SCIENTIFIC PERSPECTIVE

# Beyond PXRD Pattern Matching: Toward Rigorous Structure Determination in COFs

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**Abstract:** Widespread reliance on qualitative powder X-ray diffraction (PXRD) pattern matching has led to systematic overinterpretation of covalent organic framework (COF) structures. As a result, structure–property relationships are often obscured, mechanistic conclusions can be misleading, and reported performance is not always reproducible. In this Perspective, we take a closer look at common weaknesses in current practice, focusing on mismatches between proposed structural models and the characterization data used to support them. Through representative case studies, we show how these inconsistencies arise and why they matter. We argue that more rigorous, evidence-based approaches, achieved via complementary characterization techniques, are needed for reliable structure determination. We also emphasize the importance of transparent data reporting and deposition, and introduce a practical checklist to help authors, reviewers, and editors assess the strength of structural claims in COFs.

## 1. Introduction

Covalent organic frameworks (COFs) have emerged as an exciting class of porous, crystalline materials with potential applications in catalysis, separations, and energy conversion.[1–3] However, the rapid growth of the field has not always been matched by equal rigor in structural characterization.[4–6] In many reports, claims of crystallinity and new structure rely primarily on qualitative comparisons of PXRD patterns to idealized models, often with limited cross-validation. As a result, key features such as defects, stacking variability, phase heterogeneity, and even structural misalignment or the need for structure correction are frequently overlooked or inadequately addressed. These factors strongly influence materials discovery, properties, and reproducibility.

In this Perspective, we call for clearer, community-wide standards that better align structural claims with experimental evidence. We outline a set of best practices for robust structure determination, including: (i) quantitative powder X-ray diffraction (PXRD) analysis using Pawley or Rietveld refinement with transparent reporting of fit quality; (ii) complementary probes of local order, such as solid-state NMR analysis; (iii) electron diffraction and microscopy, including 3D electron diffraction and high-resolution transmission electron microscopy (HR-TEM) conducted with appropriate dose control; and (iv) internal consistency checks linking proposed structural

models with porosity measurements, gas-sorption data, pore-structure analysis, and computational predictions from density functional theory (DFT).

We argue that routine reporting of uncertainties, stacking disorder, and amorphous content should become standard practice, along with deposition of raw data and reproducible structural models. Finally, we discuss emerging approaches, such as continuous-rotation electron diffraction and computational validation, and provide a practical checklist intended for authors, reviewers, and editors. By adopting shared standards for structure determination, the COF community can strengthen structure–property relationships, reduce irreproducible claims, and more rapidly advance the discovery of truly crystalline and functionally reliable materials.

## 2. Why Structural Rigor Matters for COFs

Elucidating the crystal structure of covalent organic frameworks (COFs) is essential for understanding their properties and functions. Structural rigor, defined by accurate structure determination, provides meaningful insight into COF chemistry, including interlayer interactions, pore dimensions, and confined chemical environments. In 2D COFs, most structures were reported as ideal eclipsed models (AA stacking). Experimentally, COF layers are slightly slipped away, creating an offset from perfect alignment (serrated stacking).[7,8] This behavior greatly influences the electronic structure of COFs as $\pi$-$\pi$ stacking affects the interlayer interactions. Although the band gap of serrated COFs may be decreasing, their interlayer charge mobility can be increasing.[9] Interestingly, when the distinct interlayer interactions (i.e., coupling strengths) in a pyrene-based COF with nickel bipyridine as an acceptor unit are weakened, the COF can convert $CO_2$ to CO with high production yield (553.3 $\mu$mol/g/h) and 94% selectivity.[10]

Accurate determination of pore structure, which can only be achieved with the structural rigor, provides opportunities to utilize COF framework and micropore for gas capture and water vapor sorption. For example, in water sorption application, COF-432's structure determined by PXRD exhibits homogeneous micropores as small as 8 Å due to its staggered stacking.[11] The small pores of COF-432 demonstrate strong water interaction at 34% relative humidity, making it potential for water harvesting from air. Expanding the pore size helps increase the water uptake capacity, but this can also shift the water adsorption isotherm to higher relative humidity. To preserve the water sorption threshold at low relative humidity, hydrophilic active sites are introduced to the COF pores. More importantly, accessible active sites are crucial to the water harvesting application as sufficient space is required for water molecules to interact with the COF framework.[12]

Finally, confined chemical environments in COFs allow perfect installation of catalytic active centers,[13] such as cobaloxime units.[14] This approach relies on post-synthetic modification, which in turn depends on a detailed understanding of the pore structure. Similarly, mesopore COFs can serve as a platform for polymerization reaction within the pores to incorporate amine groups for carbon capture from air.[15] In conclusion, accurate structure determination is fundamental to linking COF structure with function. Failing to maintain structural rigor risks obscuring key structure–property relationships and propagating ambiguous or misleading conclusions in the literature.

Despite its importance, current practice often falls short due to an overreliance on PXRD pattern matching as the primary means of structural validation. In the following section, we examine this limitation in detail.

## 3. When PXRD Agreement Fails: Limits of Pattern-Based Validation

COFs are extended structures consisting of organic linkers linked by covalent bonds. Unlike coordinate bonds in metal complexes and metal–organic frameworks (MOFs), many covalent bonds in COFs are less reversible which is the main reason COFs generally exhibit lower crystallinity than MOFs. As a result, only imine COFs are crystallized as single crystals large enough for single-crystal X-ray diffraction (SCXRD) analysis while other COFs are often synthesized as crystalline powder. It is highly challenging to fully resolve the crystal structure of COFs due to their framework being composed of primarily light elements.

The current practice relies heavily on matching experimental and simulated PXRD patterns. For 2D COFs, reports often assume perfect eclipsed stacking and neglect common behavior in COFs, such as turbostratic disorder, preferred orientation, and solvent effects. For 3D COFs, published articles usually limit reporting of fit statistics and uncertainties, leading to many questionable new COF structures—often claimed 'unprecedented topologies in COFs.' It should be noted that the edge-transitive strategy (forming topologies based on one kind of link) has been the central focus of COF chemistry as it leads to predictable structures. In other words, this reticular design works

perfectly when COFs are formed by one kind of edge. However, the number of topology rises when kinds of edge and/or vertex are larger than one, thereby complicating the structure elucidation/selection as many topologies can be possible.

The above notion can be simply explained by increasing the degree of freedom. Several examples represent this approach: COF-790 (**fjh**),[16] COF-39 (**sql-c**),[17] and COF-904 (**hcb-c**).[18] COF-790 consists of triangular and square (more about rectangular) linkers. However, changing the dihedral angles between the central phenyl ring and adjacent rings in the triangular unit introduces an additional layer of flexibility. As a result, **fjh** is a proposed topology—it represents three kinds of vertex and two kinds of edge. Similar observation is presented in COF-39 and COF-904 (**Figure 1**). Their simplified shapes of building units may guarantee the formation of square (**sql**) and honeycomb (**hcb**) structures, respectively. But high flexibility and complexity lead to interpenetration frameworks of **sql** and **hcb**. Solving the structures of such complex COFs is challenging and requires advanced characterizations; otherwise, it may not be possible.

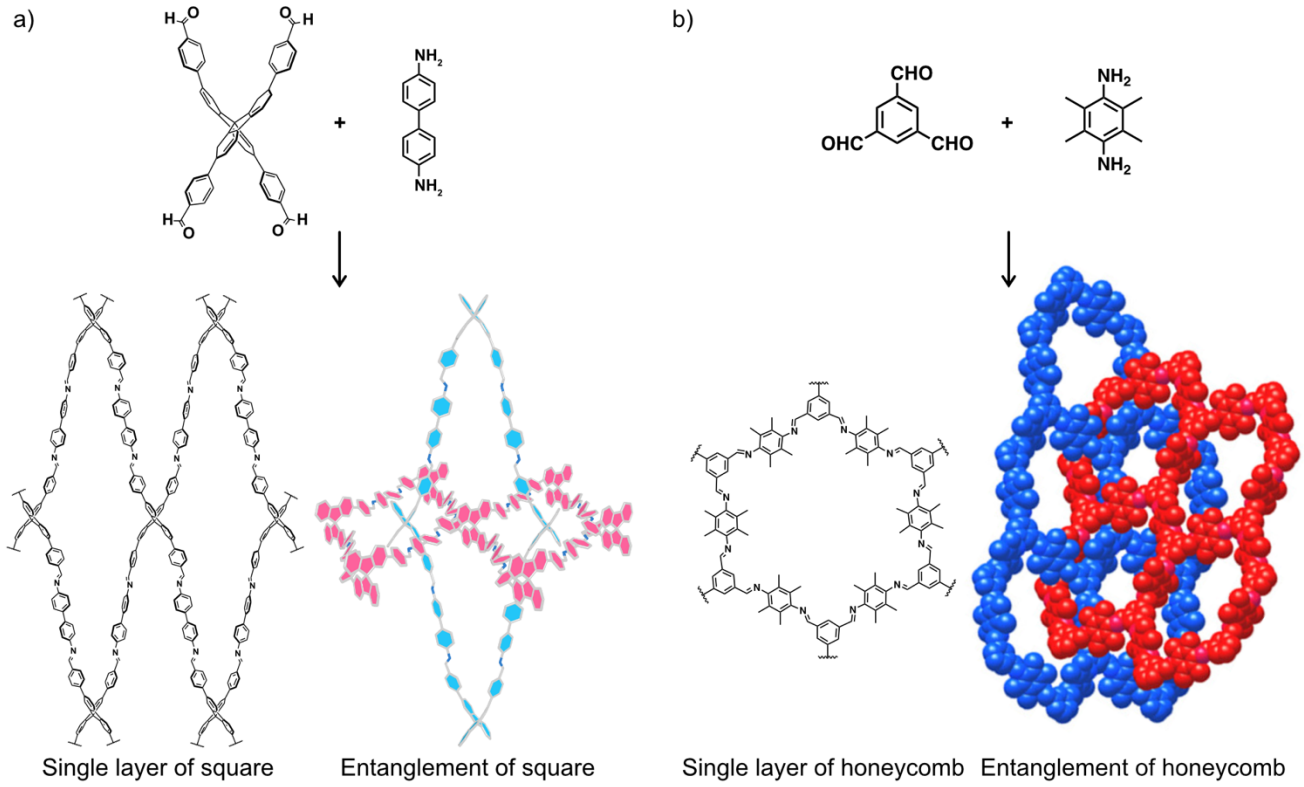


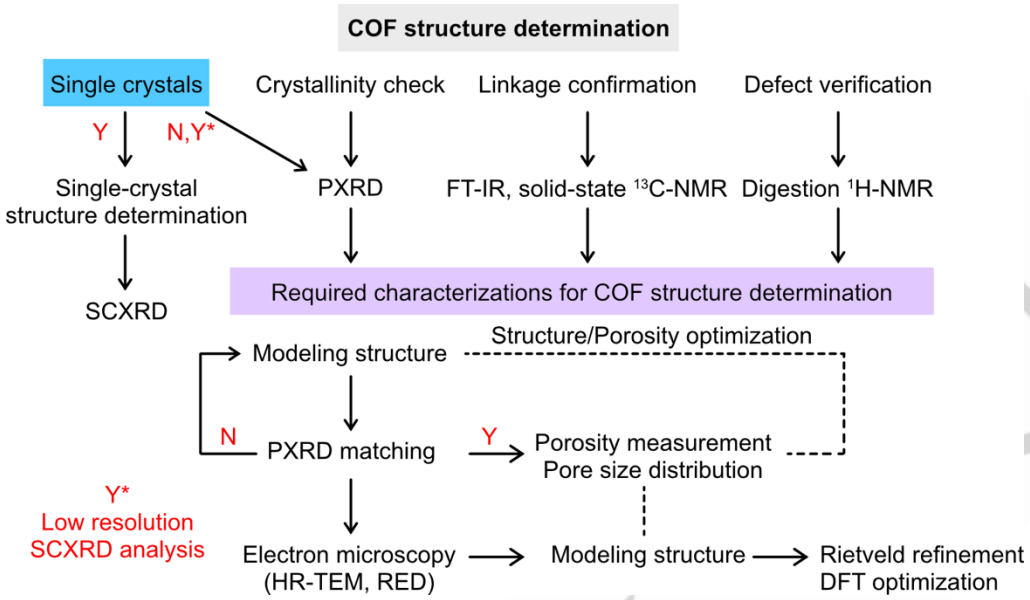

**Figure 1.** Increased linker flexibility gives rise to more complex COF structures. Formation of entanglement networks from square (a) and honeycomb (b) topologies enabled by flexible linking units.

COF-612, reported with a **kez** topology constructed from highly connected building units [(6,12)-c or (3,6,6)-c], provides another illustrative example.[19] SCXRD, even at a resolution of ~1.6 Å, determines a single-framework structure. However, to achieve close agreement between simulated and experimental PXRD patterns, it requires the application of a preferred orientation correction along the [001] direction using March–Dollase model. This case highlights the limitations of PXRD-only structural assignments and underscores the critical role of SCXRD in reliably elucidating COF structures.

## 4. A Multi-Level Validation Framework

PXRD is a powerful technique to determine the crystallinity of COFs and it is still a central characterization to validate the COFs' model structures (**Scheme 1**).[20] At this point, it is understandable that the current practice in COFs mainly depends on this method. Recent methodological article has outlined best practices for analyzing PXRD data.[5] However, these efforts primarily focus on how to perform structural validation in 2D COFs.[5] Here, we instead examine how structural claims should be interpreted, and where current assumptions may lead to

systematic misassignment. The central challenge is not the lack of structural characterization, but the overinterpretation of incomplete data. Several key considerations highlight the limitations of PXRD-based validation and the need for complementary evidence.




**Scheme 1.** Proposed workflow for COF structure determination.

In 1981, Pawley published a method to refine the unit cell parameter from a PXRD pattern.[21] This method is well-known as the Pawley refinement. In his article's abstract, he stated "In this procedure knowledge of the crystal structure is not required, and at the end of the refinement a list of indexed intensities is produced. This list may well be usable as the starting point for the application of direct methods." Pawley refinement is a whole-pattern fitting method where peak positions are determined by the lattice parameters, and the peak intensities are free variables. It is important to note that no atomic coordinates are used in Pawley refinement. For clarity in reporting, Pawley refinement may be described using statements such as 'the PXRD pattern was refined using the Pawley method, yielding good agreement factors ($R_{wp}$ ≈ X%), confirming the proposed lattice model.' However, it is important to recognize that such agreement does not uniquely validate the atomic structure, as Pawley refinement does not constrain atomic positions.

Many published articles in the COF field mislead the use of the Pawley refinement claiming that low reliability factor in this method means accurate models.[20] In fact, the low reliability factor does not necessarily mean we propose a structure close to the perfect model.[22] This conclusion can only be stated when Rietveld refinement is appropriately performed.[20,23] It is because Rietveld refinement fits the entire PXRD pattern, but peak intensities are not free. Instead, intensities are calculated from atomic positions, occupancies, thermal parameters, and symmetry constraints.[24] However, we must acknowledge that it is challenging to perform Rietveld refinement for COFs because of low scattering contrast (come from C, N, O, B, and H), disordered structure (slipping and/or turbostratic stacking), and peak overlap. As a result, a numerically "good" Rietveld fit does not guarantee a chemically meaningful structure. Instead, we should really refine using Rietveld method for COFs with high crystallinity using synchrotron PXRD data. Reliable refinement requires a sufficient number of diffraction peaks, which is often not achieved in typical low crystalline COFs. After the Rietveld refinement, experimental PXRD pattern should match with the simulated data.

The next consideration is what if the Rietveld refinement fails. As discussed above, this is a common issue in COF chemistry. There are important characterizations including local order analysis for linkage formation, porosity, and pore structure. Details of these measurements were reported in the literature.[23] Herein, we focus on how these characterizations supplement the COF structure determination.

First, linkage formation can be determined by Fourier-transform infrared and solid-state nuclear magnetic resonance (cross-polarization magic angle spinning, $^{13}$C CP/MAS NMR) spectroscopy. These two characterizations provide insightful information to identify if COF structures contain significant defects. **In this context, a few representative COFs are discussed to underscore the importance of supplementary**

**characterization in structure determination, rather than to question/criticize previously reported structures**. COF-340, highlighted here as the first example, consists of 1,3,5-tris(*p*-formylphenyl)benzene (TFPB) and tetrakis(4-aminophenyl) ethane (ETTA), and it represents a defect version of **tth** topology due to the unreacted aldehyde functional groups in TFPB.[25] Unreacted aldehyde can be recognized by $^{13}$C CP/MAS spectroscopy, showing a chemical shift at around 180 ppm. More convincingly, the sub-stoichiometry of defect **tth** is determined by digestion proton NMR, which show a ratio of 3 TFPB over 2 ETTA. However, in another work, the same combination of TFPB and ETTA results in a 3D COF structure (**ffc**)[26] which, per our perspective, is questionable as the two PXRD patterns are almost identical (**Figure 2**).[27] No digestion NMR is provided in the later publication.

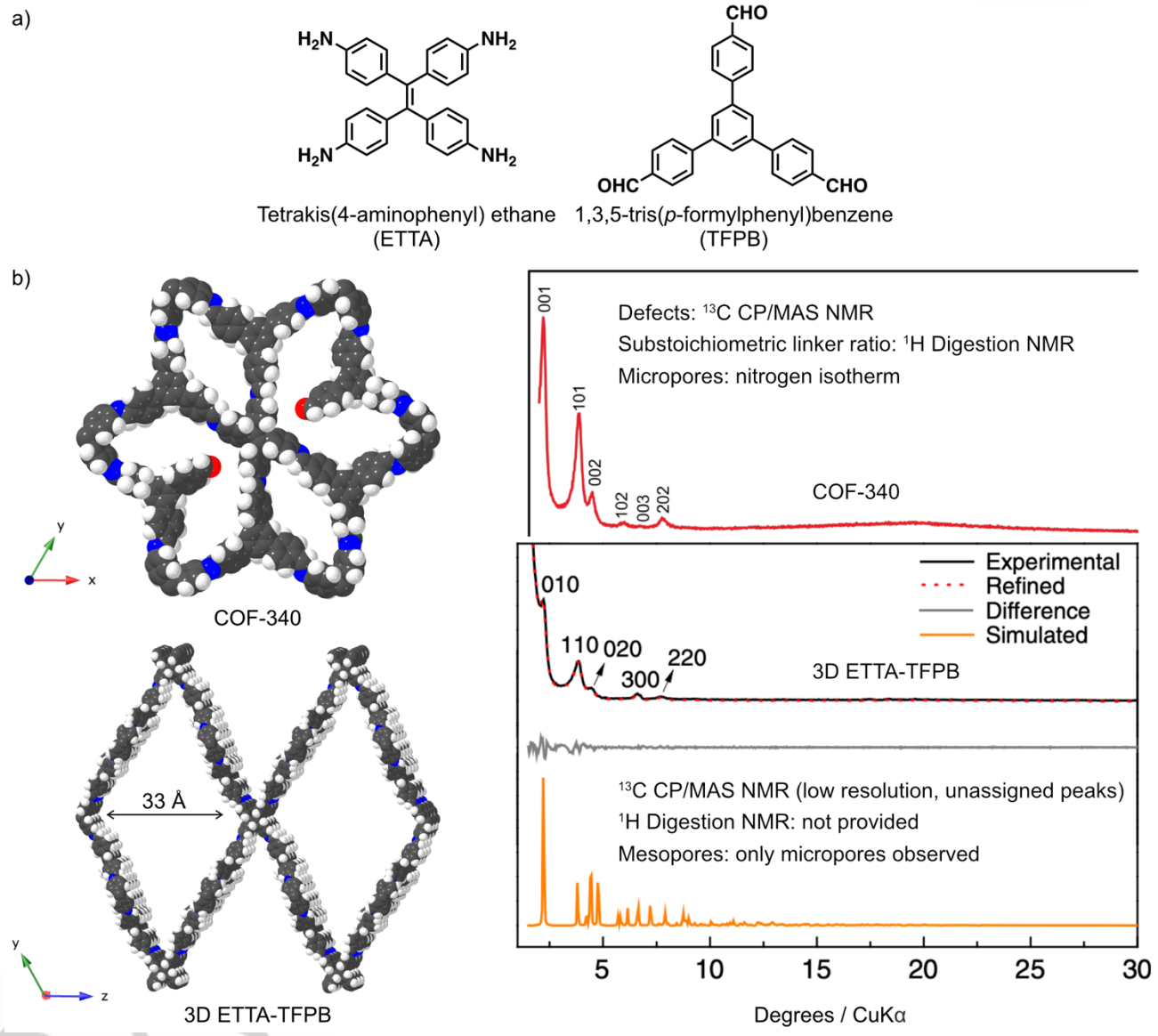



**Figure 2.** Identical building units, 1,3,5-tris(*p*-formylphenyl)benzene (TFPB) and tetrakis(4-aminophenyl) ethane (ETTA), (a) give rise to COFs that were structurally assigned as either 2D or 3D frameworks (b). Despite these different structural assignments, their PXRD patterns are highly similar, highlighting the ambiguity in structure determination and the difficulty in unambiguously validating simulated PXRD matches. PXRD data are reproduced from the original publications and overlaid after approximate alignment on the same 2θ scale.[25,26] The CIFs of COFs are downloaded from CURATED covalent organic frameworks database.[28]

Second, the model structures of COFs must be strongly supported by the porosity measurement. COFs are robust crystalline structures, and removing guest molecules in their pores does not lead to the structure collapse. Assuming that the COF crystallinity and activation protocol are optimal, a porosity calculation based on the model structure should be close to the experimental surface area measured by nitrogen or argon sorption isotherms. More

importantly, gas sorption isotherms allow simulations of the COF's pore sizes based on DFT method. This is valuable information about how many types of pores in the COF structure, and whether the COF exhibits micropores or mesopores or even both. Mismatch of pore structure (types and sizes) between model structure and experimental sorption data could be a red flag in inaccurate determination of the COF structure. For example, the **ffc** COF was proposed to be a single framework which demonstrate a mesopore structure (**Figure 2**). However, the nitrogen sorption measurement represents a type-I isotherm of microporous materials, leading to inconsistency of the structure evaluation.[26] This ambiguity in structural evaluation may have influenced later studies to assign **ffc** topology to related COFs.

In the pore-size analysis, quench solid DFT (QSDFT) is generally preferred over nonlocal DFT (NLDFT) for MOFs and COFs because it accounts for surface heterogeneity and roughness of organic pore walls, leading to smoother and more physically realistic pore size distributions, especially in the microporous regime.[29] In contrast, NLDFT assumes ideally smooth and homogeneous surfaces and can produce artificial step-like features, but it remains widely used and acceptable for comparative studies when the same model is applied consistently. The dominant pore sizes extracted from gas adsorption data match the pore dimensions predicted by the idealized framework, supporting the consistency between experimental adsorption behavior and the assigned structure. An example of pore-structure statement is "The QSDFT pore-size distribution analyses present one type of pore locating at X Å, showing good agreement with the proposed structural model." In addition, it is important to show the fitting between experimental data and calculated isotherms, with close agreement between experiment and simulation.

Finally, HR-TEM may be used cautiously to provide supporting evidence for long-range order in COFs,[30] such as the presence of periodic fringe spacings consistent with predicted lattice planes. COF-432 serves as an example, demonstrating the valuable insight of using HR-TEM to support the model structure (**Figure 3**). It is worth noting that COF-432 consists of square and triangle linkers, making it difficult to imagine a possible 2D structure could be formed.[11] Nevertheless, charge flipping method based on PXRD pattern suggests a 2D layer structure. Later, HR-TEM confirms its 2D structure, providing clear images of 2D stacking frameworks.[31]

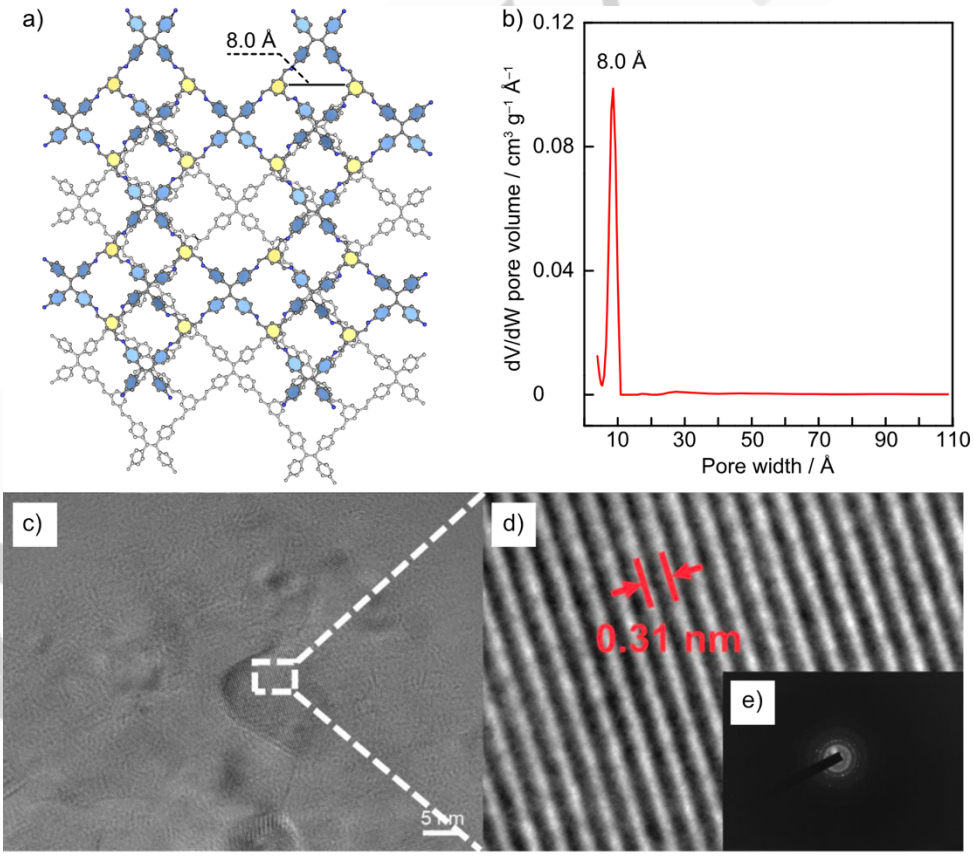



**Figure 3.** A 2D structural model of COF-432 demonstrates pore sizes of 8.0 Å (a) supported by pore size distribution estimated using nitrogen sorption isotherm at 77 K (b). The layer structure of COF-432 is consistent with HR-TEM analysis (c–e).[31] The distance between two layers in COF-432 measured by HR-TEM is 3.1 Å which is in good agreement with 3.2 Å in the model structure.

An advanced TEM technique not only provides comprehensive information about locations, orientations, and shapes of crystalline domains in 2D COFs, but also offers images of the COF pores with atomic-scale resolution.[32–34] This measurement is usually carried out through average background subtraction filter HR-TEM image of a given COF taken along a given axis. Subsequently, magnified view of the HR-TEM images allows an overlay with the COF's structure model along a particular direction. It is important to note that to be considered credible, HR-TEM observations must be acquired under strictly dose-limited conditions and correlated with simulated projections derived from the proposed structural model.[35] Given the susceptibility of COFs to electron beam, lattice fringes should only be used as corroborative evidence in conjunction with PXRD, modeling, and spectroscopic validation.

## 5. Emerging Solution for COF Structure Determination

SCXRD is certainly a technique that can fully resolve COF structures up to sub-Angstrom resolution.[36] Unfortunately, up to date, only 3D imine-linked COFs can be crystallized as single-crystals large enough for the SCXRD analysis. Nevertheless, the crystal structure of COFs with nanometer-size can still be resolved using continuous rotation electron diffraction (cRED).[37,38] cRED is a 3D electron diffraction (3DED) technique in which a single nanocrystal is continuously rotated in the electron beam while diffraction patterns are recorded as a function of tilt angle. This approach enables near-complete reciprocal-space sampling from crystals as small as tens to hundreds of nanometers, capitalizing on the strong electron–matter interaction. Compared to stepwise ED methods, cRED provides improved data completeness, reduced dynamical scattering effects through fast acquisition, and lower electron dose, which is critical for beam-sensitive COFs. The resulting datasets can be processed analogously to SCXRD, allowing reliable ab initio structure solution and refinement, including determination of lattice parameters, space group symmetry, and framework connectivity. The first COF structure resolved using cRED is COF-320 with 9-fold interpenetrated diamond structure.[37] Since 2014, different protocols have been developed across many research groups.[27,38,39] They include microcrystal ED, fast electron diffraction tomography, RED, and (cRED). Technical details of these methods are discussed in a recent review.[38]

## 6. Computational Validation

Computational simulations have become an important tool for validating COF structures, especially when experimental data alone cannot fully resolve the structure.[40] In current practice, one typically builds several plausible structural models and then uses force-field methods, usually incorporated in Materials Studio software, to optimize them and assess their relative stability, including different stacking modes such as eclipsed, staggered, or serrated layers. However, due to the limitations of force-field methods, serrated layers are usually overlooked. This can be overcome by using DFT methods, which provide a more accurate description of interlayer interactions and subtle structural distortions. For example, serrated structures are more stable in 2D COFs for water harvesting HCOFs and COF-309.[12] After COF structure optimization, simulated PXRD patterns can be generated and directly compared with experimental data; mismatches often assign to structural disorder, defects, or incorrect assignments. In this context, defects can be proven by spectroscopy methods (IR and/or NMR).

In addition, grand canonical Monte Carlo simulations allow prediction of gas adsorption isotherms, which can be matched with experimental sorption results to evaluate pore size, connectivity, and accessibility.[41] This method has been widely used to simulate water vapor isotherms in COFs.[42] Molecular dynamics simulations further help verify framework flexibility and dynamic behavior that are not visible in static models.[43,44] Taken together, computational simulations provide a more intuitive and realistic way to assess whether a proposed COF structure is physically meaningful and consistent with experimental data.

## 7. Reporting Standards, Data Transparency, and Practical Checklist

Reliable reporting and transparent data sharing are key for building confidence in COF structures and making results reproducible. In practice, this means including a clear set of essential figures and tables, including experimental and simulated PXRD patterns, full adsorption isotherms, solid-state NMR spectra, and electron microscopy images to support the proposed structure. We also suggest that underlying raw data (PXRD files, solid-state NMR spectra, and complete adsorption datasets) should be made available, rather than only showing processed plots, so others can verify and reinterpret the results if needed. Importantly, structural CIF files for all proposed models should also be shared to allow independent validation of the structural assignment, rather than relying on crystallographic coordinates provided only in the supplementary information.

It is also important to comment about material quality. Any amorphous or poorly crystalline fraction should be explicitly mentioned and, when possible, estimated using approaches such as Rietveld refinement or peak-area integration, since it can strongly affect both diffraction and adsorption behavior. Finally, authors should provide enough experimental detail to make the work reproducible: clear synthesis conditions, activation procedures, measurement protocols, and ideally some indication of batch-to-batch consistency. These practices make the work more transparent, reduce ambiguity in structural interpretation, and help ensure that the reported properties truly reflect well-defined and reproducible COF materials.

Finally, we propose a practical checklist to support a more critical and systematic evaluation of COF structure claims. This checklist ensures consistency between proposed COF models and experimental data, including careful assessment of PXRD fitting quality, agreement with complementary characterization methods (e.g., spectroscopy, gas sorption, and microscopy), and the chemical plausibility of the framework connectivity (e.g., as supported by digestion $^{1}$H-NMR). It also encourages caution against overinterpreting limited datasets, emphasizes the importance of collecting sufficient evidence to distinguish between competing structural models, and highlights the value of reporting negative or ambiguous results when appropriate.

## 8. Conclusion

In this Perspective, we outline common limitations in current COF characterization practices, particularly the ambiguity in structural assignment. These issues often arise not from a lack of data, but from insufficient cross-validation and complementary characterization. Through representative case studies, we emphasize the critical need for comprehensive evidence to support proposed structural models, especially for 3D COFs. Claims of new topologies should therefore be made with caution and supported by multiple, independent lines of evidence, rather than relying solely on PXRD pattern matching. Factors such as preferred orientation, defects, and structural disorder can lead to significant discrepancies between simulated and experimental PXRD patterns, complicating structural interpretation. Although this Perspective focuses on COFs, similar challenges are increasingly recognized across related reticular materials, suggesting that the strategies discussed here may have broad applicability.

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## Conflicts of Interest

The author declares no conflicts of interest. AI tools were used to assist with proofreading and language editing.

## Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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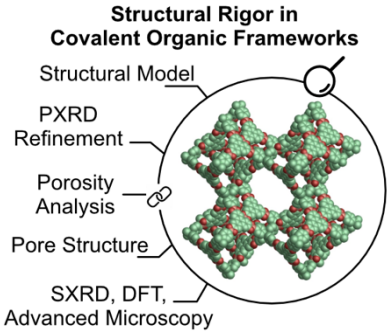
**Entry for the Table of Contents**




This Perspective identifies common limitations in current practices in COF structure determination and illustrates the importance of collecting sufficient evidence to avoid mismatches between experimental data and proposed COF models.

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