the reported results, considering this randomness?*

Response #2: Thank you for the comments. We agree that the diffusion process in our model XRDSol involves inherent randomness, which can cause variations in the results. In this work, we have considered the impact of randomness. To quantitatively assess the impact of this randomness on crystal structure solution from powder XRD patterns, we conducted multiple runs per XRD pattern ranging from 1 to 50 times on the first batch (128 samples). Then we analyzed the effect of different run counts on the performance of structure determination. As shown in Fig. S20, the XRD matching score (R_{cos}) exhibited a rising trend as the number of runs increased from the 1st to the 25th run and then it stabilized in the range of 25 to 50 runs. The result indicated that after 25 runs, the impact of randomness on the final crystal structure solution becomes minimal. Therefore, for each XRD pattern in this work, we performed 25 independent runs using XRDSol to generate 25 potential crystal structures. We then rank these solutions based on R_{cos} and select the top-ranked solution (highest R_{cos}) as the final crystal structure for the given XRD pattern. This ranking-based selection ensures that the reported results are statistically stable and minimally affected by the inherent randomness of the diffusion process.

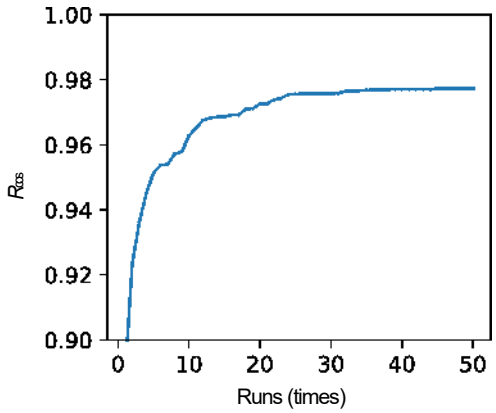

Figure S20. The R_{cos} are within 50 runs on the first batch (128 samples).

Comments #3: *Figure 2(b) shows examples with relatively low estimation accuracy. What distinguishes these "bad" examples from others? Do they share specific characteristics, such as belonging to a similar group? While the paper effectively highlights the success of using the diffusion model for accurate XRD predictions in most cases, it would be helpful to provide a more detailed analysis of these failed examples.*

Response #3: Thank you for the insightful comments. The "bad" examples, which exhibit relatively low estimation accuracy, tend to share two key characteristics:

(1) **A larger number of atoms in the unit cell**: The majority of these bad examples have a larger number of atoms. The MP-20 dataset used in this work contains compounds with up to 20 atoms per unit cell. As shown in Fig. R3-4a, the success rate remains above 96% when the atomic count is 7 or fewer. However, as the number of atoms increases, the success rate steadily declines, falling below 90%, and reaching as low as 50% for compounds with 17 atoms.

(2) **Low symmetry**: The accuracy of the diffusion model is also significantly affected by the symmetry of the crystal structure. As the symmetry decreases, the model's performance tends to degrade (Fig. R3-4b). Specifically, the success rate varies across the seven crystal systems with different symmetries (cubic 97.72%, hexagonal 90.33%, trigonal 77.86%, tetragonal 88.02%, orthorhombic 76.32%, monoclinic 68.91%, and triclinic 48.48%). Among these, the cubic crystal system shows the best performance with a success rate of 97.72%. In contrast, the triclinic system demonstrates the poorest accuracy, with a success rate of only 48.48%.

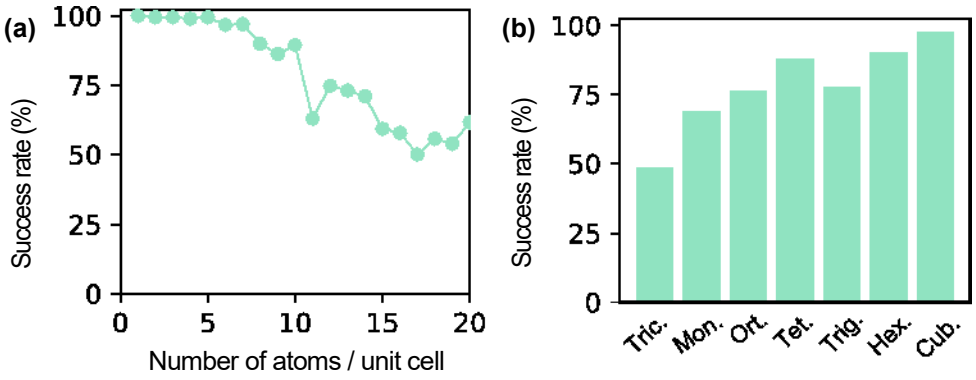

Fig. R3-4 (a) Variation in success rate as a function of atomic count in the unit cell. (b) Success rate across the seven crystal systems with different symmetries.

(Paragraph 2 of Page 19 in the revised Manuscript)

"In the future, we will focus on overcoming the current limitations in handling large-unit-cell crystals and low-symmetry systems."

Comments #4: *Does the number of cells affect estimation accuracy? Do different space groups exhibit similar accuracy trends?*

Response #4: Thank you for the comments. First, to investigate the influence of the number of cells on the estimation accuracy, we take the crystal structures with 6 atoms per unit cell as an example (Fig. R3-5). Specifically, we compared the success rates between 1×1×1 unit cell and 1×1×2 unit cell for the crystal structures. The success rate of 1×1×1 unit cell achieves 96.70%, while the success rate of 1×1×2 unit cell drops to 46.57%. This result indicates that increasing the number of cells (from 1×1×1 to 1×1×2) leads to a substantial decrease in estimation accuracy. Second, the accuracy varies across different space groups. In this work, we exclude those space groups with 10 or fewer samples in the MP-20 test dataset, which can provide a clearer picture of the accuracy trends across different space groups. As shown in Fig. R3-6, the accuracy varies across different space groups. Generally, space groups with higher symmetry tend to exhibit higher estimation accuracy. Specifically, 26 space groups achieved an accuracy of 100%, and 41 space groups had an accuracy greater than 90%. However, there are 6 space groups with accuracy lower than 50%, namely space groups 2, 19, 46, 51, 55, and 156. This suggests that symmetry plays a significant role in the model's ability to predict crystal structures accurately.

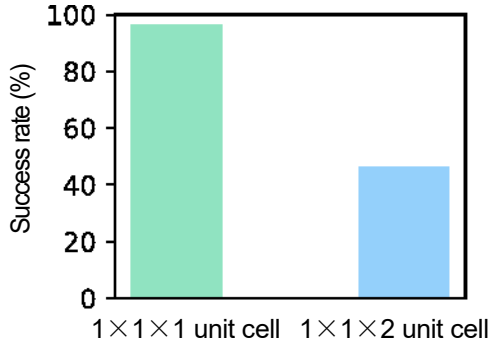

Fig. R3-5 Comparison of success rates between 1×1×1 unit cell and 1×1×2 unit cell for the crystal structures with 6 atoms per unit cell.

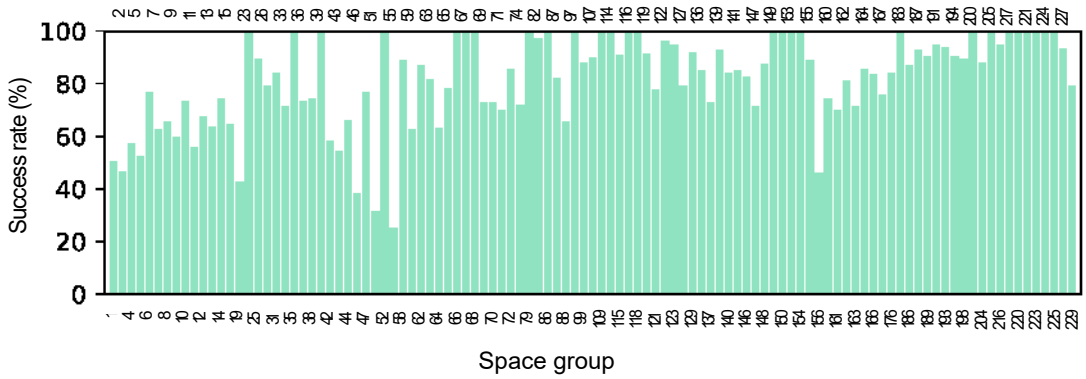

Fig. R3-6 Success rates across the 107 space groups.

Comments #5: *Is there any way to use DFT or something else to further refine the structure?*

Response #5: Thank you for the comments. In principle, using DFT to refine structures is feasible, but we do not expect it to yield satisfactory results. Structure optimization using DFT are typically performed at 0 K by minimizing system energy, ignoring temperature effects. Besides, the optimized structures depend on the choice of pseudopotentials, symmetry constraints, and other parameter choices. For instance, the commonly used PBE functional underestimates van der Waals interactions in layered structures, potentially leading to errors in interlayer spacing. Additionally, for ferromagnetic elements like Fe, Co, or Ni, different spin states can alter bond lengths. For cases where DFT cannot converge to a spin state consistent with the experiment, it will lead to incorrect bond lengths. Due to these limitations, we chose not to use DFT for further structural refinement.

We chose Rietveld refinement to refine the structures proposed by our XRDSol since Rietveld refinement can account for experimental effects (e.g., preferred orientation) while DFT cannot directly incorporate these real-world factors. We applied Rietveld refinement to an experimental XRD pattern from the ICDD database. As a representative example, we chose Li_2SrGeO_4 (Fig. S13) proposed by XRDSol in the ICDD database to demonstrate that the Rietveld refinement can further refine the structures. The crystal structure of Li_2SrGeO_4 was refined with GSAS-II software (Fig. R3-7b). The refined Li_2SrGeO_4 crystallizes in the space group $P3m1$. The refinement converged with factors: R_{wp} = 14.67%, R_{exp} = 10.05%, and χ^2 = 2.12 (Fig. R3-7b), indicating a good fit quality between the experimental and calculated diffraction patterns. This represents a substantial improvement over the fit quality without Rietveld refinement (Fig. R3-7a). We noticed that the R_{wp} is not sufficiently low. This may be attributed to the fact that the XRD pattern used in the refinement was simulated from an experimental XRD stick pattern. So the XRD pattern lacks background and noise, which are typically present in the experimental XRD data. The absence of these features leads to higher R_{wp} in the refinement process (*Powder Diffraction*, 2006, 21, 67-70). The refined Li_2SrGeO_4 structure exhibits only minor adjustments in atomic coordinates compared to the starting Li_2SrGeO_4 proposed by our XRDSol.

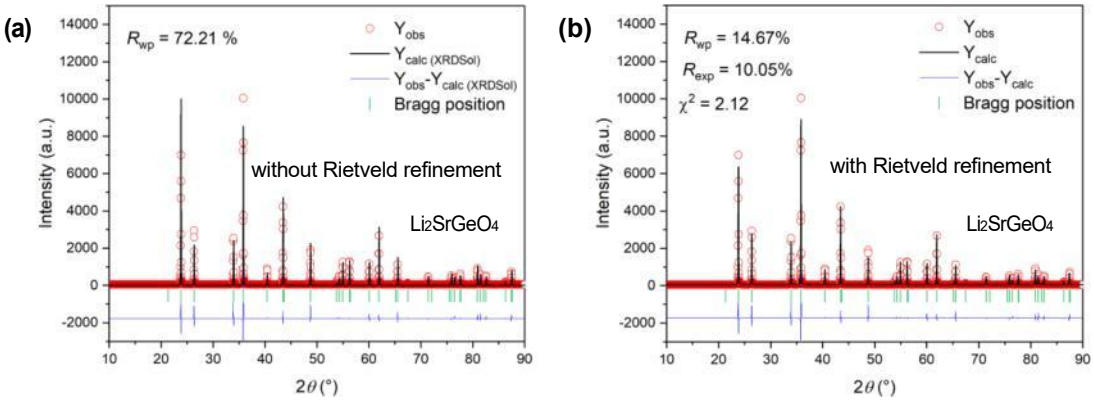

Fig. R3-7 Comparison of observed and calculated XRD patterns for Li_2SrGeO_4, (a) without and (b) with Rietveld refinement.

Comments #6: *It would be beneficial to include more details about the diffusion model to enhance clarity for the materials science community.*

Response #6: Thank you for the comments. A more detailed description of the diffusion model is now provided in the revised manuscript as follows:

(Method section in the revised Manuscript)

"The diffusion model is a generative model inspired by non-equilibrium thermodynamics. It includes a forward noising process and a reverse denoising process (Fig. S22). During the forward process, random Normal distribution noise is gradually added to the input data x_0 via T steps, thereby establishing a Markov chain $x_0 \rightarrow x_1 \rightarrow \cdots \rightarrow x_t \rightarrow \cdots \rightarrow x_T$. This noising process can be described by the transition distribution as $q(\boldsymbol{x}_t|\boldsymbol{x}_{t-1}) = \mathcal{N}(\boldsymbol{x}_t|\alpha_{t|t-1}\boldsymbol{x}_{t-1}, \sigma_{t|t-1}^2\mathbf{I})$, where the parameter α_t controls the amount of x_0 retained and σ_t controls the amount of noise added. For XRDSol, we perform diffusion on the atomic coordinates of the given structure $\boldsymbol{S}$, which defines a Markov chain $\boldsymbol{S}_0 \rightarrow \boldsymbol{S}_1 \rightarrow \cdots \rightarrow \boldsymbol{S}_t \rightarrow \cdots \rightarrow \boldsymbol{S}_T$. Due to the periodicity of stable crystal structures, we add wrapped Normal distribution noise $\mathcal{N}_W$ on the atomic coordinates to better model the periodic process. We define our forward process via transition distribution as $q(\boldsymbol{S}_t|\boldsymbol{S}_{t-1}) = \mathcal{N}_W(\boldsymbol{S}_t|\alpha_{t|t-1}\boldsymbol{S}_{t-1}, \sigma_{t|t-1}^2\mathbf{I})$. During the reverse denoising process, the equivariant graph neural network (EGNN) ϕ predicts the noise to construct the desired samples. EGNN is a type of Graph Neural Network that satisfies the equivariance constraint. In this work, the graph is initialized by a fully connected graph G based on atomic positions and lattice parameters. Each node is endowed with coordinates as well as features. The edge construction follows a fully connected graph G, where every atom in the unit cell is connected to every other atom, forming a fully connected graph. The edge features are defined as fractional coordinate differences between connected atoms. In this setting, EGNN consists of 3 EGNN blocks, each composed of equivariant convolutional layers. The noisy structure S_t is passed through the EGNN to extract structure features. And the structure features are concatenated with the PXRD features which are derived from the target PXRD pattern by using a neural network. Next, the concatenated features are fed into a neural network to predict the atomic coordinates of S_{t-1}. This process is repeated for 1000 steps and gradually restores the atomic coordinates from S_T to S_0 with the guidance of target PXRD patterns. We define the reverse denoising process via transition distribution as $p(\boldsymbol{S}_{t-1}|\boldsymbol{S}_t) = \mathcal{N}_W(\boldsymbol{S}_{t-1}|\phi(\boldsymbol{S}_t), \sigma_{t\rightarrow t-1}^2\mathbf{I})$. To solve crystal structures conditioned on given XRD patterns C, we input the XRD condition along with atomic coordinates into the neural network to guide the correct placement of atoms. The final denoising process was defined as $p(\boldsymbol{S}_{t-1}|\boldsymbol{S}_t, C) = \mathcal{N}_W(\boldsymbol{S}_{t-1}|\phi(\boldsymbol{S}_t, C), \sigma_{t\rightarrow t-1}^2\mathbf{I})$."

Remarks on code availability:

Comments #7: *The code is open-source with all data available, with good instructions to reproduce the results.*

Response #7: Thank you for the evaluation of our code.

Responses to Reviewer #5:

Comments #0: *I co-reviewed this manuscript with one of the reviewers who provided the listed reports. This is part of the Nature Communications initiative to facilitate training in peer review and to provide appropriate recognition for Early Career Researchers who co-review manuscripts.*

Response #0: Thank you for the co-reviewed comments.

Remarks on code availability:

Comments #1: *The code is clean and organized. The instructions are clean to install the software. The data is also available.*

Response #1: We appreciate your evaluation on the code and instructions.

Responses to Reviewers

(*Black italic: Reviewer's comments*; Black type: Our response; Blue type: Key revisions)

Responses to Reviewer #1:

Comments #0: *This revised manuscript details a particularly fast ML informed tool for predicting atomic positions given a PXRD pattern and unit cell data. As was noted by multiple reviewers, this paper exists in a somewhat strange intermediate space between computer science and chemistry. From a chemistry perspective, it is not written in a way to convince the field that this would be useful, although the point made about autonomous materials discovery and the particularly time efficient nature of this tool is a compelling one that should be centered in the introduction (rather than a general overview to crystallography). Although I find the manuscript improved upon revision in terms of clarity and better defining the tool developed, by not significantly revising the manuscript to address the source of reviewer comments, it still seems like a computational tool was developed first and a chemical problem was searched for second. It remains unclear what chemical problem is actually being solved, and the question remains how the authors envision it will be used? Can the authors include a demonstration/provide an example of how it can be implemented completely autonomously? Or how the process of correcting a database would be performed (it is not stated how the potentially incorrect ICSD structures were identified, or can an entire database be screened at once?). I find this issue embodied by the lack of chemical analysis presented in the discussion section, which is too speculative in ways that are not specific enough to bridge the disconnect.*

Response #0: We truly appreciate your thorough evaluation and the opportunity to clarify the chemical relevance of our work. We fully recognize the importance of clearly articulating the chemical problem. To address concerns regarding the lack of chemical focus, here we provide a detailed description of how our XRDSol can be used for the inspection and correction of entries in large-scale inorganic structural databases.

Demonstration of the inspection and correction of structural databases (e.g., ICSD)

In response to the reviewer's request for a concrete example of a quality control step for entries in structural databases, we have added more details in the Results and Supplementary Information that describe a complete workflow for screening and correcting potentially incorrect database entries.

In the original manuscript, we indeed conducted a systematic screening and correction of the ordered structures of the ICSD database. The workflow is shown in Fig. S7a, i.e., Fig. R1-1a. We began by collecting **ordered structures** from ICSD (Table S2, i.e., Table R1), which

are available through the Materials Project database. All of them are ordered structures (**49283 structures**), and with DFT-calculated energy above the convex hull (E_{hull}) available. We screened these entries for ones with poor thermodynamic stability (high E_{hull}). We set the E_{hull} threshold to 0.1 eV/atom, which is a commonly used criterion for assessing thermodynamic stability. Crystal structures with high E_{hull} values (> 0.1 eV/atom) were identified as high-energy structures that are potentially erroneous.

Due to the architectural constraints of our XRDSol model (limited to primitive cells containing 20 atoms or fewer), we filtered these high-energy structures accordingly, yielding **3,122 candidate structures for re-evaluation**. For each of them, we simulated the powder XRD patterns based on the available structure and extracted the lattice parameters and the number and type of atoms. They are used as inputs for XRDSol. XRDSol then predicted the atomic coordinates to reconstruct the crystal structures. Among the resulting predictions, **1429 proposed structures differ from the original ICSD structures** (Table R1). Within this subset, **588 structures** exhibited good agreement with the target simulated XRD patterns ($R_{cos} > 0.9$) and were selected to perform further DFT calculations. Only those candidates that exhibit both low E_{hull} and high XRD matching quality were retained as plausible corrected structures for manual inspection. Finally, **39 high-confidence corrections** that we report in the original manuscript are identified (Table R1).

It is worth noting that within the 588 structures with good XRD agreement, some still have E_{hull} values exceeding 0.1 eV/atom. Although these might be classified as unstable by strict thermodynamic standards, they may still represent valid metastable or experimentally realizable phases. Nevertheless, to uphold rigorous crystallographic standards, we conducted manual inspections and extensive literature reviews. As a result, only the 39 most reliable corrected structures are presented in the manuscript. The remaining candidates, while promising, will require further experimental validation or manual inspection to confirm their correctness and chemical plausibility.

Another issue worth noting is that we used simulated PXRD patterns based on available ICSD entries. Ideally, it would be better if we could use the original PXRD patterns, which are unavailable from ICSD, since the simulated PXRD pattern may also be problematic if the structures are potentially incorrect.

Case study: $CsIO_3$ (ICSD-33665)

We illustrate this process using $CsIO_3$ (ICSD-33665) reported in 1928 from the ICSD database as an example (Fig. S7b, i.e., Fig. R1-1b). In this early study, $CsIO_3$ was reported to be a covalent perovskite material with a cubic perovskite structure in the $Pm\bar{3}m$ space group, where Cs occupies the six-coordinate B-site. The calculated E_{hull} of this original structure (ICSD-

33665) is extremely high at 1.97 eV/atom, which strongly suggests an incorrect atomic arrangement. We simulated the corresponding XRD pattern and extracted the lattice parameters and the number and type of atoms based on the originally reported $CsIO_3$ structure. We used these as inputs to XRDSol. 5 atoms (1 Cs, 1 I, and 3 O atoms) with random atomic coordinates were initialized in a primitive cell ($a = b = c = 4.67$ Å, $\alpha = \beta = \gamma = 90°$). XRDSol then predicted atomic coordinates to reconstruct the $CsIO_3$ crystal structure. In the $CsIO_3$ structure proposed by XRDSol, the larger Cs cations are moved to the twelve-coordinate A-sites. Subsequent DFT calculations confirmed the thermodynamic stability of this solution with a significantly lower E_{hull} of 0.02 eV/atom. Moreover, the structure solution is very close to the experimentally resolved single-crystal structure of $CsIO_3$ (*Chemistry of Materials*, 2018, 1136-1145). The

study clarified that the earlier assignment of *Pm3 m* space group in 1928 using powder X-ray diffraction was inaccurate. Thus, this case demonstrated XRDSol's capability to identify and correct some suspicious structure reports.

Furthermore, we believe our work goes beyond merely providing a new tool for chemistry or materials science. Rather, this study is inherently interdisciplinary, spanning chemistry, materials science, and computer science. As AI for chemistry and materials science is an emerging and rapidly evolving field, the terminology in this interdisciplinary domain is less mature and well-defined compared to established fields like crystallography. Therefore, we strive to describe our work in language accessible to researchers across all these disciplines. We have also included a more detailed discussion in the Introduction section of the main text about the advancements of AI tools in crystal structure generation and PXRD analysis to better position our own work within the context of community progress as follows:

(Introduction in the revised Manuscript)

"Recently, machine learning approaches, particularly generative diffusion models, have provided a new paradigm for materials structure generation. Xie et al. built the Crystal Diffusion Variational Autoencoder (CDVAE), which employs score matching to generate realistic crystal structures by learning from the data distribution of known stable materials (Tian Xie et, al. Crystal Diffusion Variational Autoencoder for Periodic Material Generation, *ICLR*, 2022) . Without any predefined prototypes, CDVAE shows its ability to generate valid and diverse crystal structures that captures the physical inductive bias of material stability."

"Equivariant diffusion can effectively preserve reflection, translation, rotation, and mirror symmetries, enabling generation of physically reasonable crystal structures. Such equivariant denoising models were employed to generate inorganic crystal structures and molecules, and showed remarkable performance. Besides generating crystal structures without constraints, conditioning diffusion models allow crystal generation with desired chemistry, mechanical,

electronic, or magnetic properties, paving the way towards generative AI-assisted materials design paradigms."

"Recently, Lipson et al. proposed a generative diffusion model, PXRDnet, to determine the crystal structures from nanocrystalline powder diffraction patterns. This approach addresses the challenge of peak broadening effects due to nanosized crystallites, and solved 200 structures of varying symmetry and complexity from simulated nanocrystalline PXRD patterns. Consequently, the conditional equivariant diffusion model holds tremendous potential for determining atomic coordinates under PXRD pattern conditions."

Table R1-1. The statistics of solved entries in ICSD.

Structures	Number
Ordered structures in the ICSD database	49283
Potentially incorrect structures with unit cell ≤ 20 atoms (E_{hull} > 0.1 eV/atom)	3122
XRDSol proposed structures that differ from the original ICSD structures	1429
XRDSol proposed structures that show good XRD match (R_{cos} > 0.9)	588
XRDSol proposed structures that show low energy (E_{hull} < 0.1 eV/atom)	39

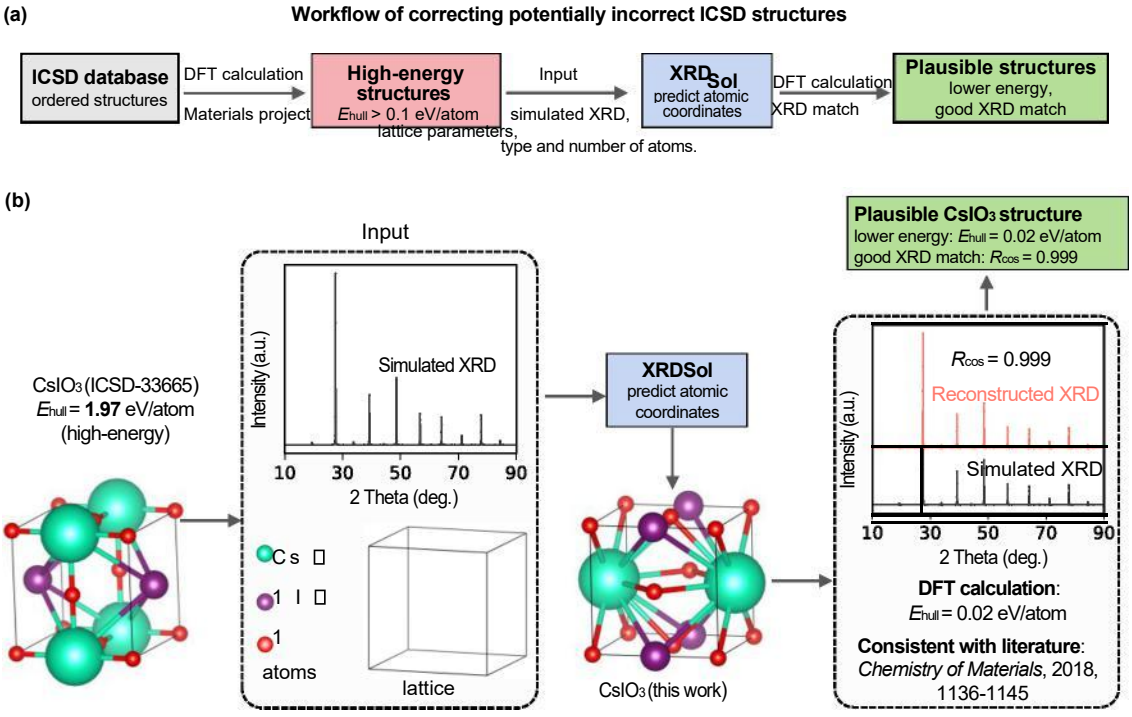

Fig. R1-1 (a) Workflow of XRDSol as the inspection and correction for entries in ICSD. (b) Illustration using $CsIO_3$ (ICSD-33665) from the ICSD database as an example.

Responses to Reviewer #2:

Comments #0: *I co-reviewed this manuscript with one of the reviewers who provided the listed reports. This is part of the Nature Communications initiative to facilitate training in peer review and to provide appropriate recognition for Early Career Researchers who co-review manuscripts.*

Response #0: We thank the Reviewer for the co-reviewed comments.

Responses to Reviewer #3:

Comments #0: *The authors have worked hard to address my comments, but I still feel that they fall somewhat short. I am not sure if they have a professional crystallographer among the authors, but tha paper still lacks insights that I would expect from such a person, and since the paper is really about developing a tool for crystallographers to do their crystallography, this is a significant shortcoming. A reading of the comments of the other referees and the author responses doesn't do anything to allay this impression. With that said, the paper is greatly improved from the original version. I focus primarily on responses to my comments.*

Response #0: We thank the Reviewer for the thoughtful and constructive feedback. We acknowledge the previous limitations in crystallographic depth. We have followed your advice and actively sought collaborations with a professional crystallographer, who has since joined as a co-author. With his expertise, we have further revised the manuscript to strengthen its crystallographic rigor. We hope these improvements address your concerns, and we will respond to your concerns point by point below.

Comments #1**:** *I appreciate their efforts to place their work in context of the PXRDNet paper that was mentioned. This is mostly handled well, though I note that the version that has now appeared in print does have a post-validation step which invalidates one of their comments in the rebuttal.*

Response #1: Thank you for your insightful comments. We acknowledge that the published version of PXRDNet includes a post-validation step.

Comments #2: *In Response 3 the authors attempt a justification of the reason for mismatched Bragg peak intensities in some of their solutions. They mention experimental things such as temperature and absorption effects. However, these cannot explain the differences in relative Bragg peak intensities that are a characteristic of atoms being in incorrect positions that I was referring to in my original comment, and so they have not successfully addressed my comment, unfortunately and this issue still remains. They did work hard to incorporate a Rietveld post-processing step, at least on one representative sample. As one might expect, it did result in an improvement of metrics like Rwp. However, they did not select one of the patterns that had problematic relative peak intensities. It is therefore not quite clear whether this would have corrected the problematic cases that showed success by the MaxDist (thanks for fixing the description of this in the manuscript) measure, but which were almost certainly not actually correct in some key way based on a visual assessment of the diffraction pattern. I also find their rebuttal on the basis that their data are from simulated data so the Rietveld will give a lower*

Rwp, with a citation to a paper in Powder Diffraction journal, to be a bit lazy and to be an attempt to evade the question rather than address it head on as a serious scientist would seek to do. All in all, these responses reinforce an impression that the crystallography expertise in the group is lacking. The authors have worked hard on this work and it deserves better. In summary, the authors did not address the key point of my original objection in comment #5 with any of their responses.

For reference, we also paste your previous comment #3 and comment #5 here.

Previous Comments #3: *This is a significantly simplifying assumption because it results in the Bragg peaks being in the right positions and the model simply changes the intensities of the peaks when it atoms around. It gives a subjective impression that the model is working better than it is because the Bragg peaks are all in the right locations, but close inspection of the figures shows that even "successful" solutions have the intensities that don't match. It is not so clear that a crystallographer would be satisfied with these structure solutions. This is expanded on a bit below.*

Previous Comments #5: *In general, the structure solution field needs better measures of when structures are successfully solved. The problem with this is that there is disagreement even among crystallographers about the exact definition. For example, an Rcos of 0.899 sounds pretty good (almost 90% good!), but a crystallographer looking at the powder patterns in figure S7 of the supplementary would be pretty surprised with how bad it is. Clearly wrong. Even the Rcos of 0.974 in figure S2 has a bunch of problems. These could possibly be fixed by a final Rietveld refinement step, which was not done by these authors, but this would normally be part of a minimal requirement from a crystallographer.*

Response #2: Thank you for your insightful comments. We now better understand the core of your original comment: namely, that in some of our solutions, the "relative Bragg peak intensities" differ significantly from those in the reference data, in a way that suggests not just experimental noise (e.g., temperature effects, absorption effects, preferred orientation, crystallite size, and instrument settings), but **may due to incorrect atomic positions**. We acknowledge that our previous response did not fully address this concern, and we appreciate the opportunity to clarify.

First, we explain why we did not perform Rietveld refinement for the previous Figure S7 and S2 (corresponding to the HoAgGe and NbP in the main text Figure 3), and why visual assessments of these diffraction patterns look bad. Both entries were documented in ICSD, and DFT calculations suggested poor thermodynamic stability for these two structures (high E_{hull},

0.17 eV/atom for HoAgGe, 0.6 eV/atom for NbP), indicating that the documented structures might be incorrect. Ideally, we should attempt to solve these structures using the original experimental PXRD patterns. However, ICSD is a structural database that only provides structure information, but no diffraction data is available. We also looked into the original literature (*Journal of Alloys and Compounds*, 1998, 92-98 and *Acta Chemical Scandinavica*, 1954, 226-239). We found that for HoAgGe, only neutron diffraction data is documented, while PXRD data is not available. For NbP, the PXRD pattern is relatively low quality, as the experiment was performed more than 70 years ago. Below is the original diffraction data for NbP (*Acta Chemical Scandinavica*, 1954, 226-239).

Table 3. Calculated and observed intensities for the β-NbP phase.

hkl	I_{calc}	I_{obs}	*hkl*	I_{calc}	I_{obs}
1,0,1	51	40	1,1,10	28	25
0,0,4	65	85	2,0,9	4	0
1,0,3	26	25	3,0,5	4	0
1,1,2	117	125	1,0,11	3	0
1,0,5	12	10	2,1,9	6	0
2,0,0	31	40	0,0,12	5	5
1,1,6	52	60	3,1,6	39	40
2,1,1	17		3,2,1	6	
1,0,7	8	5	3,0,7	3	0
2,0,4	52	60	2,2,8	18	15
0,0,8	13	15	3,2,3	6	0
2,1,3	6	5	3,2,5	6	0
2,1,5	12	10	2,1,11	5	0
1,0,9	5	5	1,0,13	3	0
2,2,0	16	25	3,0,9	3	0
3,0,1	6	5	4,0,0	10	10
2,1,7	9	5	4,1,1	9	10
2,2,4	28	25	3,2,7	9	10
2,0,8	28	25	4,0,4	34	40
3,0,3	4	0	4,1,3	10	10
3,1,2	56	60			

We observed that all intensities I_{obs} are multiples of 5. After consulting with professional crystallographers' opinions, we believe this may be because early experiments did not use digitized intensity recordings, but rather researchers estimated diffraction intensities visually. Therefore, we gave up the attempt to perform Rietveld refinement on the original PXRD pattern.

As we explained, since the ICSD lacks diffraction data, we adopted an alternative strategy. For structures in the ICSD that we deemed suspicious (with extremely high E_{hull} based on DFT calculations), we hypothesized the existence of different but more reasonable structures that have similar PXRD patterns to the suspicious structures documented in the ICSD. In this case, we can first calculate a PXRD pattern based on the documented structure in the ICSD and then use our XRDSol to solve it. Since these calculated PXRD patterns are based on a suspicious crystal structure documented in the ICSD, which may be incorrect, rather than on

experimentally measured PXRD patterns, we believe that performing Rietveld refinement in this case is not reasonable, even from a crystallographic perspective.

Now we address your concern about whether these inconsistencies in peak intensities originate from incorrect atomic positions. In other words, whether the solutions we provided are indeed correct. We mainly rely on two evaluation methods. First, DFT calculations confirmed that our proposed structures in Figure 3 have much lower energy compared to the previously documented ones. Second, we conducted a comprehensive literature review and directly compared our proposed crystal structures with those reported in the literature. This directly addresses your concern about **whether our proposed structures have incorrect atomic positions**.

We now use **root mean square deviation (RMSD) of atomic positions**, which is widely accepted in crystallography as a metric, to directly compare our proposed structure with some recently validated structures. As can be seen, the structures given by our model are almost identical to these correct structures. Therefore, in most cases, we have **replaced XRD pattern comparison with direct structure comparisons**. To provide a more rigorous analysis, we now present detailed case-by-case discussions of the **total present 6 ICSD corrected structures**.

(1) HoAgGe: HoGeAg was originally reported in 1998 based on neutron diffraction (ICSD-86732, *Journal of Alloys and Compounds*, 1998, 92-98), but the reported structure has an E_{hull} of 0.17 eV/atom. This E_{hull} is extremely high for an intermetallic compound, indicating poor thermodynamic stability. The original work did not provide an experimental PXRD pattern. The solution proposed by XRDSol is thermodynamically stable (E_{hull} = 0 eV/atom). Recently, Zhao *et al.* (*Science*, 2020, 1218-1223) determined the crystal structure of HoGeAg using high-confidence single-crystal XRD at 15 K. Although the lattice parameters reported in that study (a = 4.1864, c = 7.0862Å) differ slightly from ours (a = 4.1136, c = 7.3431Å) which was measured in ambient conditions, the atomic coordinates predicted by XRDSol exhibit good agreement with the experimental structure, with an RMSD of **0.04 Å**. Instead of comparing simulated XRD patterns of the incorrect ICSD structure and our solution, we present a structural comparison in Fig. S17, i.e., Fig. R2-1. This highlights the difference between the incorrect ICSD structure (Fig. R2-1a) and XRDSol prediction (Fig. R2-1c), and demonstrates the consistency between the XRDSol prediction and the experimentally validated structure (*Science*, 2020, 1218-1223) (Fig. R2-1b).

Fig. R2-1 Structural comparison of HoGeAg. (a) ICSD-reported structure (ICSD-86732, *Journal of Alloys and Compounds*, 1998, 92-98); (b) Recently reported experimental structure (*Science*, 2020, 1218-1223); (c) Structure proposed by this work, consistent with (b).

(2) $SrPbF_6$: $SrPbF_6$ (ICSD-25629) was first synthesized and characterized by Hoppe in 1958 (*Zeitschrift für anorganische und allgemeine Chemie*, 1958, 251-263). It was originally proposed to crystallize in space group $P4_2/mmc$. However, the original report noted that the presence of **several unindexed peaks in the XRD diffraction pattern which were attributed to another unknown phase**. First principles calculations reveal that the original structure has a high E_{hull} of 0.16 eV/atom. The crystal structure proposed by XRDSol is predicted to be a stable compound (E_{hull} = 0 eV/atom). In 2018, the compound characterized by Hoppe in 1958 was experimentally revisited, and its space group was corrected to be $P4_2/mcm$ (*Zeitschrift für anorganische und allgemeine Chemie*, 2018, 1721-1726), where Sr is eight-coordinated instead of ten-coordinated by F**. This revisited structure perfectly matches the PXRD profile obtained from the experiment with no unindexed peaks, suggesting its correctness**. In the original manuscript (Fig. S3), we compared simulated XRD patterns of the incorrect 1958 ICSD structure and our corrected XRDSol structure, which led to unmatched peaks due to structural discrepancies. We now present a direct structural comparison among the 1958 ICSD structure, the 2018 reported structure, and our XRDSol prediction (Fig. S18, i.e., Fig. R2-2). The structure proposed by our XRDSol (Fig. R2-2c) closely matches that of the 2018 revisited structures (**RMSD = 0.08 Å**) (Fig. R2-2b).

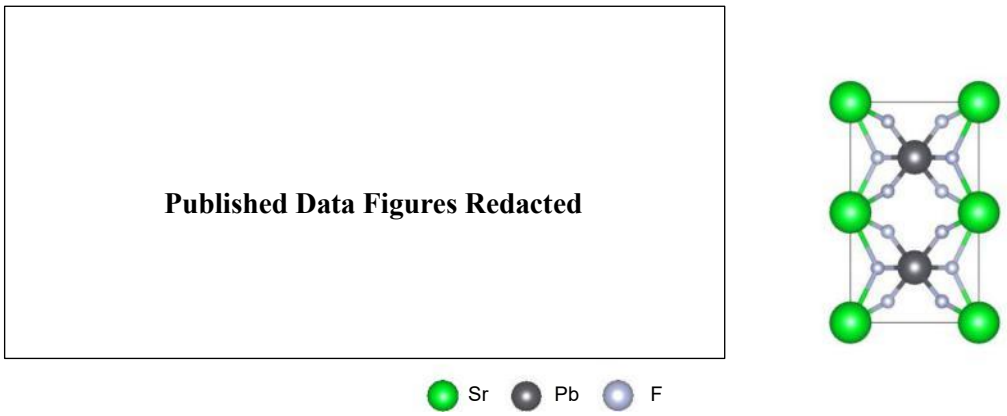

Fig. R2-2 Structural comparison of $SrPbF_6$. (a) ICSD-reported structure (ICSD-25626, *Zeitschrift für anorganische und allgemeine Chemie*, 1958, 251-263); (b) Revisited structure by Bandemehr *et al.* (*Zeitschrift für anorganische und allgemeine Chemie*, 2018, 1721-1726); (c) Structure proposed by this work, consistent with (c).

Half-Heusler compounds (NbSnRh and HoPdSb): NbSnRh and HoPdSb are both Half-Heusler. In this structure type, three equal molar elements form three interpenetrating face-centered cubic sublattices, and only one element is eightfold coordinated. The originally reported NbSnRh (ICSD-105220, *Metallurgical Transactions*, 1970, 3159-3162) and HoPdSb (ICSD-108547, *Journal of the Less Common Metals*, 1980, 25-28) exhibit high E_{hull} of 0.704 and 0.276 eV/atom, respectively. These extremely high E_{hull} values indicate poor thermodynamic stability. XRDSol proposed different site assignments for the two Half-Heusler compounds. The structures predicted by XRDSol have much lower E_{hull} (0 eV/atom for both), suggesting the solutions from XRDSol are more plausible. As shown in Fig. R2-3, the solutions by XRDSol also match the recently reported results (*Advanced Materials*, 2023, 2210788), with RMSD values of nearly **0 Å** in both cases, respectively.

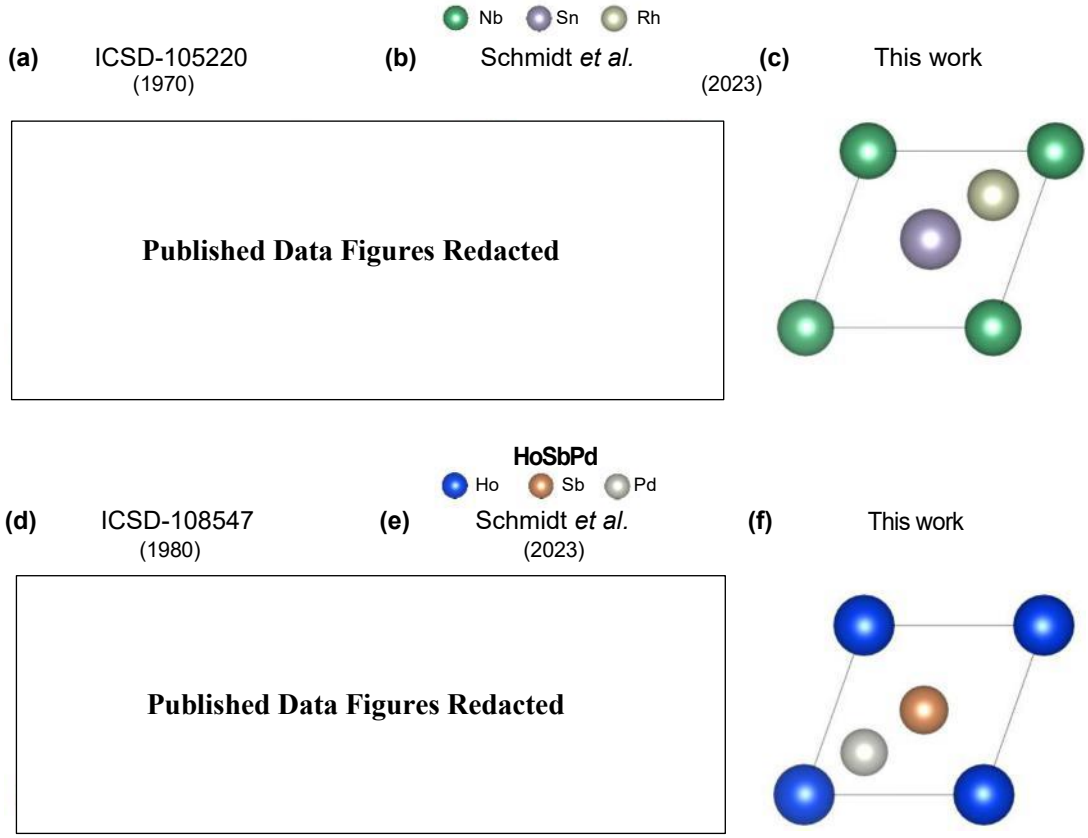

Fig. R2-3 Structural comparison of (a-c) NbSnRh and (d-f) HoPdSb. (a) ICSD-reported structure (ICSD-105220, *Metallurgical Transactions*, 1970, 3159-3162); (b) Recently reported structure (*Advanced Materials*, 2023, 2210788); (c) Structure proposed by this work, consistent with (b). (d) ICSD-reported structure (ICSD-108547, *Journal of the Less Common Metals*, 1980, 25-28); (e) Recently reported structure (*Advanced Materials*, 2023, 2210788); (f) Structure proposed by this work, consistent with (e).

$CsIO_3$: $CsIO_3$ (ICSD-33665) is a covalent perovskite material. It was first reported in 1928 with a cubic perovskite structure (space group *Pm3 m*), where Cs occupies the six-coordinate B-site (Fig. S19a, i.e., Fig. R2-4a). However, the calculated E_{hull} of this original structure is extremely high at 1.97 eV/atom. In contrast, our solution from XRDSol exhibits a much lower E_{hull} of 0.02 eV/atom. The larger Cs cations are moved to twelve-coordinate A-sites, and the original ICSD structure incorrectly swapped the positions of Cs and I atoms. Our structure solution (Fig. S19c, i.e., Fig. R2-4c) is very close to the recently synthesized and experimentally characterized structure (Fig. S19b, i.e., Fig. R2-4b) from a single crystal (*Chemistry of Materials*, 2018, 1136-1145), with an RJ'VISD of **0.28 Å**. Although RJ'VISD is slightly larger due to minor deviations in atomic positions caused by different extents of distortions, a direct comparison between the reported structure (Fig. R2-4b) and our predicted structure (Fig. R2-4c) demonstrates the correctness of our structure.

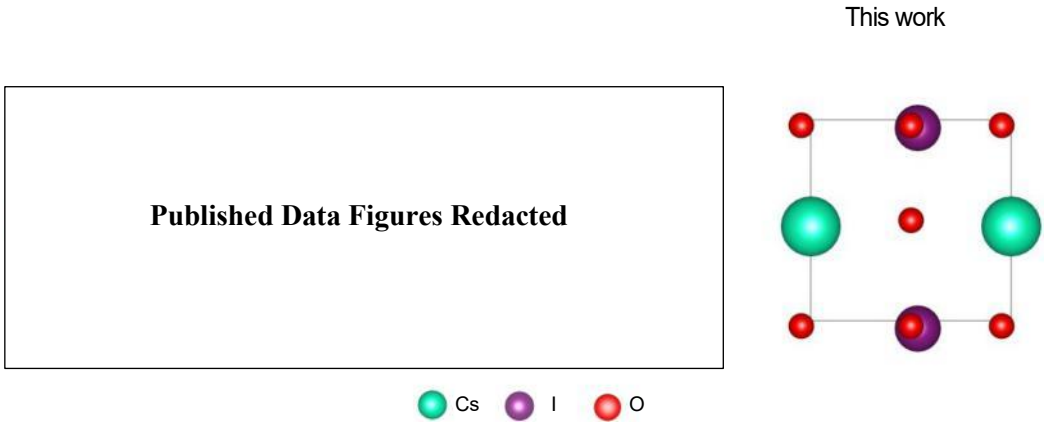

Fig. R2-4 Structural comparison of $CsIO_3$. (a) ICSD-reported structure (ICSD-33665, *Angewandte Chemie*, 1928, 797-797); (b) Structure recently reported by Zhang *et al.* characterized based on a single crystal sample (*Chemistry of Materials*, 2018, 1136-1145); (c) Structure proposed by this work, consistent with (b).

NbP: NbP was first characterized by PXRD in 1954 and reported as centrosymmetric with $I4_1/amd$ space group (ICSD-76027, *Acta Chemical Scandinavica*, 1954, 226-239). It contains a very uncommon four-fold square planar coordination for Nb and P (Fig. S20a, i.e., Fig. R2-5a). DFT calculation reveals an extremely high E_{hull} of 0.6 eV/atom, further raising doubts about the validity of this structure. In contrast, XRDSol suggests a non-centrosymmetric structure with a different space group $I4_1md$, where Nb is in a trigonal prismatic coordination environment with six P atoms (Fig. S20c, i.e., Fig. R2-5c). DFT calculation confirms this proposed structure is stable (E_{hull} = 0 eV/atom), and it agrees with the previous literature report with an RMSD value of **0.07 Å** (*Inorganic Chemistry*, 1996, 845-849) (Fig. S20b, i.e., Fig. R2-5b).

Fig. R2-5 Structural comparison of NbP. (a) ICSD-reported structure (ICSD-76027); (b) Previously reported experimental structure from a single crystal sample (*Inorganic Chemistry*,

1996, 845-849); (c) Structure proposed by this work, consistent with

(b). **Comparison with ICDD XRD patterns**

This category also includes structure comparisons. To rigorously assess the accuracy of the atomic coordinates predicted by XRDSol, we compare our proposed structures to experimentally determined structures reported in the literature. Our predicted structures show good agreement **in atomic arrangement**. This supports the validity of our solutions. We now present a **total of 5 structures** in the original manuscript.

$(NH_4)CoF_3$: $(NH_4)CoF_3$ was originally reported in 1970 without atomic coordinates. XRDSol solved its structure as a cubic perovskite (Fig. S23b, i.e., Fig. R2-6b), with cobalt at the B-site and ammonium at the A-site. Nitrogen is tetrahedrally coordinated with hydrogen, forming the correct ammonium structure. The structure has a low E_{hull} of 0.03 eV/atom. It also aligns well with the structure later reported from single-crystal XRD by Siebeneichler *et al.* with an RMSD value of **0.28 Å** (*The Journal of Chemical Physics*, 2020, 104501) (Fig. R2-6a and b). This validates the plausibility of our solution.

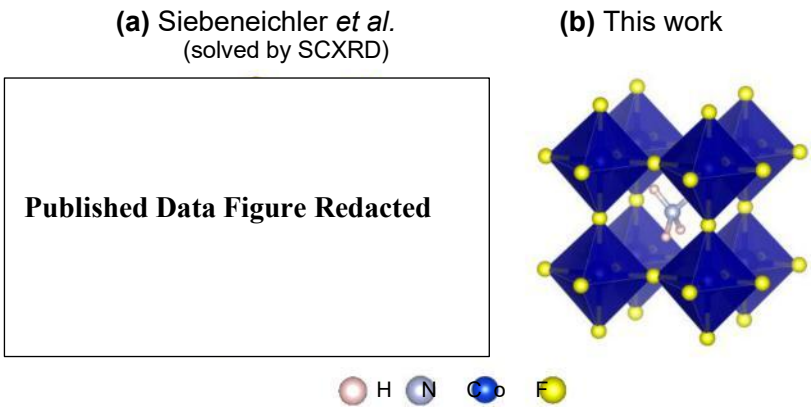

Fig. R2-6 Structural comparison of $(NH_4)CoF_3$. (a) Previously reported experimental structure from a single crystal (*The Journal of Chemical Physics*, 2020, 104501); (b) Structure proposed by this work, consistent with (a).

Li_2SrGeO_4: Li_2SrGeO_4 was characterized in 1986 as a tetragonal phase with *I*-42*m* space group but without atomic coordinates. The XRDSol predicts a stable Sr-analog of Li_2CaGeO_4 phase (E_{hull} = 0 eV/atom). Our solution agrees with the recently reported structure by Griesemer *et al.* with an RMSD of **0.08 Å** (Fig. S25a and b, i.e., Fig. R2-7a and b). Therefore, our proposed structure is highly plausible.

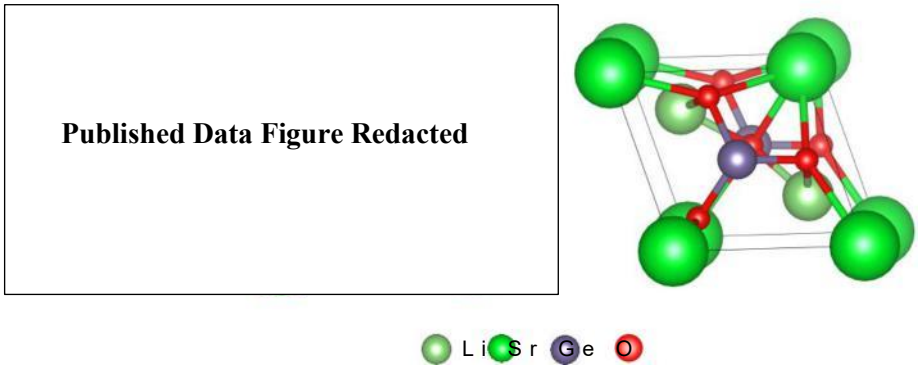

Fig. R2-7 Structural comparison of Li_2SrGeO_4. (a) Previously reported structure (*Physical Review Materials*, 2021, 105003); (b) Structure proposed by this work, consistent with (a).

MnO_2: Natural ramsdellite MnO_2 was documented by ICDD without atomic coordinates. And the structure solved by XRDSol has a low E_{hull} of 0.009 eV/atom. The structure proposed by XRDSol is consistent with the literature report by Post *et al.* with an RMSD of **0.1 Å** (*American Mineralogist*, 2004, 969-975) (Fig. S27, i.e., Fig. R2-8). We believe the proposed structure is highly plausible.

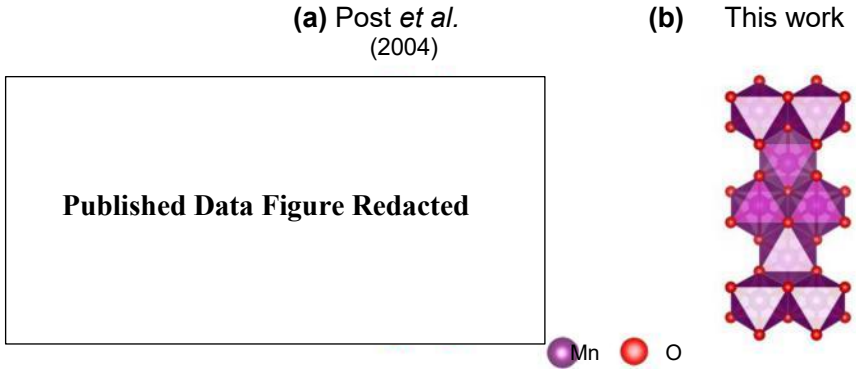

Fig. R2-8 (a) Previously reported experimental structure (*American Mineralogist*, 2004, 969-975); (b) Structure proposed by this work, consistent with (a).

$NaSrPO_4$: $NaSrPO_4$ is a natural olgite mineral discovered in 1980. Early XRD experiments revealed that it belongs to the hexagonal lattice system and was originally assumed to have the *P*3 space group. Lattice parameters were extracted from diffraction patterns, but without atomic coordinates. XRDSol provided a solution with a different space group *P*3*m*1. Despite that the reconstructed pattern matches most of the major peaks, strong intensity deviation was observed. This is probably due to the strong texture of the sample and potentially associated impurity phases. DFT calculation confirms that the structure is highly plausible with a low E_{hull} of 0.01 eV/atom. We confirmed that our proposed structure agrees with a recent report on olgite crystal

structure, except that one lattice site might be co-occupied by Na or Sr (*Canadian Mineralogist*, 2005, 1521-1526).

$Sr_{0.5}Ca_{0.5}TaO_2N$: $Sr_{0.5}Ca_{0.5}TaO_2N$ is an oxynitride perovskite material, in which complex anion order behavior may exist. The A-site is co-occupied by Sr and Ca (*Journal of the Korean Ceramic Society*, 2020, 432-439). In contrast, in the structure proposed by XRDSol, two A-sites in a supercell are occupied by Sr and Ca, respectively. For the anion-sites, XRDSol proposed an ordered *trans*-type anion configuration, in which nitrogen occupies axial sites while oxygen occupies the equatorial sites. Remarkably, this is in excellent agreement with recent neutron diffraction results (*ACS nano*, 2017, 3860-3866).

We hope that we have convinced you that we are doing our utmost to be serious about the validity of our solutions. The approach we have adopted is neither a lazy one nor an attempt to evade the question. It is our firm belief that the reliability of results is more important than whether the paper is published. Therefore, we have confidence in allowing our solutions to undergo rigorous questioning or challenging. Additionally, we sincerely thank you, as a crystallography expert, for your critical review and questioning of our solutions, which greatly benefits our results and algorithms.

Comments #3: *Further, on the point of the use of structureMatcher/MaxDist to assess structures: This metric has not been validated in any meaningful way by the crystallographic community, and whilst it is widely used by the ML community, this is an issue that needs to be urgently addressed. this is not the fault of the current authors, and they are following practices used by others in this regard, but with respect to the specific scientific claims of the paper, this measure is so flawed as to make them highly dubious. Increasing the crystallographic domain knowledge in the team would, again, greatly help.*

Response #3: Thank you for your insightful comments. We agree that the use of structureMatcher/MaxDist has not been systematically validated or accepted by the crystallographic community as a standard for structural assessment. We consulted crystallography experts and re-evaluated our evaluation strategy. To address this concern, we have revised our manuscript to incorporate **RMSD**, a metric that is broadly recognized and commonly used by the community. We calculated the RMSD values for 9,046 structures solved by XRDSol in the MP-20 test set. The distribution of RMSD is shown in Fig. S4, i.e., Fig. 2-9. 72.15% of the structures achieved an RMSD less than 0.1 Å, and 78.13% achieved an RMSD less than 0.3 Å. Among the structures with RMSD < 0.1 Å, the mean RMSD is 0.0215 Å, the median RMSD is 0.0129 Å, the first quartile is 0.0024 Å, and the third quartile is 0.0325 Å. These results demonstrate that XRDSol can reproduce most crystal structures with high fidelity

in the MP-20 test set. The description of RMSD has been provided in the revised manuscript.

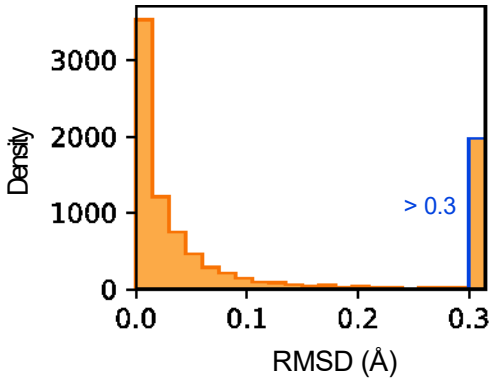

Fig. R2-9 Distribution of RMSD for 9046 structures solved by XRDSol in the MP-20 test dataset, reflecting the reconstruction quality of the crystal structures.

Comments #4: *I appreciate the efforts of the authors to increase the clarity of the presentation. Also, they report at making a better effort of acknowledging the inspiration for their work (e.g., CDVAE) in the methods section, but I still find this inadequate. I would rather expect to see it high up in the paper (e.g., the Introduction) and with a bit more fanfare. There is no harm in a full bodied celebration of the work of others. It does not diminish in any way the developments made by the authors. Perhaps they feel pressure to publish in a high profile journal, and they feel they need to try and make their work stand out to accomplish that. But this is bad for science in general, and counter-productive for the authors as it makes it harder for others to cite their work if it doesn't do a fair job of explaining how it fits in to the broader community.*

Response #4: Thank you for your comments. We fully agree that the prior materials generative models (e.g., CDVAE) deserve more prominent recognition as a key source of inspiration for our work. We are grateful for the foundational work of CDVAE, which significantly influenced our thinking in designing a diffusion-based structure generation model. While we have cited CDVAE (Reference 12) in both the Introduction and Method sections of our original manuscript, we realize that this did not sufficiently highlight the foundational role of CDVAE. To clearly articulate how the CDVAE inspired the design and development of our model, we have now revised the **Introduction** section to explicitly and prominently describe the contribution of CDVAE as follows:

(Introduction in the revised Manuscript)

"Recently, machine learning approaches, particularly generative diffusion models, have provided a new paradigm for materials structure generation[12-15]. Xie et al. built the Crystal Diffusion Variational Autoencoder (CDVAE), which employs score matching to generate

realistic crystal structures by learning from the data distribution of known stable materials[12]. Without any predefined prototypes, CDVAE shows its ability to generate valid and diverse crystal structures that captures the physical inductive bias of material stability. Equivariant diffusion can effectively preserve reflection, translation, rotation, and mirror symmetries[12-16], enabling generation of physically reasonable crystal structures. Such equivariant denoising models were employed to generate inorganic crystal structures[12,14,15] and molecules[13,16], and showed remarkable performance. Besides generating crystal structures without constraints, conditioning diffusion models allow crystal generation with desired chemistry, mechanical, electronic, or magnetic properties, paving the way towards generative AI-assisted materials design paradigms."

***Comments* #5:** *I thank the authors for their efforts at better benchmarking. Just a note that I am more interested in benchmarking prediction performance, in part as a way to understand how the model is working, where it is getting information from, and so on, and less interested in computation time. It is clear that a trained ML model will work in production much quicker than any regression method, but getting an answer is of greater interest in structure solution rather than wall-clock time in most applications and so understanding the performance is more important than how quickly it gets there. Overall, given the challenges of not really having good success metrics in general, the benchmarking work that the authors have done is about as good as we can hope for.*

Response #5: We thank the reviewer for the valuable feedback. The concerns regarding benchmarking prediction performance have been addressed in our revised responses to *Comments #2 and #3,* where we provide detailed analyses using meaningful metrics (e.g., RMSD) in the crystallographic community to evaluate the accuracy and quality of the predicted structures.

Some small points:

***Comments* #6:** *In one response the authors mention that better performance can be obtained by incorporating "'domain knowledge (e.g., space group information)". This an incorrect use of the term 'domain knowledge' which refers to the general knowledge of a domain expert rather than incorporating additional information in a particular input. I sugget to just delete mention of domain knowledge at that point.*

Response #6: Thank you for pointing this out. We agree that the term "domain knowledge" is misused. We have removed the term and now refer directly to "space group information" as additional input.

Comments #7: *In a later comment they also mention p'eak distinction'. Do they mean p'eak extinction here'? Again, bolstering their crystallography domain expertise might help this paper.*

Response #7: Thank you for pointing this out. We acknowledge that the term “peak distinction” was incorrectly used. Wha we originally intended to express was indeed “peak extinction”. Upon further discussion with our co-auther, a crystallographer, we realized that the term “systematic absence” is more precise and widely accepted in the crystallography community. We appreciate the opportunity to clarify.

Comments #8: *In methods they describe how they run the model 25 times with different random seeds and pick the best solution. This is fine, it is fairly standard practice, but then they call it 'Top-1', but I find this a bit misleading. I think more normally this would be called 'Top-25'. Clearly you measure the model performance with the best model of your sample and report that performance, but I think of 'top-1' as how well the model performs at a guess of one sample, Top-10 when you let it guess 10 times and take the best one, and so on. So I would think that what the authors are doing is better described as Top-25. They justify very nicely why they do that, so it is no criticism of the approach, just the naming.*

Response #8: Thank you for pointing this out. We agree that the term “Top-25” better reflects our evaluation protocol, which involves running the model 25 times and selecting the best result. To avoid misunderstanding, we have revised the term “Top-1” to “Top-25” in the revised manuscript.

Comments #9: *They call their approach "end-to-end" on page 3 but requiring knowledge of the lattice parameters suggests that this is more mid-to-end than end-to-end. I recommend simply to remove this statement. It doesn't add much.*

Response #9: Thank you for your insightful observation. We agree that the term “end-to-end” could be misleading, as our approach requires the unit cell parameters as input. We have removed the phrase “end-to-end”.

Responses to Reviewer #4:

Strength:

Comments #0: *I appreciate the authors' detailed responses. My main concerns, including the graph initialization, diffusion step selection & potential randomness, and failure case analysis, have been well addressed.*

Response #0: We truly appreciate the Reviewer' positive feedback. We are glad that our revisions have addressed your main concerns regarding graph initialization, diffusion step selection, potential randomness, and failure case analysis.

Comments #1: *To further improve clarity, I suggest the authors consider simplifying the presentation of the diffusion model in the final revision. Including a clear formulation of the forward and reverse steps, perhaps via a concise pseudo-code for one noising and denoising step, would help a lot.*

Response #1: Thank you for the helpful suggestion. In the revised manuscript, we have added concise pseudo-code (Table S6, i.e., Table R2-1) to illustrate the noising and denoising steps.

Table R2-1 Pseudo-code of XRDSol for crystal structure solutions using powder XRD data.

Input: PXRD pattern C , initial structure $S_0 = [L, A, P_0\}$, diffusion steps T, schedule $[\alpha t, \sigma t\}$
$fC \leftarrow \mathrm{MLP}(C)$
Noising process:
for t = 1 to T do
    $\varepsilon t \sim \mathcal{N}w\ (0, I)$
    $St \leftarrow \alpha t \cdot St-1 + \sigma t \cdot \varepsilon t$
end for
Denoising process:
$ST \leftarrow [L, A, PT\}$
for t = T to 1 do
    $fstruct \leftarrow \mathrm{EGNN}\ (St)$
    $fcat \leftarrow \mathrm{concat}(fstruct, fC)$
    $\varepsilon t\wedge \leftarrow \varphi(fcat)$
    $St-1 \leftarrow St - \sigma t \cdot \varepsilon t\wedge$
end for
Output: $S_0 = [L, A, P_0\}$

Remarks on code availability:

Comments #2: *The code is clear and runnable with good instructions to reproduce the results.*

Response #2: Thank you for the evaluation of our code.

Responses to Reviewer #5:

Comments #0: *I co-reviewed this manuscript with one of the reviewers who provided the listed reports. This is part of the Nature Communications initiative to facilitate training in peer review and to provide appropriate recognition for Early Career Researchers who co-review manuscripts.*

Response #0: Thank you for the co-reviewed comments.

Remarks on code availability:

Comments #1: *The code is runnable with clear instructions.*

Response #1: We appreciate your evaluation of the code and instructions.

Responses to Reviewers

(*Black italic: Reviewer's comments*; Black type: Our response; Blue type: Key revisions)

Responses to Reviewer #1:

Comments #0: *This manuscript presents a fast machine-learning model for predicting structures in a polycrystalline sample from powder x-ray diffraction data. This is a promising application of machine learning within the expanding interface between chemistry and computer science, highlighting the need for input by both machine-learning experts and experienced crystallographers. I believe that this work has substantially improved from the initial manuscript in its presentation of the effectiveness and shortcoming of XRDSol.*

Response #0: We thank the Reviewer for the thoughtful and constructive feedback. We greatly appreciate your recognition of the improvements in the revised manuscript. Your comments are valuable in helping us further refine this work. We address your concerns point by point below.

Comments #1**:** *The crux of my critique against this paper that remains unaddressed is that I disagree with the author's statement regarding "solving" structures from powder x-ray diffraction data: "determining atomic coordinates is the most crucial and challenging step." Such a statement reflects a lack of understanding of how a Rietveld refinement works, in terms of refining against models (rarely are candidate structures generated from scratch), and reveals a core weakness of the manuscript.*

Response #1: Thank you for pointing out that our original statement might have been overclaimed. We agree that our original phrase, "determining atomic coordinates is the most crucial and challenging step," was imprecise. We have revised it to "determining atomic coordinates is **one of** the most crucial and challenging steps."

We also want to note that our work is not intended to replace Rietveld refinement. Instead, we aim to use our algorithm to provide an initial model that can serve as a good enough starting point for the following Rietveld refinement. At its current stage, XRDSol has no chance to replace an experienced crystallographer. We agree that, for experienced crystallographers, they can come up with candidate structure models based on the PXRD patterns and their prior knowledge of structure prototypes, etc. However, for complex structures or those lacking prior information, even experienced crystallographers may require multiple rounds of tedious trial-and-error attempts to arrive at the correct structure. In these cases, XRDSol could accelerate this process largely and reduce the crystallographer's effort.

Besides, we also note that most of the researchers who perform structural characterization

and analysis using PXRD, focus on specific material systems of their own interests and are not experienced crystallographers. An automated algorithm like XRDSol could potentially benefit such a community as well.

In summary,We emphasize that our solver is designed to assist not only crystallographers but also a broader community of researchers working in the physical sciences who utilize powder X-ray diffraction analysis as a tool within their specific research domains. For expert crystallographers, our model can provide an initial model that serves as a sufficiently good starting point for subsequent Rietveld refinement, saving them time and effort. For researchers who focus more on specific materials than on crystallography itself, our model can provide a reasonable baseline model for them to start with. Such assistance from our model helps to ensure that the final structural model is reliable.

Comments #2**:** *Instead, most of the high energy structures highlighted in the manuscript could likely be easily corrected by inspection, once identified as a high energy structure. There may be utility in this approach if the algorithm could solve entirely new structure types (ones without models for refining against), but given the chemical constraints of the examples presented, this seems to be outside the scope of the tool developed.*

Response #2: Thank you for the comments. We agree that an experienced crystallographer can often correct high-energy structures by inspection. We made this point explicit in the text and clarified that XRDSol is not intended to replace judgment from experts. The meticulous manual inspection by professional crystallographers and rigorous peer review should serve as the best and final safeguard for the accuracy of structural analysis.

However, we respectfully note that this is not always as “easy” as it appears to be. Training an expert crystallographer often requires years of rigorous study and extensive hands-on experience. Therefore, they are scarce compared to the large number of structures to be examined and solved. Taking ICSD database as an example, this is one of the leading structure databases in the world. Despite that the energy calculation (done by Materials Project) for tens of thousands of ICSD structures have been performed for more than 10 years, structural errors still persist for decades before being noticed and revised by experts. The structure of $SrPbF_6$ was first reported by Hoppe in 1958 from experiments, but a correction of the structure based on the same sample was not available until sixty years later in 2018. As one can see, such a correction is on a time scale of tens of years. We agree with the Reviewer that the correction could be “easy” if it is identified as suspicious and presented to an experienced crystallographer. However, there is a huge gap between the scale of the structural database and the limited number of human-experienced crystallographers.

In the context, automated tools like XRDSol are suited to fill this gap. XRDSol is not designed to replace manual expertise, but rather to reduce the scale of manual effort by automatically generating chemically reasonable candidate structures. If the solution offered by XRDSol is different from the one offered by a researcher, he and she could still perform manual analysis and decide to adopt or refuse the solution from XRDSol. This automated step is most beneficial in database scale (e.g., quality control of ICSD database), where manual correction is time-consuming and labor-intensive.

Finally, we appreciate the Reviewer's point about truly novel structure types. Extending XRDSol to discover new structure types is an important direction. At present, such examples are rare, and our XRDSol is limited to relatively small primitive cells ($\leq$ 20 atoms). We have added these limitations to the Discussion section.

Comments #3**:** *Instead, I maintain that the utility of the approach is overstated, and while it lays a good groundwork, it is disingenuous for the authors to claim that it significantly improves on other approaches because it requires less input when not all input is created equal. Instead, the authors state XRDSol requires stoichiometry and "periodic lattice" as inputs, although I do not think the latter is a standard crystallography term (maybe unit cell is meant instead?). This information may indeed prove quite difficult to obtain depending on the quality of a diffraction pattern or sample purity, something that is not adequately considered throughout the manuscript.*

Response #3: We thank the Reviewer for urging us to raise potential applications of our approach. It helps us reflect more deeply on the potential applications, current limitations, and potential future development directions of XRDSol.

We agree with the Reviewer that the term "periodic lattice" is not a standard term. And we have replaced it with the standard crystallography term "unit cell" in the revised manuscript. We also clarified that unit cell determination is treated as a separate preprocessing step. As the Reviewer noted, the unit cell determination can be affected by the quality of samples or the quality of diffraction patterns. We appreciate this constructive comment and acknowledge that requiring the unit cell as input is an important limitation of the current version of XRDSol. Indeed, we are actively developing a newer version of XRDSol that can work without requiring the unit cell as input.

We also acknowledge that the input requirements of XRDSol differ from some other approaches. XRDSol requires the target PXRD patterns, lattice parameters, and the number and type of atoms as inputs. Our intention is not to claim that XRDSol surpasses existing methods in all respects, but rather to present it as a complementary new approach. For an experienced

crystallographer, XRDSol can provide an initial model that can serve as a starting point for the following Rietveld refinement. A good initial guess of the structural model can help the researcher save time and effort. For a researcher who focuses on a specific material and is not so experienced in crystallography, XRDSol can provide a baseline model that is "not so bad" for them to start with. Such assistance from XRDSol provides a potential guarantee that the final structure model is more or less reasonable.

Action #1: To clarify the applications of XRDSol and the descriptions of the unit cell, we have now added the related descriptions in the revised manuscript as follows:

(Introduction in the revised Manuscript)

"Specifically, determining atomic coordinates usually relies on prior knowledge, prerequisite information, and the expertise of expert crystallographers. As a result, for complex structures or those lacking prior information, even experienced crystallographers may require multiple rounds of tedious trial-and-error attempts to arrive at the correct structure. Besides, most researchers who perform PXRD analysis focus on specific materials of their interests rather than crystallography. In these cases, structural analysis based on PXRD could be challenging, potentially resulting in incomplete, controversial, or even incorrect solutions. For example, the ICSD database, which is the largest database for completely identified inorganic crystal structures, contains about 300,000 entries. However, a previous study suspected that among the unique entries with ordered structures, about one-fifth may be spurious. The ICDD database, one of the most widely used diffraction databases, contains more than 480,000 sets of inorganic diffraction data. Nevertheless, it also includes tens of thousands of entries without atomic coordinates in their associated structures (Supplementary Table S1). Given that these two databases already represent cutting-edge resources for structural data on inorganic materials, developing efficient and accurate approaches to solve crystal structures from PXRD is urgently important."

(Discussion in the revised Manuscript)

"For experienced crystallographers, XRDSol can provide high-quality initial models that can serve as a starting point for the following Rietveld refinement, saving time and effort from human experts. For researchers who focus on specific materials rather than crystallography, XRDSol can provide a baseline model with good quality that can potentially satisfy their need for routine structural characterization in their research. For large-scale structural databases, XRDSol can be valuable for database maintenance and quality control, by providing an initial screening of suspicious entries, identifying potential errors in existing records, supplementing missing structural parameters, and offering cross-validation for ambiguous cases. Besides, the

automated nature of our algorithm also makes it suitable for potential integration into autonomous materials discovery platforms, since it requires minimal human intervention and has a rapid processing capability."

We have also removed the previous descriptions of the unit cell as follows:

(Introduction in the revised Manuscript)

"Determining the unit cell parameters is a relatively well-established step. In contrast, determining atomic coordinates is much more difficult due to the vast number of possible atomic arrangements in the configurational space."

Comments #4: *Accordingly, the authors failed to satisfactorily address my prior comments concerning how this model could be implemented for materials discovery. Indeed, the success rate of ~1-3% on correcting database entries speaks to the fact that the authors have developed a tool with limited ability to fix outstanding challenges in crystallography. I reiterate the suggestion of the reviewers that for further work on PXRD-informed structure prediction they collaborate with an experienced crystallographer to provide additional perspective on the problems that they aim to solve.*

Response #4: We thank the Reviewer for this important comment and for the suggestion to collaborate with experienced crystallographers.

Our tests focused on 3,122 high-energy structures, which were only potentially incorrect, where XRDSol provides different crystal structure solutions for about half of the entries (Table S2). However, there is no automated or high-throughput way to determine if our solution is correct for manual inspection and comprehensive literature search. Therefore, we selectively performed such manual inspection and literature search only on a very small portion of these candidate structures. For this reason, the success rate (~1-3% success rate noted by Reviewer) alone may not fully reflect XRDSol's performance. Although incorrect crystal structures make up only a small fraction of the overall database, encountering such a structure in research on the relevant material system can have a significant impact.

We greatly appreciate the Reviewer's suggestion and will actively pursue collaborations with experienced crystallographers to gain additional perspectives for future improvements. A practical application of XRDSol in crystallography is its integration into traditional structure determination workflows. Once the unit cell and the number and type of atoms are determined, XRDSol can provide a good initial guess for atomic positions.

We appreciate the Reviewer's assessment. It has helped us sharpen the presentation of

XRDSol's scope, limitations, and future directions.

Comments #5: *Lastly, the manuscript contains some typos (ex: On lines 206-208, the authors repeat the phrase "All these structure analysis were performed with pymatgen"). I suggest the authors perform one more review of the prose in their manuscript.*

Response #5: Thanks for the comments. We appreciate the Reviewer's careful reading. We have thoroughly proofread the entire manuscript and corrected the typos throughout.

Responses to Reviewer #2:

Comments #0: *I co-reviewed this manuscript with one of the reviewers who provided the listed reports. This is part of the Nature Communications initiative to facilitate training in peer review and to provide appropriate recognition for Early Career Researchers who co-review manuscripts.*

Response #0: We thank the Reviewer for the co-reviewed comments.