

Data-driven Inverse Design of Multifunctional Bicontinuous Multiscale Structures

Corresponding Author: Dr Xiaoya Zhai

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)

The manuscript "Data-driven Inverse Design of Bicontinuous Multiscale Structures" presents an approach for the inverse design of bicontinuous, elastic multiscale structures. This method focuses on constructing datasets of cubic symmetric, bicontinuous microstructures with identical boundaries to ensure seamless connectivity across scales. Using topology optimization, denoising diffusion models, and active learning, four extensive datasets are generated. These datasets enable the selection of microstructures based on matching elastic coefficients, facilitating the design of multiscale structures with tailored properties.

The concept of creating extensive datasets of bicontinuous microstructures with identical boundaries, along with the reported applications, is intriguing. However, the performance, impact, and novelty of the proposed approach compared to existing methods remain unclear.

Comments.

1. In the introduction, the authors state that commonly employed techniques to enhance connectivity between microstructures lead to "increased computational costs and limited properties", struggling to "effectively address the above two key challenges". Can the authors discuss and quantify these challenges? How does the proposed approach solve them? Does the proposed approach outperform them?
2. Related to 1., benchmarks with existing methods, including graded spinodoid microstructures (<https://doi.org/10.1038/s41524-020-0341-6> ; <https://doi.org/10.1016/j.cma.2021.113894>) or growth-based approaches <https://doi.org/10.1038/s41467-024-47831-2> , are missing. Can the proposed approach outperform these methods? What does this method achieve that other approaches cannot?
3. Related to 1. and 2., are interpolations between microstructures more computationally expensive and have limited property range compared to the proposed method? If yes, can the authors show a benchmark?
4. Why is the initial dataset optimized by maximizing the elastic moduli (bulk, shear, Young's modulus, etc)? Do most of the proposed applications require stiffness values not achievable by using non-optimized microstructures with compatible 3D-printed materials (e.g., biocompatible)?
5. Have any of the designs presented in the case studies been compared to existing commercial designs?
6. The selection of the four masks is not entirely clear: "We evaluated the generated structures based on quality, Poisson's ratio coverage, and bicontinuous." How did you exactly select these masks? How do you define "quality"?
7. Regarding the multiscale design, how is the distribution of elastic coefficients in the design domain determined? Looking at the bone implant as an example, to the best of my knowledge, the implant's stiffness (entire stiffness matrix) should match that of the bone to promote cell growth and tissue regeneration. In the reported example as well as in all other case studies, stiffness is maximized, rather than matched with that of the bone. Furthermore, should the stress distribution within the implant be as uniform as possible?
8. Following up on point 7, does the assumption of cubic symmetry pose limitations for certain applications, such as bone implants?
9. About the filtering device example, the datasets were constructed accounting only for the stiffness. However, the main performance metric for such devices seems to be permeability. Would using other conditioning properties, such as permeability, in the diffusion model help finding better designs?

(Remarks on code availability)

Reviewer #2

(Remarks to the Author)

1. The paper does not discuss how errors in the generative model (e.g., boundary misalignment or failure to meet elastic tensor constraints) propagate through the multiscale optimization process. Quantifying this could identify potential pitfalls in applications.
2. The reliance on predefined elastic tensors and masks could limit the model's ability to generalize. Techniques like unsupervised learning or meta-learning could enhance adaptability for unseen property spaces.
3. Include automated metrics for validating bicontinuity and boundary alignment during dataset generation, such as a) Fourier transform-based spatial analysis for structural periodicity, and b) Stress-testing using finite element analysis on randomly sampled outputs.
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5. Embedding physical constraints (e.g., Navier-Stokes equations for permeability or heat transfer equations for thermally conductive structures) directly into the model could improve performance on application-specific tasks.
6. Use latent space analysis to identify how different latent dimensions correlate with specific structural properties, aiding in targeted property tuning.
7. Instead of static boundary masks, incorporate adaptive masks that evolve during training to explore broader structural designs.

(Remarks on code availability)

The github repository link provided by the authors does not contain the main code.

Reviewer #3

(Remarks to the Author)

The study investigates the machine learning (ML)-enabled design process of large-scale, boundary-identical, bicontinuous structures. While the study addresses an important research area, the current results fail to clearly demonstrate the novelty of the work. Several critical issues should be addressed to enhance its scientific contribution and overall quality.

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1. The manuscript shows no significant advantages in active learning or microstructure generation compared to their prior studies (reference 56 and <https://doi.org/10.1002/adv.202410428>). If the novelty lies in adding boundary conditions to achieve large-scale structure assembly, the authors must clarify how their approach improves computational efficiency or structure performance. Such as directly large-scale topology optimization methods (<https://doi.org/10.1038/nature23911>) or other ML-based methods (<https://www.nature.com/articles/s41467-024-47831-2>, <https://www.nature.com/articles/s41467-023-42415-y>)
2. The two examples of bone implants (segmental implant and fusion cage) differ from actual requirements, and the performance description is insufficient.
 - (a) The base material for constructing the structures is unclear. As load-bearing bone implants, materials such as PEEK or Ti are typically used, and optimization objectives differ significantly depending on the base material.
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 - (c) What is the difference between assembling the final implant by selecting different structures within a defined range and repeatedly constructing it using a single structure optimized for the target performance?
 - (d) The authors optimized the microstructures, but do the assembled large-scale structures still meet the target performance? In other words, the final porosity, mechanical properties, and other performance metrics of the large-scale structures should be clarified and compared. A good example would be the permeability test in this paper.
3. How do the principles of microstructure arrangement enhance or control properties such as permeability? Such summaries or discussions should be provided to support the advancement of the field.

Minor Concerns:

4. The transitions between units with the preset boundary conditions are good. And the internal structures appear to have rounded transitions near the boundaries. How were these transitions considered and achieved?
5. On Page 7, the authors claim that smaller pores contribute to faster cell seeding and that high curvature improves nutrient flow, cell attachment, and tissue regeneration. These statements are inaccurate. Accurate discussions of these can be referred to <https://doi.org/10.1016/j.matt.2022.06.003> and <https://doi.org/10.1038/s42254-024-00700-9> for accurate

discussions of these phenomena.

(Remarks on code availability)

Code is not yet updated

Version 1:

Reviewer comments:

Reviewer #1

(Remarks to the Author)

The authors have thoroughly addressed all of my previous comments and concerns. The revised manuscript is significantly improved and is now suitable for publication in Nature Communications.

(Remarks on code availability)

I briefly reviewed the code without installing or running it locally. The repository seems to have clear instructions for installation and execution.

Reviewer #3

(Remarks to the Author)

The authors have made substantial revisions that address most major concerns. I think this paper can be accepted after addressing some issues remained blow:

The reply to their novelty is reasonably thorough and includes performance comparisons, e.g., in mechanical cloak design (5 minutes vs. 10 hours). Still, A more explicitly contrast the new boundary-aware generation strategy with their previous “boundary-free” designs should be clarified.

About the discussion part,the author experimentally compared the permeability of two LBBM structures and four TPMS structures, achieving a wide range of permeability results. And the addition of application such as thermal conductivity to the permeability discussion is good. However, the author still have not addressed my previous question: Does this contribute to some theoretical understanding of the relationship between structural design and permeability, rather than merely comparing different results? For example, among parameters such as porosity, pore size, pore shape, and orientation, how do they rank in terms of influence on permeability? The authors do not need to experimentally or numerically verify each factor, but should at least provide a theoretical discussion.

(Remarks on code availability)

The code is uploaded, and the README file has enough instructions.

Reviewer #4

(Remarks to the Author)

Comment 1: In general this is a quality piece of work. The manuscript and figures are well constructed. Most, but not all prior reviewer concerns appear to have been addressed.

Comment 2: I am confused by the need to resolve connectivity in conventional periodic lattices. This must stem from the discretization of the design domain, but why this is necessary for conventional lattice design is not explained. Continuous fields can be used to efficiently drive periodic lattice design variable such as cell size/shape, density, and tiling.

Comment 3: There are still some concerns over novelty. If the term “open cell” is substituted (quite appropriately) for bi-continuous, much of the implications of this work can be more readily understood.

Comment 4: There are too many complex multi-panel figures. To be fair these figures are executed extremely well, and are visually pleasing, but many features become too small to see, making interpretation of results difficult at times. A more straightforward quantitative presentation of results may help make direct comparisons, and remove any obfuscation.

Comment 5: I am also curious about the choice of boundary masks. Can the authors provide more detail on how they were selected and enforced. What order connectivity is enforced at the boundary, geometric, tangent, continuous (C0, C1, C2)? Can the authors comment more about the impact of boundary mask on properties? Is it useful to construct 100,000 internally different iterations of 4 boundary configurations, or would more performance gains be made by constructing 1000 different boundary masks with 100 internal designs each? The re-entrant boundary mask showing such wide spread in poissons ratio is telling that this initial constraint is significantly blocking/unlocking property spaces. Until the boundary conditions can be fully understood and modified where possible by machine design, human designs will often remain superior.

(Remarks on code availability)

Version 2:

Reviewer comments:

Reviewer #3

(Remarks to the Author)

The authors have well addressed my concerns and significantly improved the manuscript. I think it is now suitable for publication in Nature Communications.

(Remarks on code availability)

The code is well structured.

Reviewer #4

(Remarks to the Author)

The modifications to this manuscript make it much better and address all the reviewer comments. It is clear the authors have done quite a bit of technical work, and work in preparation of the manuscript.

(Remarks on code availability)

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Revision summary

“Data-driven Inverse Design of Multifunctional Bicontinuous Multiscale Structures”

Lili Wang, Jingxuan Feng, Xiaoya Zhai, Jiacheng Han, Kai Chen,
Winston Wai Shing Ma, Ligang Liu, Xiao-Ming Fu

April 15, 2025

REVIEWER COMMENTS

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Remarks on code availability:

Code is not yet updated.

General Response

We are grateful to all three reviewers for their constructive and insightful comments. Based on the feedback from the reviewers, we have thoroughly revised the main manuscript and the Supplementary Information according to all comments, primarily including

- This study considers two types of bone: compact bone and cancellous bone. To highlight the advantages of our optimization results in terms of computational efficiency and performance metrics, we compare them with parametric microstructure models, including the body-centered cubic symmetry (BCC) truss, Schoen’s I-graph-wrapped package (IWP), and spinodal structures. In both cases, our optimized designs demonstrate clear advantages.
- We develop and implement a novel experimental protocol that integrates numerical analysis, simulation modeling, and experimental testing to comprehensively validate the broad range of permeability represented in our dataset. Both simulation and experimental results demonstrate the outstanding performance of the constructed dataset.
- We further enrich the dataset by incorporating a comprehensive set of properties, including mechanical characteristics (Young’s modulus, Poisson’s ratio, shear modulus, and bulk modulus), as well as permeability, porosity (volume fraction), pore size, and surface-to-volume ratio (S/V).

Please see below for a point-by-point response to the reviewers’ comments and concerns. All page/figure/table/line numbers refer to the revised manuscript file with tracked changes. All paragraphs that appear in the revised manuscript or supplementary are marked in **red**.

Response to Reviewer #1

- **Reviewer #1 General Comment:** The manuscript “Data-driven Inverse Design of Bicontinuous Multiscale Structures” presents an approach for the inverse design of bicontinuous, elastic multiscale structures. This method focuses on constructing datasets of cubic symmetric, bicontinuous microstructures with identical boundaries to ensure seamless connectivity across scales. Using topology optimization, denoising diffusion models, and active learning, four extensive datasets are generated. These datasets enable the selection of microstructures based on matching elastic coefficients, facilitating the design of multiscale structures with tailored properties.

The concept of creating extensive datasets of bicontinuous microstructures with identical boundaries, along with the reported applications, is intriguing. However, the performance, impact, and novelty of the proposed approach compared to existing methods remain unclear.

Response: We are extremely grateful for your thorough review of our manuscript and the valuable feedback you have provided. We are delighted that you have shown interest in our data-driven inverse design approach and the concept of bicontinuous microstructures. In response to your questions regarding performance, impact, and novelty. Following, we have made point-by-point responses regarding the specific comments.

- **Reviewer #1 Comment #1:** In the introduction, the authors state that commonly employed techniques to enhance connectivity between microstructures lead to “increased computational costs and limited properties”, struggling to “effectively address the above two key challenges”. Can the authors discuss and quantify these challenges? How does the proposed approach solve them? Does the proposed approach outperform them?

Response: We are very grateful for the valuable comments provided by the reviewer and fully agree on the necessity of conducting a specific quantitative analysis of the two key challenges: “increased computational costs and limited properties.” Based on this, we elaborate on how our method addresses these challenges in a targeted manner and discuss whether our approach can effectively surpass these limitations. In the following, we provide a detailed response to the three specific questions raised by the reviewers, focusing on (1) computational costs and (2) properties.

(1) Computational costs

To systematically evaluate the computational cost of the multiscale optimization process, we divide the entire multiscale computational workflow into five stages:

- Inverse optimization: The elastic tensor of the macroscopic element is employed as the design variable for inverse optimization targeting at application-dependent objectives.
- Matching: Microstructures are matched according to the optimized elastic tensor.
- Assembly: The selected microstructures are equipped to form a macrostructure.
- Connectivity processing: Interpolation is applied to address discontinuities at the microstructure boundaries to ensure boundary connectivity of the optimized structures.
- Intersection operation: The final results are obtained from the intersection of the optimized macrostructure and predefined solid domain.

A detailed statistical analysis is performed to quantify the time consumption at each stage.

Compact and cancellous bone design We compare the computational time of the multiscale optimization process with that of three representative microstructures: BCC truss, IWP structure and spinodal structure. The total time of designing a compact bone implant using our method is 8.54 seconds for a multiscale optimization problem of $3 \times 3 \times 9$ unit configuration. However, for optimization problems with the same scale and design objectives, addressing boundary connectivity issues such as those required by interpolation algorithms [1] like BCC truss, TPMS (Triply Periodic Minimal Surfaces), and spinodal structures typically takes more than 2.5 times longer. For a larger-scale optimization task with a configuration of $5 \times 7 \times 4$ units, our method requires approximately one-quarter of the computation time compared to other multiscale approaches, including the BCC truss, IWP, and spinodal methods.

It is worth emphasizing that as the resolution increases, our method consistently maintains high computational efficiency, avoiding the exponential growth in computation time typically caused by boundary processing and interpolation in traditional approaches. This significant reduction in computational time demonstrates the outstanding efficiency of our optimization method and further confirms its applicability to large-scale, high-resolution multiscale design tasks.

Mechanical cloak Most notably, in a large-scale invisibility cloak design case with $20 \times 20 \times 20$ units, our complete multiscale design process takes under 5 minutes—substantially faster than the 37,014.26 seconds (over 10 hours) reported by Yang et al.[3] for multiscale mechanical cloak optimization. This significant computational advantage is attributed to the unified boundaries of all structural units in our framework, which eliminate the need for boundary connectivity processing during the initial design phase, effectively reducing the time for this step to zero. Detailed comparative results are provided in Figure R1.

(2) Properties

Regarding performance evaluation, we conducted a multiscale optimization design of bone structures using the Young’s modulus of 5000 MPa for compact bone and 2500 MPa for cancellous bone as benchmarks [4].

For compact bone, numerical results show that the multiscale structure we designed closely matches the mechanical properties of compact bone. In comparison, the IWP structure and truss structure also perform well but show slightly lower compatibility, while the spinodal structure performs the worst. Additionally, analysis of volume and S/V reveals that our optimized structure is lighter than the IWP and spinodal structures, with a higher S/V compared to the BCC truss and spinodal structures, demonstrating superior structural characteristics (Figure R2).

Furthermore, in our design, the average pore size (APS) of the compact bone structure is $286.64 \mu\text{m}$, which falls within the optimal range of $200\text{--}400 \mu\text{m}$. In contrast, the APS of the other three structures lie outside this ideal range. It is noteworthy that the average pore size of the designed cancellous bone structure is $299.31 \mu\text{m}$, which also falls within the ideal range. In contrast, the other three structures exhibit greater deviations from this range, resulting in larger discrepancies (Figure R2).

For compact bone, our method favors plate-like structures, while for cancellous bone, it produces truss-like forms that better mimic real bone. Although the optimization depends on initial conditions, our dataset makes the results less sensitive compared to IWP, BCC truss, and spinodal structures (Figure R3-R4).

Multiscale design		Unit cell count	Optimization /s	Matching /s	Assembly /s	Interpolation /s	Intersection /s	Total /s	Total /min
Compact bone	Mask 3	$3 \times 3 \times 9 \times 128^3$	2.89	0.11	2.2	—	3.34	8.54	0.14
	IWP		2.56	0.09	2.57	22.97	3.39	31.58	0.53
	BCC truss		2.71	0.09	2.36	23.32	3.31	31.79	0.53
	Spinodal		3.51	1.49	4.39	23.21	3.37	35.97	0.60
Cancellous bone	Mask 3	$5 \times 7 \times 4 \times 128^3$	3.34	0.13	5.18	—	11.46	20.11	0.34
	IWP		3.06	0.10	5.06	55.34	11.85	75.41	1.26
	BCC truss		3.11	0.11	5.52	56.16	10.23	75.13	1.25
	Spinodal		7.22	3.67	8.51	54.89	11.60	85.89	1.43
Mechanical cloak	Mask 2	$20 \times 20 \times 20 \times 128^3$	68.56	0.30	223.2	—	—	292.06	4.87
	Yang et al. [3]		67.18	0.42	235.35	—	37014.26	37317.21	621.95

Figure R1: Time consumption statistics for optimization, matching, assembly, interpolation, and intersection processes, along with a comparison of optimization results.

Multiscale design		Unit cell count	Porosity	Vol	S/V	Young's modulus /MPa	Minimum Distance	Maximum Distance	Average Distance	Average pore size μm	Displacement
Compact bone	Mask 3	$3 \times 3 \times 9 \times 128^3$	0.6347	0.37	0.67	4968.1	1	48.7032	10.9303	284.6437	—
	IWP		0.6234	0.38	0.70	4624.9	3	29.8998	17.8103	463.8111	—
	BCC truss		0.6380	0.36	0.29	4767.6	1	62.1128	22.7392	592.1670	—
	Spinodal		0.5770	0.42	0.59	5835.8	1	15.6525	1.5840	41.2497	—
Cancellous bone	Mask 3	$5 \times 7 \times 4 \times 128^3$	0.7781	0.22	0.67	2511.3	1	41.1218	9.5778	299.3076	—
	IWP		0.7998	0.20	0.55	2668.8	6	31.1769	20.3875	637.1079	—
	BCC truss		0.7403	0.26	0.27	2377.6	1	61.3514	27.6850	865.1556	—
	Spinodal		0.6773	0.32	0.68	3120.3	1	15.6525	1.9849	62.0268	—
Mechanical cloak	Mask 2	$20 \times 20 \times 20 \times 128^3$	—	—	—	—	—	—	—	—	0.3393→0.0523
	Yang et al. [3]		—	—	—	—	—	—	—	—	0.3417→0.0581

Figure R2: Performance comparison and analysis of compact bone, cancellous bone, and mechanical cloaks.

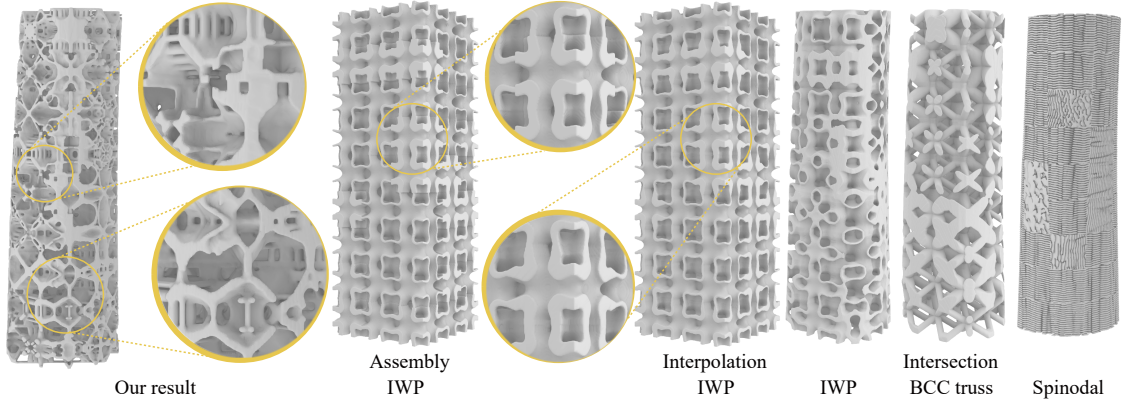


Figure R3: Our optimization results compared with the details of compact bone, along with the assembly and interpolation results of the IWP structure, as well as the intersection results of the IWP, BCC truss, and spinodal structures.

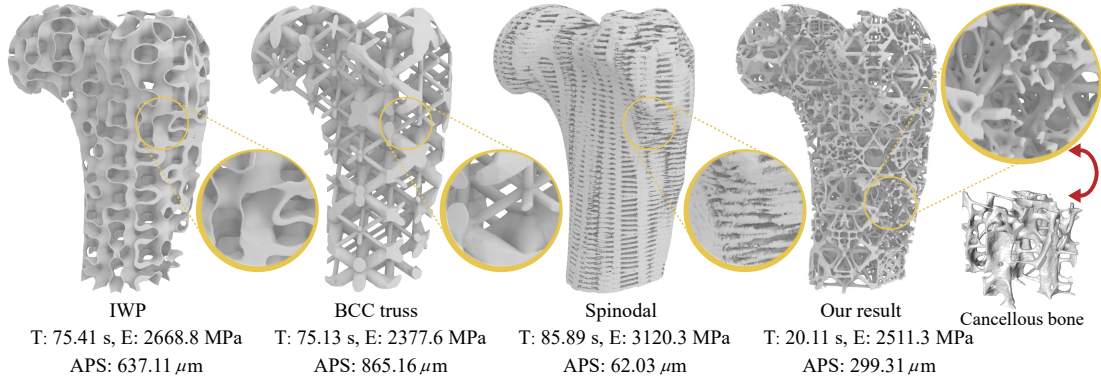


Figure R4: The multiscale results of IWP, BCC truss, and spinodal structures are presented, along with our optimization results, which are compared in detail with cancellous bone [2].

In the cloak design case, quantitative evaluation of displacement distortion indicates that our optimized cloak achieves comparable invisibility effect as the study by Yang et al. [3], further validating the effectiveness and feasibility of the proposed method.

- **Reviewer #1 Comment #2:** Related to 1., benchmarks with existing methods, including graded spinodoid microstructures (<https://doi.org/10.1038/s41524-020-0341-6>; <https://doi.org/10.1016/j.cma.2021.113894>) or growth-based approaches <https://doi.org/10.1038/s41467-024-47831-2>, are missing. Can the proposed approach outperform these methods? What does this method achieve that other approaches cannot?

Response: Thank you for your valuable comments. A comparison with the current benchmark example is indeed necessary, and we provide a comprehensive response to the reviewer's comments from three perspectives: (1) property range, (2) data density, and (3) boundary consistency.

(1) Wide property range and large design space

To investigate the property range of spinodal structures, we follow the methodology presented in the reviewer-suggested reference [5] and generate 20,000 spinodal structure samples. Among them, we select 8,193 bicontinuous structures. Figure R5 illustrates the relationships among Poisson's ratio, Young's modulus, and the Zener ratio. It shows that the Zener ratio of anisotropy for the spinodal structure remains below 1.5. The distribution of microstructures within the

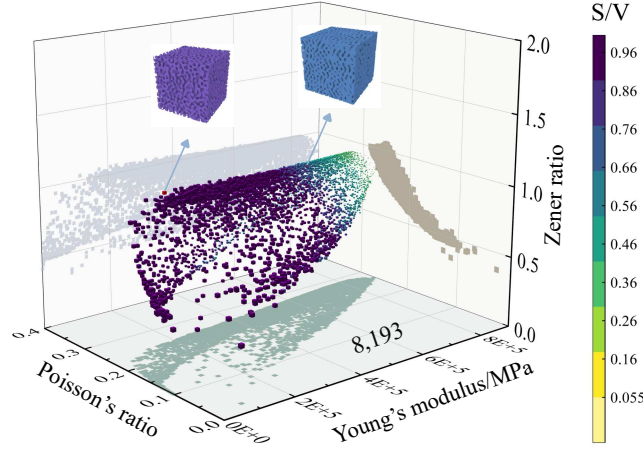


Figure R5: Bicoutinous datasets of spinodal.

Microstructural parameters	Mask 1 (106445)		Mask 2 (142980)		Mask 3 (75350)		Mask 4 (79580)		Spinodal (8193)	
	min	max	min	max	min	max	min	max	min	max
Vol	0.0572	0.8312	0.0446	0.8114	0.0365	0.8593	0.0721	0.7923	0.3227	0.9434
Poisson's ratio	-0.1969	0.4514	-0.0514	0.4117	-0.0422	0.4406	0.0421	0.4005	0.0260	0.2848
Young's modulus/MPa	5166.97	571996.43	17027.53	385256.79	5142.20	494472.80	13710.11	590058.67	632.26	895138.70
Zener ratio	0.1214	7.4311	0.0239	3.9076	0.1158	6.4073	0.1695	3.6147	0.3532	1.0534
S/V	0.0523	0.9252	0.0553	0.8424	0.0458	1.0045	0.0768	0.7764	0.1546	2.2626

Figure R6: Statistical analysis of the datasets mask 1-4 and spinodal.

attribute space is sparse, with certain target properties lacking corresponding microstructures.

We further compare the mechanical metrics of our four constructed datasets with those of the spinodal dataset, as shown in Figure R6. The results show that our datasets cover a broader range of key mechanical properties, which is further demonstrated in Figure R7. Taking mask 1 as an example:

- Volume fraction: 0.06 – 0.83
- Poisson's ratio: $-0.20 - 0.45$
- Young's modulus: 5.16×10^3 MPa – 5.72×10^5 MPa
- Zener ratio: 0.12 – 7.43
- S/V : 0.05 – 0.95

However, the bicontinuous spinodal structure, while offering a relatively large range in Young's modulus (6.32×10^2 MPa – 8.95×10^5 MPa), is significantly limited in other properties such as Poisson's ratio (0.03 – 0.28), Zener ratio (0.35 – 1.05), and volume fraction (0.32 – 0.94), particularly lacking in structures with volume fractions below 0.3 [6]. This is especially insufficient for lightweight multiscale designs, such as those of cancellous bone, where spinodal structures deviate not only in performance but also in morphology from the actual biological counterparts.

Additionally, structures designed based on growth-based approaches [7], although lightweight, are often too regular in form, making it difficult to achieve complex mechanical behaviors, for example, in the design of multiscale functional materials with negative Poisson's ratio (Figure R8).

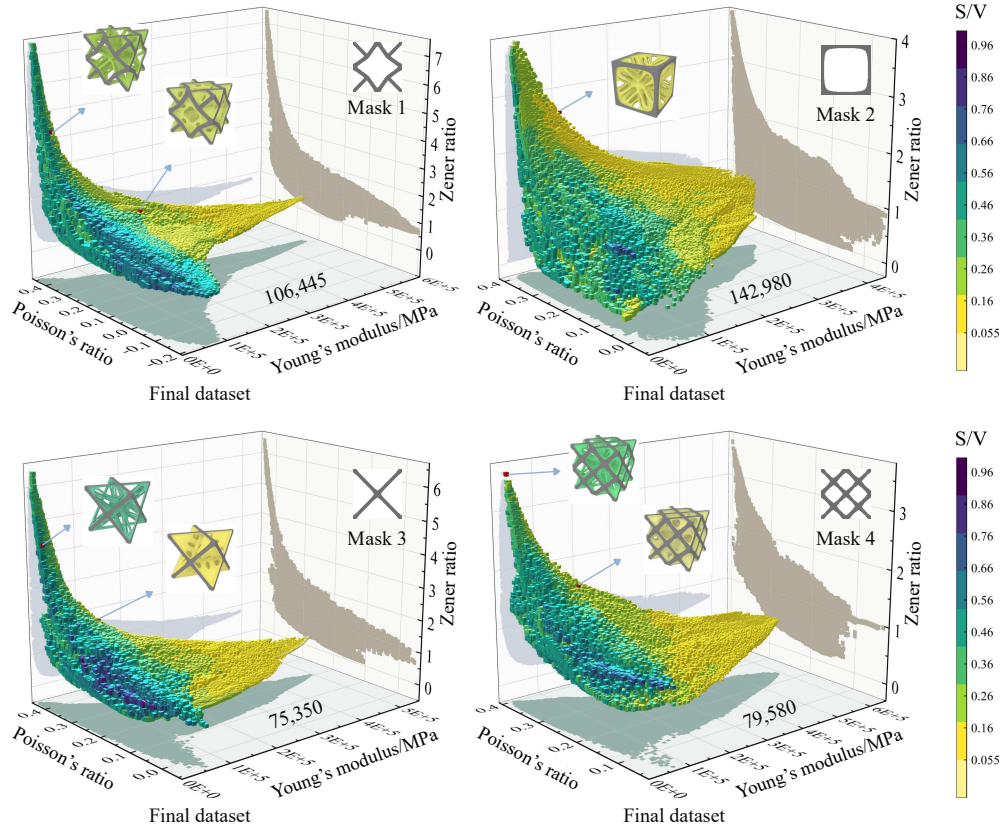


Figure R7: Large-range, Boundary-identical, Bicontinuous Microstructure (LBBM) datasets of mask 1-4.

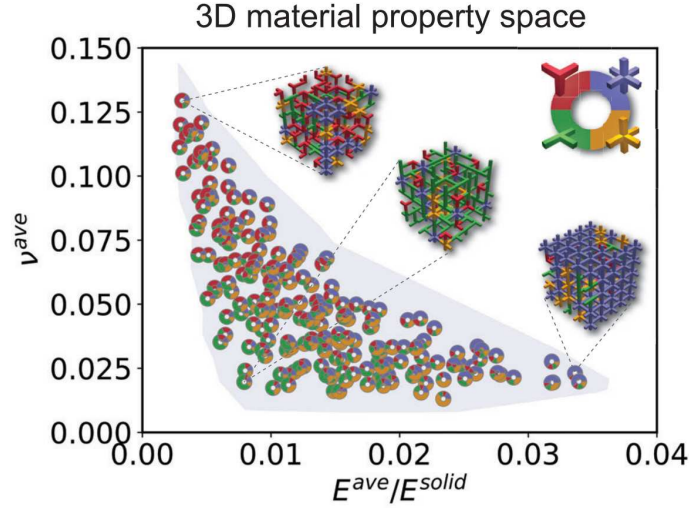


Figure R8: **Material property space in 3D cases.** The x -axis represents the relative average Young's modulus ($E^{\text{ave}}/E^{\text{solid}}$), and the y -axis denotes the average Poisson's ratio (ν^{ave}). The color wheels indicate the frequency combinations in the material database, and their positions correspond to the averaged $E^{\text{ave}}/E^{\text{solid}}-\nu^{\text{ave}}$ pairs over specimens with the same frequency combination. The shaded regions illustrate the actual material properties achieved by all specimens, while the insets show examples of the generated microstructures. [7]

In contrast, our dataset demonstrates a clear advantage in both the breadth and diversity of structure-performance modulation.

(2) Well-covered property space

As illustrated in Figure R7, our dataset features a well-covered property space, offering an even distribution across various combinations of volume fraction and mechanical metrics. This makes it ideally suited for multiscale inverse design. This even sampling not only helps minimize errors during property lookup in multiscale inverse design but also significantly enhances the dataset’s practicality, enabling more precise and reliable design outcomes. Although the optimization depends on initial conditions, the constructed dataset makes the results less sensitive compared to IWP, BCC truss, and spinodal structures.

(3) Fully consistent boundaries for enhanced computational efficiency

Although the spinodal dataset demonstrates an advantage in terms of the numerical values of Young’s modulus, boundary mismatches between units remain one of the most time-consuming challenges in practical multiscale modeling tasks (Figure R1). Conventional methods often suffer from inconsistent boundaries, making seamless boundary connections difficult. However, our Large-range, Boundary-identical, Bicontinuous Microstructure (LBBM) dataset is designed with boundary consistency, significantly reducing complexity and computational cost associated with boundary processing.

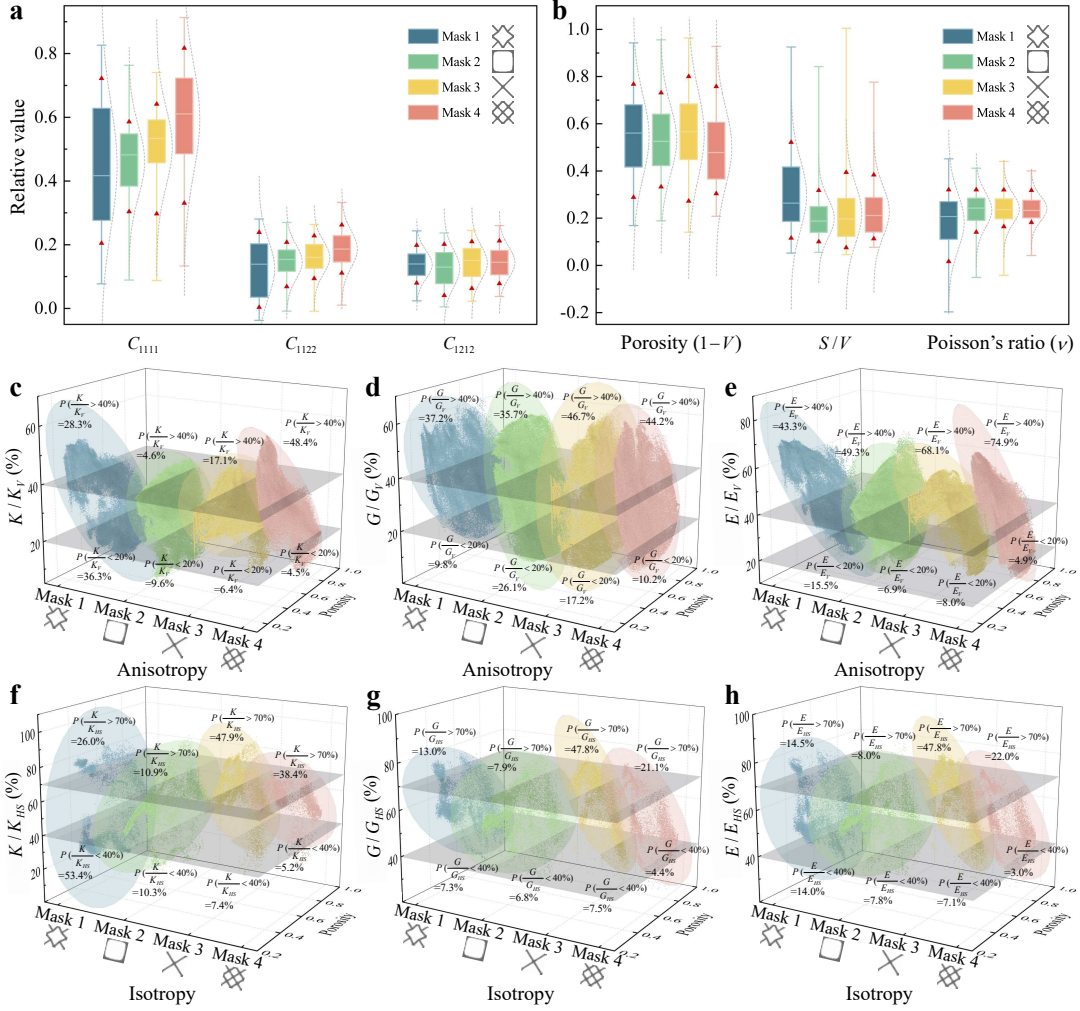
Therefore, the LBBM dataset demonstrates clear advantages in terms of property range, sampling density, and boundary consistency. It is well-suited to support a wide array of structural design tasks, including but not limited to lightweight and high-strength materials, bio-inspired structures, complex mechanical behavior control, and multiscale functional devices, showcasing excellent scalability and real-world applicability.

- **Reviewer #1 Comment #3:** Related to 1. and 2., are interpolations between microstructures more computationally expensive and have limited property range compared to the proposed method? If yes, can the authors show a benchmark?

Response: We appreciate your valuable feedback. In the revised manuscript, we include comparative experiments involving BCC truss, IWP, and spinodal structures, and provide detailed statistics on the computational time required for each stage of the multiscale design process, including optimization, matching, assembly, interpolation, and intersection, as shown in Figure R1. For a multiscale design task with $3 \times 3 \times 9$ units, interpolation between microstructures alone takes more than 2.5 times the total time required for our optimization process.

As the design scale increases, the computational overhead grows accordingly, particularly when the diversity and variation of microstructure boundaries are high, making interpolation extremely costly. For instance, in a $20 \times 20 \times 20$ unit mechanical cloaking design, our complete multiscale design process takes less than 5 minutes, which is significantly faster than the 37,014.26 seconds (over 10 hours) reported by Yang et al. [3].

Regarding the limitations in property coverage, we provide a detailed response to reviewer Comment 2, where we compare the attribute range (Figure R6), data coverage (Figure R7), and boundary consistency across different datasets.



- **Reviewer #1 Comment #4:** Why is the initial dataset optimized by maximizing the elastic moduli (bulk, shear, Young's modulus, etc)? Do most of the proposed applications require stiffness values not achievable by using non-optimized microstructures with compatible 3D-printed materials (e.g., biocompatible)?

Response: Thank you for the insightful question. For the dataset construction, the primary goal is to generate a broad coverage of mechanical properties to support the selection of microstructures for different functional requirements. In practice, we have designed a total of 10 different optimization problems, as detailed in Supplementary Material 3 “microstructure optimization model.” Statistical analysis of the optimization results shows that the microstructures we generate not only include high stiffness regions but also encompass areas with medium and low stiffness, negative Poisson's ratio, and significant anisotropy, among other diverse mechanical responses (Figure R9).

Relying solely on the material itself is insufficient to meet practical engineering requirements, and geometric design optimization becomes particularly crucial. As a result, the optimization

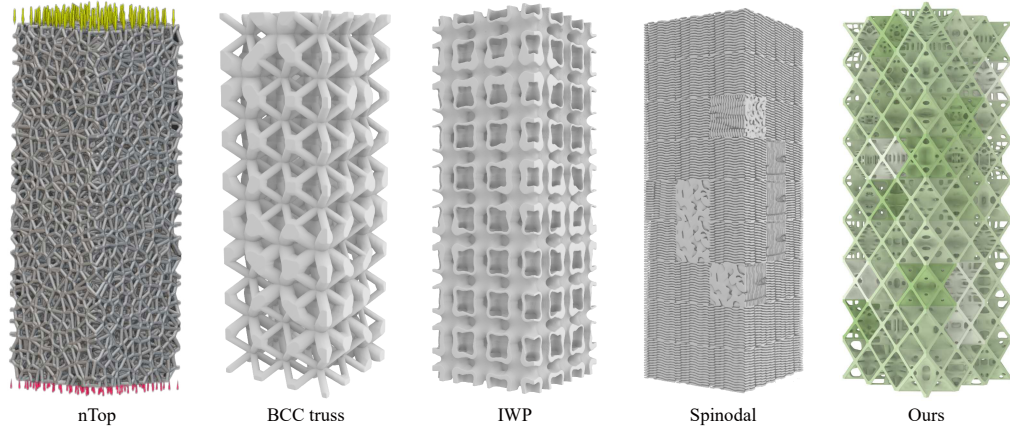


Figure R10: The optimization results generated using nTop, as well as the multiscale structural optimizations of IWP, BCC truss, and spinodal structure, are presented and compared with our own design outcomes.

framework we propose is not only aimed at achieving maximum stiffness but also focuses on constructing a microstructure database with a wide property range and consistent boundaries, efficiently supporting multiscale and multifunctional complex structural design tasks.

- **Reviewer #1 Comment #5:** Have any of the designs presented in the case studies been compared to existing commercial designs?

Response: We sincerely appreciate the reviewer’s insightful comments. In response to the suggestion regarding comparisons with existing commercial designs, we conduct a comprehensive investigation and analysis. Currently, mainstream commercial design software (e.g., nTop). However, such tools present clear limitations when applied to highly complex and multiscale design problems, such as 3D invisibility cloaks and functionally graded materials.

In our study, as illustrated in Figure R10, we present a comparative evaluation involving the optimization results obtained using nTop (with a design domain of $30\text{mm} \times 30\text{mm} \times 90\text{mm}$, employing the Voronoi Volume Lattice module and a beam diameter of 1mm), several classical microstructures (such as BCC truss, IWP, and spinodal), and those generated by our constructed dataset within a multiscale optimization framework. The results show that nTop typically generates simplified, truss-like structures, which fail to capture optimizations with specific tasks such as mechanical invisibility cloak design.

By contrast, our proposed method efficiently explores complex design spaces and identifies microstructures that satisfy specific functional optimization requirements. It is particularly well-suited for multiscale structural design tasks with special performance demands, such as the mechanical cloak shown in Figure R11. Therefore, compared with existing commercial approaches, our method demonstrates enhanced adaptability and superior performance in addressing complex, function-driven design scenarios.

- **Reviewer #1 Comment #6:** The selection of the four masks is not entirely clear: “We evaluated the generated structures based on quality, Poisson’s ratio coverage, and bicontinuous.” How did you exactly select these masks? How do you define “quality”?

Response: We sincerely apologize for the lack of clarity in our description regarding the selection of the four fixed boundaries, and we are grateful for your thorough review. We construct the

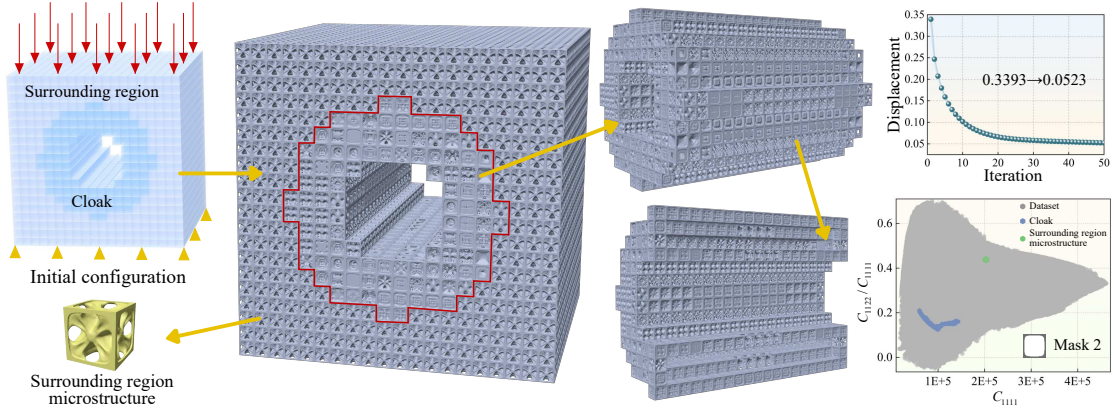


Figure R11: The initial setting and final results of the mechanical cloak ($20 \times 20 \times 20$ units). Design domain, final design results, iteration curves, and the property distribution of structures used in the second dataset across the entire dataset for the mechanical cloak.

four types of microstructure boundaries through the following workflow: first, collecting extensive boundary data from diverse sources, then performing clustering-based deduplication, and finally conducting generation tests based on the streamlined data to finalize the four boundary types. Detailed descriptions can be found in Section 2 of the Supplementary Information.

(1) Multi-source boundary design and feasibility analysis

The boundary data primarily originate from three sources: the 3D microstructure dataset [3], the 2D microstructure dataset [8], and user-designed boundaries, as shown in Figure R12a.

For the 3D microstructure dataset, we extract the boundaries of each structure as boundary data. Since 2D microstructure patterns exhibit high similarity to the boundaries of 3D microstructures, 2D microstructure images are also utilized as boundary data. Additionally, to enrich the boundary data, we collected some user-specified boundaries.

The selection of boundaries significantly influences the potential property range of the ultimately generated bicontinuous dataset. Therefore, we need to test microstructure generation with different boundaries. However, given the substantial scale of the boundary data, it is impractical to perform generation tests for each boundary. To address this, we employ clustering methods to streamline the boundary data.

(2) Cluster analysis and candidate boundary extraction

We perform cluster analysis on the boundary data obtained in the previous step using K-means clustering. Focusing on microstructures with a low volume fraction (0.1–0.4), we extract 15 representative cluster centers as candidate boundary patterns for 3D microstructure generation.

(3) Screening and evaluation according to quality metrics

Building on the above explorations, we refer to existing 3D boundary design schemes [9, 10, 11] and select approximately 30 boundary patterns for further testing (Figure R12b). For the microstructures generated from these candidate boundaries, we perform a systematic evaluation based on two key metrics:

- **Proportion of bicontinuous structures:** To ensure that the generated 3D microstructures possess the requisite connectivity, we employed a connected component labeling algorithm to verify whether these structures are bicontinuous and then calculated the proportion of bicontinuous architectures.

The connected component labeling algorithm is used to assess independently the number of connected components in both the solid and void regions of a microstructure. A microstructure is considered bicontinuous if and only if both its solid and void parts exhibit

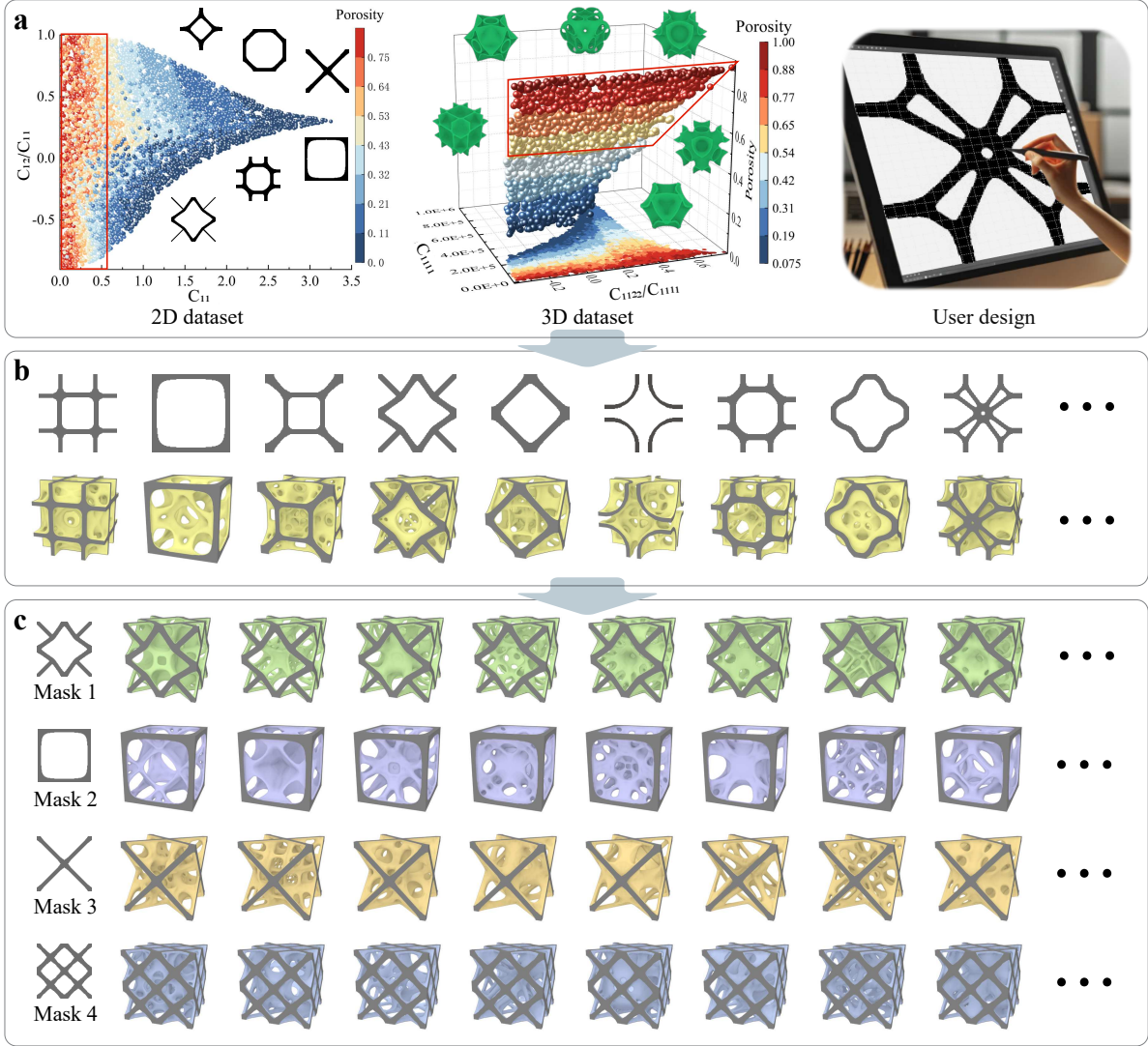


Figure R12: **Boundary construction.** **a** Three sources of boundaries. The left panel shows the relationship between C_{12}/C_{11} and C_{11} for a 2D dataset, while the middle panel displays C_{1111} and C_{1122}/C_{1111} along with porosity data for a 3D dataset. The red box in the 2D and 3D datasets identifies the candidate boundary regions. The right panel illustrates user-specified boundaries. **b** Part of boundaries and their corresponding example microstructures. **c** The four finally selected boundaries and their associated example microstructures.

exactly one connected component each; otherwise, it is deemed non-bicontinuous. Details of the connected component labeling algorithm are provided below:

· **First scan**

For each element p at coordinate (i, j, k) , assign a label $L(i, j, k)$ to the output through the following procedure:

$$L(i, j, k) = \begin{cases} \text{a new label} & \text{if neighboring elements } N(p) \text{ are unlabeled;} \\ \min(N(p)) & \text{if neighboring elements } N(p) \text{ are labeled;} \end{cases}$$

where $N(p)$ denotes the neighboring elements of p . When multiple labels exist in $N(p)$, select the minimum label and record these labels as equivalence relationships;

· **Second scan**

Traverse each element p again and update labels to unify all equivalent labels into a single label:

$$L(i, j, k) = \text{find}(L(i, j, k)),$$

where the find function retrieves the minimum equivalent label associated with $L(i, j, k)$, thereby achieving label consolidation.

A high proportion of bicontinuous structures indicates that boundaries are more likely to be leveraged to generate stable and functional 3D microstructures, which is crucial for achieving target performance in specific applications.

- **Poisson’s ratio coverage:** We calculate and compare the Poisson’s ratios of structures generated from different boundaries to assess the diversity of their mechanical properties. Specifically, this process involves performing mechanical analysis on each microstructure generated from the candidate boundaries to determine their Poisson’s ratio values. The goal is to identify boundaries that could produce a wide range of Poisson’s ratios, indicating their suitability for designing materials with diverse mechanical responses.

Based on the evaluation results from these two key metrics, we conduct multiple rounds of testing and screening and ultimately identify four optimal fixed boundaries, as shown in Figure R12c. The four boundary configurations not only demonstrate excellent coverage of Poisson’s ratios but also achieve a high proportion of bicontinuous architectures, thereby facilitating the subsequent generation of high-quality datasets.

- **Reviewer #1 Comment #7:** Regarding the multiscale design, how is the distribution of elastic coefficients in the design domain determined? Looking at the bone implant as an example, to the best of my knowledge, the implant’s stiffness (entire stiffness matrix) should match that of the bone to promote cell growth and tissue regeneration. In the reported example as well as in all other case studies, stiffness is maximized, rather than matched with that of the bone. Furthermore, should the stress distribution within the implant be as uniform as possible?

Response: We appreciate the reviewer’s comment regarding the distribution of elastic coefficients in the multiscale design and bone implant optimization. In the revised manuscript, we have added a clearer explanation to address this point. The details are as follows:

(1) Elastic coefficients optimization

Multiscale topology optimization is a design method that optimizes both the overall shape and internal material layout to meet specific performance goals under constraints. It consists of

two stages: first, computing the elastic tensor for each macro unit; second, finding a matching microstructure that achieves this tensor. The optimization model for the first stage is formulated as follows,

$$\begin{aligned} \min_{\mathbf{C}} \quad & f(\mathbf{C}) \\ \text{subject to} \quad & \mathbf{K}(\mathbf{C})\mathbf{U} = \mathbf{F}, \\ & \text{SDF}(\mathbf{C}_e) \leq 0, \quad \forall e \in \{1, \dots, N\}. \end{aligned}$$

Here, f is the application-dependent objective function. In designing bone implants and spinal fusions, our goal is to meet specific stiffness requirements while staying within set porosity limits (see Supplementary Section 6.1). For the chair design, we aim to maximize stiffness at a given porosity level (see Supplementary Section 6.3). $\mathbf{C} = \{\mathbf{C}_1, \dots, \mathbf{C}_N\}$ represents the elastic tensor and is taken as a design variable. N is the number of macroscale elements. $\mathbf{U}$ denotes the displacement field, and $\mathbf{F}$ represents the applied external force. The inequality constraint $\text{SDF}(\mathbf{C}_e \leq 0)$ is used to ensure that $\mathbf{C}_e$ is within the feasible range of the dataset. Then, we find $\mathbf{s}_e \in \mathcal{D}$ where $\mathcal{D}$ is the constructed dataset that minimizes

$$\mathbf{s}_e = \arg \min_{\mathbf{s} \in \mathcal{D}} \|\mathbf{C}(\mathbf{s}) - \mathbf{C}_e\|_2,$$

Here $\mathbf{s}_e$ is the material distribution of the e -th optimized microstructure. $\mathbf{C}(\mathbf{s})$ is calculated by homogenization theory [12].

(2) Bone implant optimization

We thank you for your profound insights on the stiffness matching of bone implants. We fully agree with your point that, ideally, the stiffness (the entire stiffness matrix) of the implant should match that of the bone to promote better cell growth and tissue regeneration. At the same time, we also recognize the importance of stiffness matching in the multiscale optimization of bone implants. In the revised version of the manuscript, we have made a comprehensive modification to the optimization problem of the bone implant. Specifically, in the multiscale design study of the rabbit femoral implant, the optimization problem is as follows:

Multiscale optimization is currently divided into two parts: The first phase screens the data that meets the requirements, and the second phase performs gradient optimization on this dataset.

Data filtering We first filter the data from the third dataset that satisfies the following criteria from all the data sets: $d_{\min} - d_e \leq 0$ and $p_{\min} \leq p_e \leq p_{\max}$. $d_{\min}$ represents the minimum required pore size of the implant, and d_e denotes the porosity of the e -th unit cell. $p_{\max}$ and $p_{\min}$ refer to the maximum and minimum porosity thresholds, respectively, and p_e is the porosity of the e -th unit cell. To promote cell growth and material exchange, we select microstructural units from the database with an average pore size exceeding $26 \mu\text{m}$ (specifically calculated as $1 \text{ cm} \div 3 \div 128 \approx 0.0026 \text{ cm} = 26 \mu\text{m}$, where 1 cm represents the macroscopic size of the compact bone implant and 128 represents the microstructure resolution) and a porosity ranging from 0.2 to 0.85 during the design process.

Gradient-based optimization The optimization model for femoral implants and lumbar interbody fusion cages is formulated as follows:

$$\begin{aligned} \min_{\mathbf{C}} \quad & f(\mathbf{C}) = \frac{|E_{\text{eff}}(\mathbf{C}) - E_{\text{target}}|}{E_{\text{target}}} \\ \text{s.t.} \quad & \mathbf{K}(\mathbf{C})\mathbf{U} = \mathbf{F}, \\ & \text{SDF}(\mathbf{C}_e) \leq 0. \end{aligned}$$

Here, $\mathbf{C} = \{\mathbf{C}_1, \mathbf{C}_2, \dots, \mathbf{C}_N\}$ is the elastic tensor of macroelement. The total number of macroelements are denoted as N . E_{target} denotes the target Young's modulus of bone tissue. $K(\mathbf{C})$ is the stiffness derived from the assembly from the elastic tensor of the macroelement. $\mathbf{U}$ and $\mathbf{F}$ are the displacement and the external force, respectively. The inequality constraint $\text{SDF}(\mathbf{C}_e \leq 0)$ [13, 3] is used to ensure that $\mathbf{C}_e$ is within the feasible range of the dataset.

In the multiscale design of rabbit femoral implants, titanium is selected as the base material, with the objective of minimizing the relative stiffness mismatch between the implant and the target bone to achieve mechanical compatibility. This study focuses on compact bone implants for the femoral shaft and cancellous bone implants for the femoral head. In the compact bone design domain, the structure consists of $3 \times 3 \times 9$ units, with a target Young's modulus of 5000 MPa and a Poisson's ratio of 0.3. The cancellous bone design domain consists of $5 \times 7 \times 4$ units, with a Young's modulus of approximately 2500 MPa and a Poisson's ratio of 0.3. The optimization problem is solved using MMA, as mentioned in section 3.1. The optimization process terminates when the number of iterations reaches 50 or when the design variable change between two consecutive iterations is less than 0.001.

Then, the closest matching microstructure is identified by calculating the distance to the pre-defined dataset, thereby determining the final microstructure for each design unit. Based on these matching indices, the corresponding microstructures are retrieved and assembled into the complete structure. Finally, the designed implant structure is intersected with the femoral implantation region to generate the final multiscale implant.

The optimization goal of the lumbar interbody fusion device is similar to that of the femoral implant, we select structures with a negative Poisson's ratio for comfort design. The design domain is divided into $11 \times 8 \times 3$ units. The total computational time for the entire multiscale design process does not exceed 50 seconds (Figure R1).

Finally, regarding the stress distribution issue, although we do not make uniform stress distribution an optimization objective, we can perform screening within the constraints because the dataset is sufficiently complex. During the screening process, we can avoid the minimum size condition and try to prevent stress shielding as much as possible.

- **Reviewer #1 Comment #8:** Following up on point 7, does the assumption of cubic symmetry pose limitations for certain applications, such as bone implants?

Response: Thank you for your suggestions and comments. We acknowledge that cubic symmetry may have certain limitations in some applications, particularly in bone implant design, mainly due to its restricted range of properties. However, using the same optimization combined with active learning generation method, we can extend and generate databases with richer symmetries or asymmetries to better accommodate a wider range of application needs. It should be noted that although this extension can provide greater design flexibility, the increased consumption of computational resources and complexity is indeed an unavoidable challenge.

In our design, however, we have conducted multiscale optimization separately for compact bone and trabecular bone. In terms of performance, compared to other structures (such as BCC Truss,

IWP, Spinodal structures), our designed implants exhibit high adaptability to the corresponding bone structures. From the unit cell characteristics of the optimization results, the assembled microstructure of the compact bone predominantly takes the form of plate-like structures to match its higher Young's modulus (Figure R13), while the assembled microstructure of the trabecular bone predominantly takes the form of rod-like structures to adapt to its lower Young's modulus (Figure R14). These optimized microstructures not only meet specific mechanical performance requirements but also maximize similarity to bone tissue, validating the great potential of our design method in bone implant design.

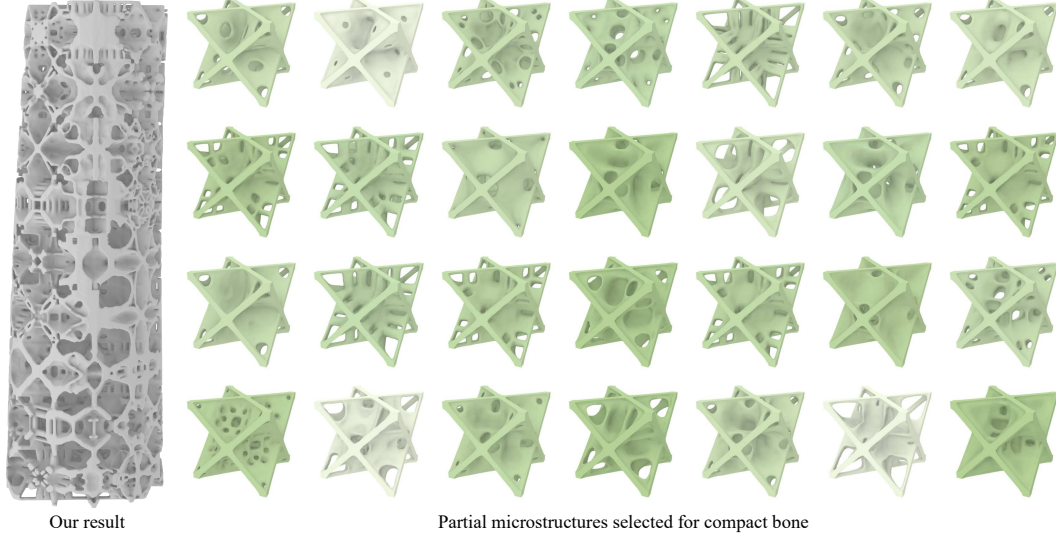


Figure R13: **Examples of microstructure quality evaluation.** Top row: structures with disconnected solid phases. Middle row: structures with disconnected void phases. Bottom row: bicontinuous structures with both phases fully connected.

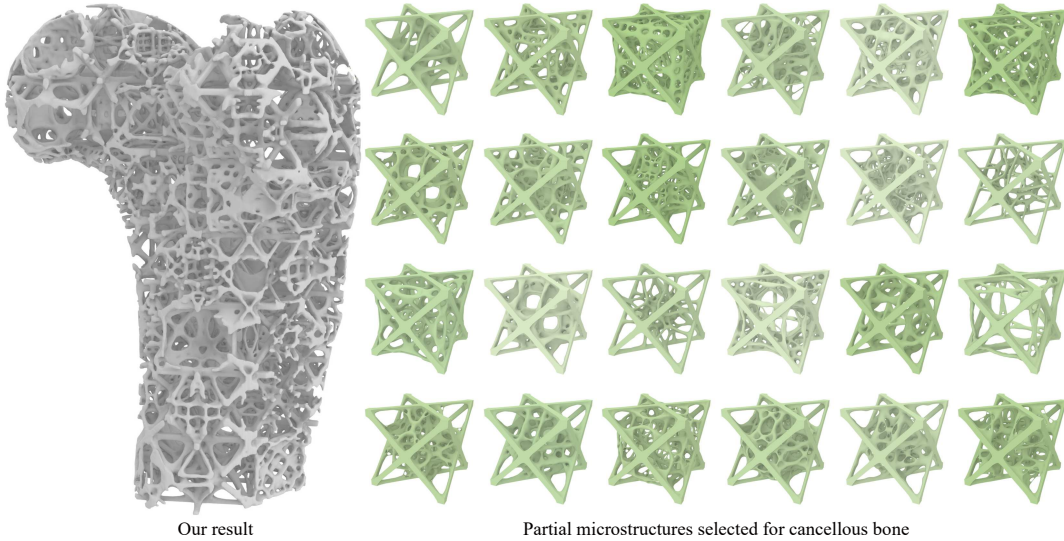


Figure R14: **Examples of microstructure quality evaluation.** Top row: structures with disconnected solid phases. Middle row: structures with disconnected void phases. Bottom row: bicontinuous structures with both phases fully connected.

- **Reviewer #1 Comment #9:** About the filtering device example, the datasets were constructed accounting only for the stiffness. However, the main performance metric for such devices seems to be permeability. Would using other conditioning properties, such as permeability, in the diffusion model help finding better designs?

Response: The authors sincerely thank the reviewer for the valuable comments, which give us the opportunity to further improve and clarify our design philosophy. Regarding the permeability experiments, our original intention was to leverage the existing structural and mechanical attributes in the dataset (such as stiffness, porosity, S/V , Young’s modulus, and Poisson’s ratio) to further explore and extract potential multiphysical properties, including permeability, electrical conductivity, and thermal conductivity. We believe that uncovering the deep correlations in this high-dimensional structure-property space is of great significance for achieving more efficient and comprehensive multiphysical performance control.

To further demonstrate the feasibility and potential of our dataset for exploring additional physical properties, particularly the underlying relationship between porosity, S/V , and permeability, we have redesigned and supplemented the relevant experiments in the revised manuscript. Detailed descriptions can be found in Section 6.6 of the Supplementary Information.

In this section, we present the results of our study on the design of structures with extensive permeability characteristics. To verify the permeability properties of the designed multiscale structures, the research process is divided into three stages: computational analysis, simulation validation, and experimental testing.

(1) Computational analysis

In the computational analysis stage, we perform detailed calculations on the permeability and S/V of four datasets and triply periodic minimal surface (TPMS) structures [14, 15]. The second dataset is selected for a more detailed illustration of the microstructural features. The results indicate that, compared to TPMS structures, our designed multiscale structures exhibit a broader range of variations in both permeability and S/V ratio (Figures R15- R18).

(2) Simulation validation

The next stage, simulation validation, aims to assess the permeability performance and flow streamline distribution of the multiscale designs. The porosity of the structures is fixed at four levels: 0.5, 0.6, 0.7, and 0.8, and corresponding structures are selected from the chosen dataset for further analysis. By comparing the permeability of these structures with Gyroid, Diamond, and IWP structures, five microstructures with high S/V ratios are selected for in-depth investigation. Box plots of porosity versus S/V ratio are generated for these structures.

Fluid simulation experiments are conducted using COMSOL software. For each design group, the steady-state response of four structures is tested under unidirectional creeping flow conditions. Water is used as the testing fluid, with an inlet positioned at the top of a $4 \times 4 \times 1$ structure and an applied pressure of 500 Pa. The outlet is located at the outer surface of four microstructures at the bottom center, where the pressure is set to 0 Pa. The permeability of each design group is calculated using Darcy’s law.

To further validate the effectiveness of the multiscale design, comparisons are made with three classical TPMS structures, Gyroid, Diamond, and IWP, which are known for their high surface-to-volume ratios. The results of these comparative experiments are summarized in Figures R15- R18, demonstrating that our designed multiscale structures exhibit a broader range of variation in porosity and S/V ratio than TPMS structures.

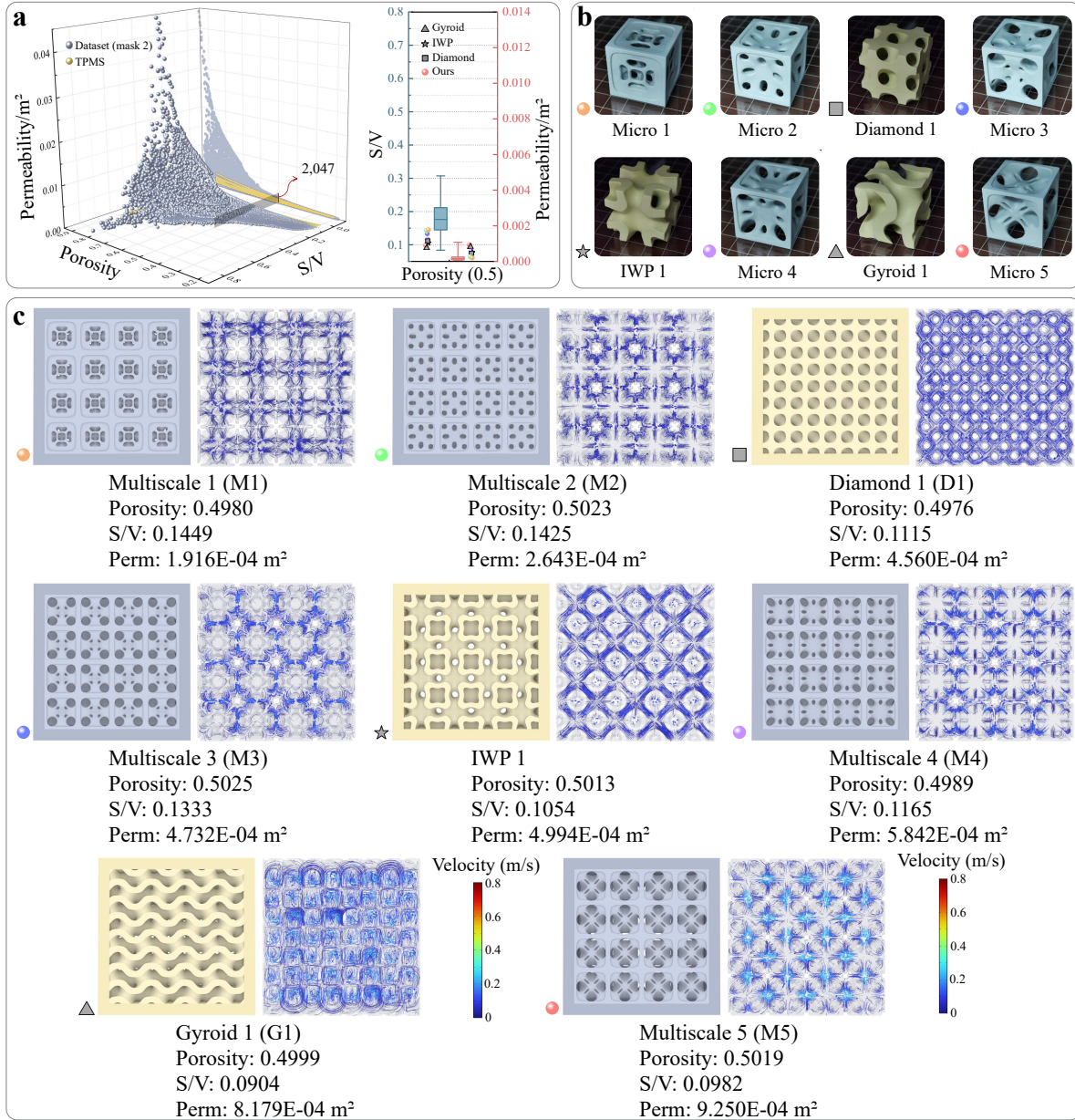


Figure R15: **Figure S10. Permeability test results of the structures at a porosity of 0.5.** **a** The left panel illustrates the relationships among porosity, S/V , and permeability for all structures in the second dataset and the TPMS dataset. A gray plane marks the data with a porosity of 0.5, totaling 2,047 samples. In the right panel, blue box plots represent the relationship between porosity and S/V , while red box plots depict the correlation between porosity and permeability. Individual points denote test results from different datasets. **b** The 3D-printed samples of the selected microstructures, with a printing size of 3 cm. **c** Multiscale structures and their simulated velocity streamlines.

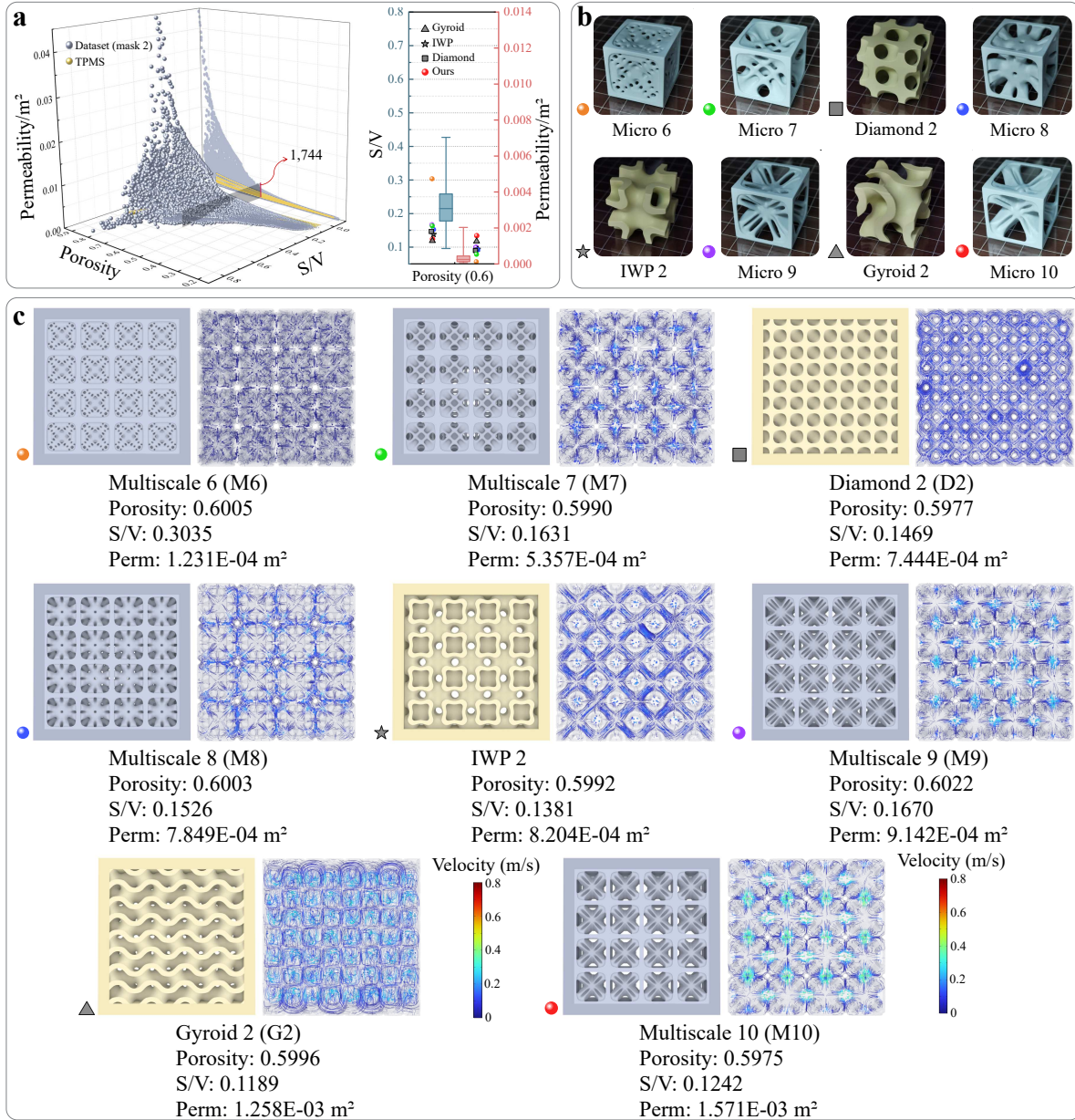


Figure R16: **Permeability test results of the structures at a porosity of 0.6.** **a** The left panel illustrates the relationships among porosity, S/V , and permeability for all structures in the second dataset and the TPMS dataset. A gray plane marks the data with a porosity of 0.6, totaling 1,774 samples. In the right panel, blue box plots represent the relationship between porosity and S/V , while red box plots depict the correlation between porosity and permeability. Individual points denote test results from different datasets. **b** The 3D-printed samples of the selected microstructures, with a printing size of 3 cm. **c** Multiscale structures and their simulated velocity streamlines.

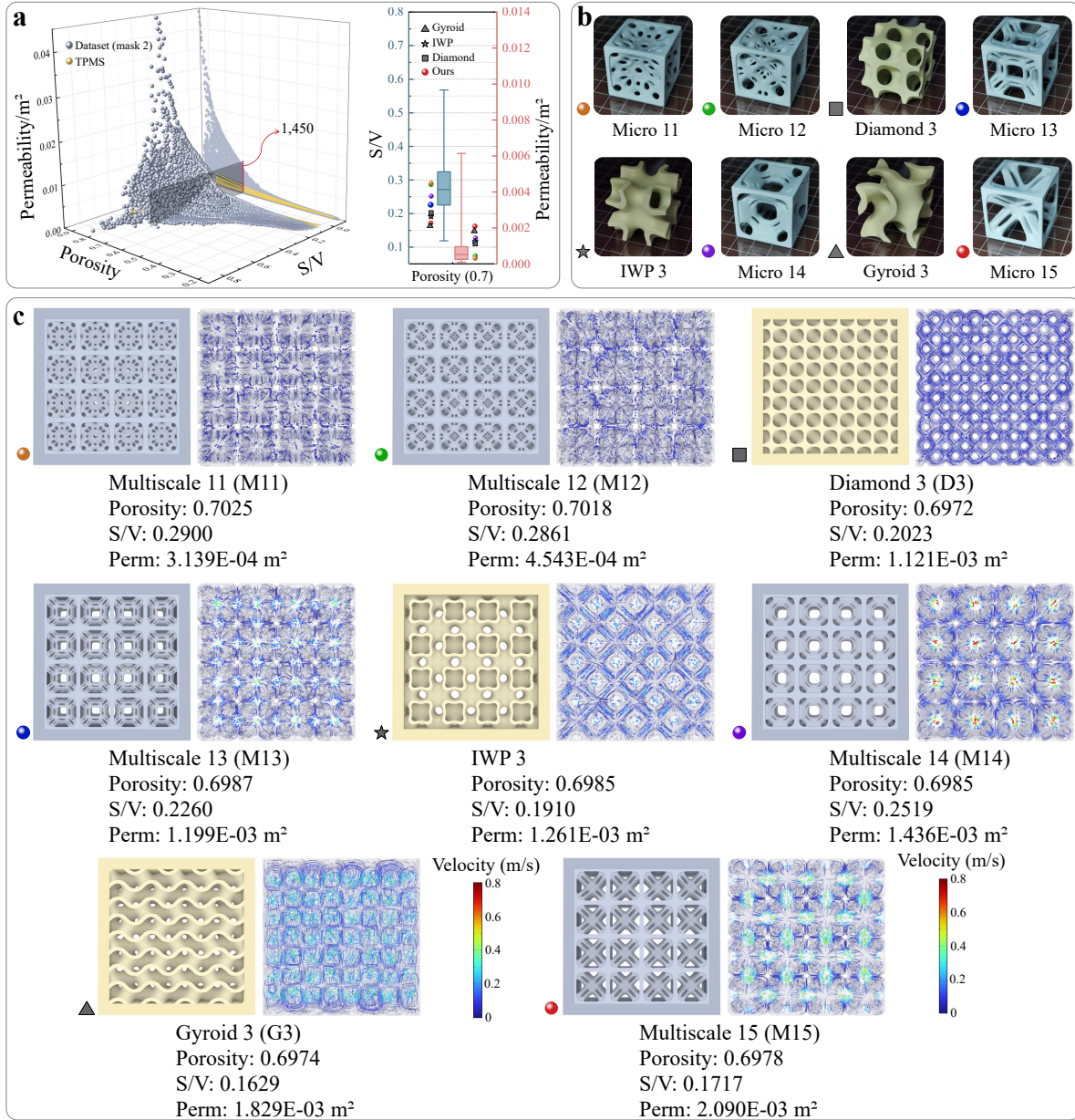


Figure R17: **Permeability test results of the structures at a porosity of 0.7.** **a** The left panel illustrates the relationships among porosity, S/V , and permeability for all structures in the second dataset and the TPMS dataset. A gray plane marks the data with a porosity of 0.7, totaling 1,450 samples. In the right panel, blue box plots represent the relationship between porosity and S/V , while red box plots depict the correlation between porosity and permeability. Individual points denote test results from different datasets. **b** The 3D-printed samples of the selected microstructures, with a printing size of 3 cm. **c** Multiscale structures and their simulated velocity streamlines.

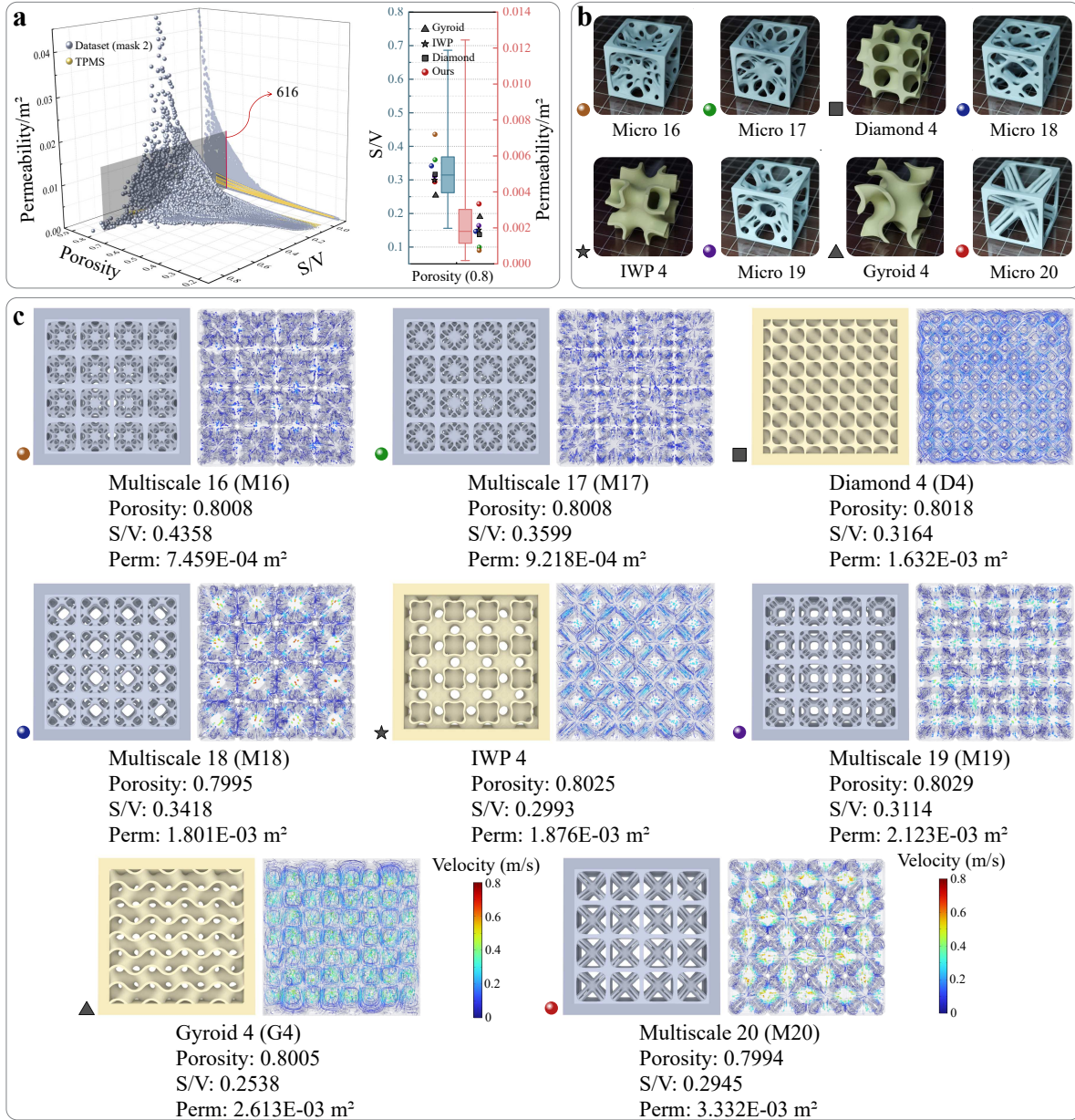


Figure R18: **Permeability test results of the structures at a porosity of 0.8.** **a** The left panel illustrates the relationships among porosity, S/V , and permeability for all structures in the second dataset and the TPMS dataset. A gray plane marks the data with a porosity of 0.8, totaling 616 samples. In the right panel, blue box plots represent the relationship between porosity and S/V , while red box plots depict the correlation between porosity and permeability. Individual points denote test results from different datasets. **b** The 3D-printed samples of the selected microstructures, with a printing size of 3 cm. **c** Multiscale structures and their simulated velocity streamlines.

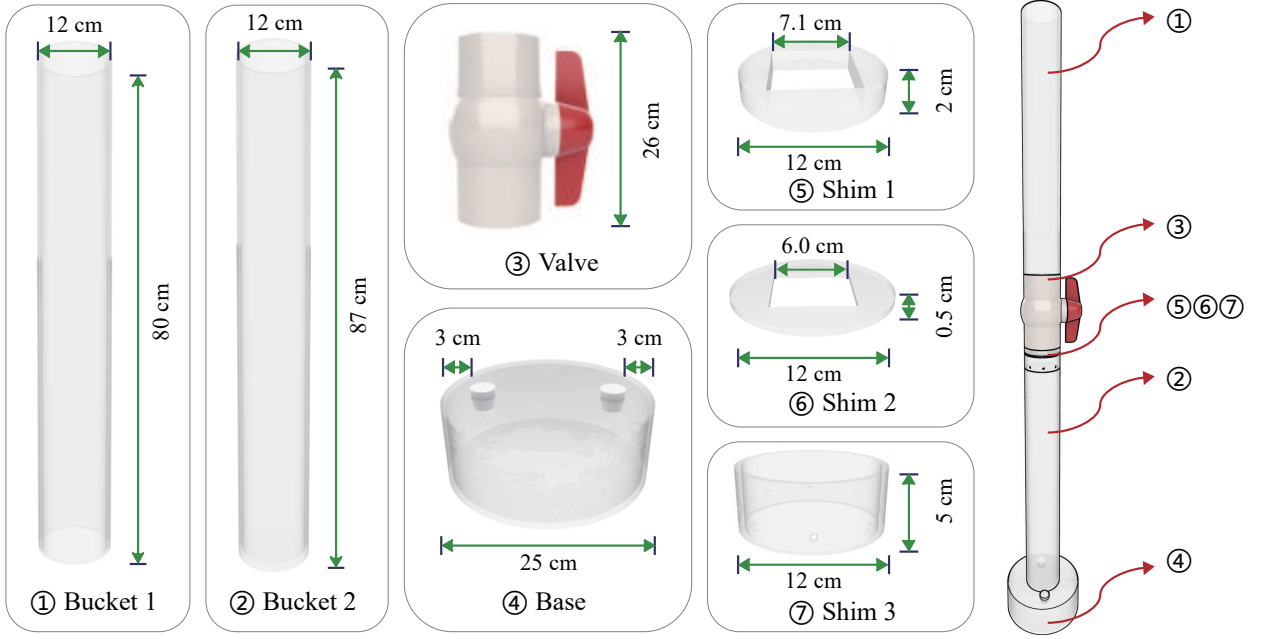


Figure R19: Design of experimental apparatus.

(3) Experimental testing

In the experimental testing stage, a specialized experimental setup is designed (Figure R19) to physically measure and validate the permeability differences among various structures. The setup evaluates the permeability performance of different structures by monitoring water flow velocity. It consists of seven key components: two buckets (one for water injection and the other for water collection), a valve for controlling water flow, a base for stability, and three spacers used for sample fixation and flow regulation.

The first bucket (bucket 1) supplies water to the system, while the second bucket (bucket 2) collects the outflow. To ensure precise variable control, both buckets are marked with an 80 cm scale on their sides. The valve regulates the water flow, and the base provides structural stability. The first spacer has a central square hole with a side length of 7.1 cm, fitting the 7 cm test structures while leaving a 0.1 cm gap for securing the structures with double-sided tape. This setup simulates ideal fluid boundary conditions. Additionally, double-sided tape is applied at the bottom of the test structures to ensure consistent inlet and outlet boundary conditions, creating a tight seal to prevent leakage and reduce experimental error. The second spacer features a 6 cm square hole to adjust the outlet position, while the third spacer includes eight 0.5 cm diameter holes to maintain pressure balance inside and outside the buckets.

The experimental procedure quantifies the permeability of different structures by measuring the time required for a predetermined volume of water to pass through the system and reach a specified height in the collection bucket. The steps are as follows:

- (1) The test structure is placed in the square hole of the first spacer, and the valve is closed.
- (2) A fixed volume of water is added to the injection bucket.
- (3) The valve is opened, allowing water to flow through the test structure into the collection bucket.
- (4) The time required for the water level to reach the predefined height is recorded.
- (5) The permeability is calculated based on the recorded time data.

After completing the computational analysis and simulation validation, our multiscale structures demonstrated a broader permeability and S/V range than TPMS structures. To further confirm

this, experimental tests are conducted on three multiscale structures with high, medium, and low permeability at a porosity of 0.8. These are compared with Gyroid, Diamond, and IWP structures. Detailed experimental procedures can be found in Video 5. The experimental results indicate a strong correlation between measured water flow velocity and simulated permeability behavior, confirming the validity of our design across different structures. Through systematic computational, simulation, and experimental validation, we have demonstrated that the designed multiscale structures possess significantly enhanced permeability characteristics.

Moreover, we fully agree with your insightful comment: it is indeed feasible to incorporate additional conditioning properties—such as thermal conductivity, electrical conductivity, and permeability—into the diffusion model, thereby guiding the generation of microstructures tailored for a broader range of application scenarios, including multiphysics-coupled problems. In fact, this represents one of the key directions of our future research. We also add the discussion below:

While the LBBM datasets demonstrate advantageous properties, there remain unexplored opportunities in expanding toward more multifunctional capabilities and asymmetric microstructure datasets. To explore multifunctional properties, integrating physical constraints such as the Navier–Stokes equations for permeability or heat transfer equations for thermally conductive structures into the model can enhance performance in application-specific tasks. For asymmetric microstructure datasets, the theory of 3D space groups offers a pathway to relax cubic symmetry constraints, thereby enabling the generation of comprehensive, full-space microstructure datasets. This study marks a meaningful step toward realizing the broader vision of multiphysical, multifunctional, and multiscale bicontinuous structural design. These designs hold significant promise for applications in bone implants, environmental protection, health and wellness, and next-generation engineering solutions.

Response to Reviewer #2

- **Reviewer #2 General Comment:** Thank you very much for your thoughtful feedback. We sincerely appreciate your valuable comments and the time you have taken to review our work. Your insights have helped us to reflect more deeply on our methodology and presentation. We take your concerns seriously and are committed to addressing them thoroughly in our revised manuscript. We hope that the revisions will clarify our intentions and strengthen the overall contribution of our work.
- **Reviewer #2 Comment #1:** The paper does not discuss how errors in the generative model (e.g., boundary misalignment or failure to meet elastic tensor constraints) propagate through the multiscale optimization process. Quantifying this could identify potential pitfalls in applications.

Response: Thank you for your thorough review and response. In the top-down data-driven multiscale design process, we utilize a pre-generated dataset rather than generating microstructures on the fly during the design process. Consequently, the generative accuracy of the model has no impact on the precision of the multiscale design. However, the generative accuracy of the model affects the efficiency of dataset expansion when employing active learning strategies. We conduct experimental tests on the generative accuracy of the model, and the results demonstrate that our model achieves a generation accuracy of approximately 95% or higher for both the tasks of specifying elastic tensors and boundary masks. Relevant experimental results are presented below.

1) The top-down data-driven multiscale design process proceeds as follows: For a given problem, we first perform macroscale topology optimization to obtain the spatial distribution of elastic tensors. Subsequently, microstructures satisfying target elastic tensor requirements are selected from the dataset for multiscale structure filling and assembly. Since this process does not involve real-time data generation via neural networks, the accuracy of generative models does not influence the multiscale design outcomes.

2) The generative model accuracy primarily impacts the active learning-based dataset expansion process. During iterative dataset augmentation, we employ predefined elastic tensors and boundary masks as conditional inputs for microstructure generation. Poor generative accuracy tends to produce results resembling unconditional generation, thereby reducing dataset expansion efficiency and potentially causing data scarcity for specific property-microstructure mappings. To demonstrate the generative accuracy of our model, conditional generation tests are conducted on four networks mentioned in the text.

We evaluate the accuracy of the generation based on two metrics: the R^2 -score between the elastic tensors of the generated results and the target elastic tensors, and the degree of match (DoM) between the boundary masks of the generated structures and the specified boundary masks. The R^2 -score between the generated elastic tensors and the target elastic tensors is defined as:

$$R^2(\mathbf{Y}, \mathbf{Y}') = 1 - \frac{\sum_{i=1}^N \|\mathbf{y}_i - \mathbf{y}'_i\|^2}{\sum_{i=1}^N \|\mathbf{y}_i - \bar{\mathbf{y}}\|^2},$$

where $\mathbf{Y}$ and $\mathbf{Y}'$ are the generated and target elastic tensor matrix, respectively, each with the dimension of $3 \times N$. $N (= 1000)$ is the number of generated microstructures. $\mathbf{y}_i$ is the i -th column of $\mathbf{Y}$ which presents the elastic tensor vector ($[C_{1111}, C_{1122}, C_{1212}]$) of the i -th generated microstructure. $\mathbf{y}'$ follows a similar explanation. $\bar{\mathbf{y}}$ is the mean of the generated properties.

DoM is calculated as:

$$\text{DoM}(\mathbf{b}, \mathbf{b}') = 1 - \frac{\|\mathbf{b} - \mathbf{b}'\|_2}{\|\mathbf{b}\|_2},$$

Algorithm 1 Joint training a diffusion model with classifier-free guidance

Require: p_{uncond} : probability of unconditional training

```
1: repeat  
2:    $(\mathbf{x}, \mathbf{c}) \sim p(\mathbf{x}, \mathbf{c})$   $\triangleright$  Sample data with conditioning from the dataset  
3:    $\mathbf{c} \leftarrow \emptyset$  with probability  $p_{\text{uncond}}$   $\triangleright$  Randomly discard conditioning to train unconditionally  
4:    $\lambda \sim p(\lambda)$   $\triangleright$  Sample log SNR value  
5:    $\epsilon \sim \mathcal{N}(\mathbf{0}, \mathbf{I})$   
6:    $\mathbf{z}_\lambda = \alpha_\lambda \mathbf{x} + \sigma_\lambda \epsilon$   $\triangleright$  Corrupt data to the sampled log SNR value  
7:   Take gradient step on  $\nabla_\theta \|\epsilon_\theta(\mathbf{z}_\lambda, \mathbf{c}) - \epsilon\|^2$   $\triangleright$  Optimization of denoising model  
8: until converged
```

Figure R20: Training process of classifier-free guidance [16].

where $\mathbf{b}$ represents the target boundary mask, and $\mathbf{b}'$ is the boundary mask of the generated microstructure.

The test results for the R^2 -score and DoM are presented in Table 1.

Table 1: Generation accuracy evaluated by the R^2 -score and DoM of different models.

Models	$R^2 - score$	DoM
Mask 1	0.958	0.987
Mask 2	0.971	0.992
Mask 3	0.941	0.974
Mask 4	0.962	0.981

- **Reviewer #2 Comment #2:** The reliance on predefined elastic tensors and masks could limit the model’s ability to generalize. Techniques like unsupervised learning or meta-learning could enhance adaptability for unseen property spaces.

Response: We appreciate your valuable feedback. In fact, our conditional diffusion model considers generalization during training, and the generation results demonstrate that our network can produce data richer than the training dataset. The model’s generalization capability is primarily achieved through three aspects: the unconditional model training in classifier-free guidance, interpolation enabled by positional encoding, and dataset iterative expansion via active learning strategies.

First, our conditional diffusion model employs classifier-free guidance to incorporate specified elastic tensor during generation. As shown in Figure R20 referencing [16], the training process involves:

During training, we nullify the elastic tensor with a specific probability (20% in our implementation). This converts the training process into an unconditional diffusion model with unsupervised learning characteristics. Thus, our conditional generation model combines both conditional and unconditional generation capabilities rather than relying solely on supervised learning.

Second, we utilize Learnable Sinusoidal Embedding (LSE) [17] to incorporate elastic tensors into the denoising network. This encoding can represent positional relationships between arbitrary real numbers, enabling our model to generate microstructures with "intermediate elastic tensors" that fill gaps in the training dataset’s elastic tensor space. The interpolation effects can be observed from Figure R21. Our implementation of LSE is as follows:

$$PE_{(pos,2i)} = \sin(pos \cdot w_i \cdot 2\pi), PE_{(pos,2i+1)} = \cos(pos \cdot w_i \cdot 2\pi),$$

where w_i is a learnable parameter initialized as:

$$w_i = \frac{1}{10000^{2i/d}}.$$

This initialization mimics conventional Sinusoidal Positional Encoding (SPE) [18] while enabling subsequent optimization during training. Specifically, we normalize the C_{1111} , C_{1122} , and C_{1212} components before embedding, encode them separately using LSE, and sum the three encodings as the final elastic tensor representation.

Finally, our active learning strategy enables iterative dataset expansion. As shown in Figure R21, the iterations extend the property coverage boundaries of the original data, empirically verifying our model’s generalization capability through progressively expanded elastic tensor space coverage.

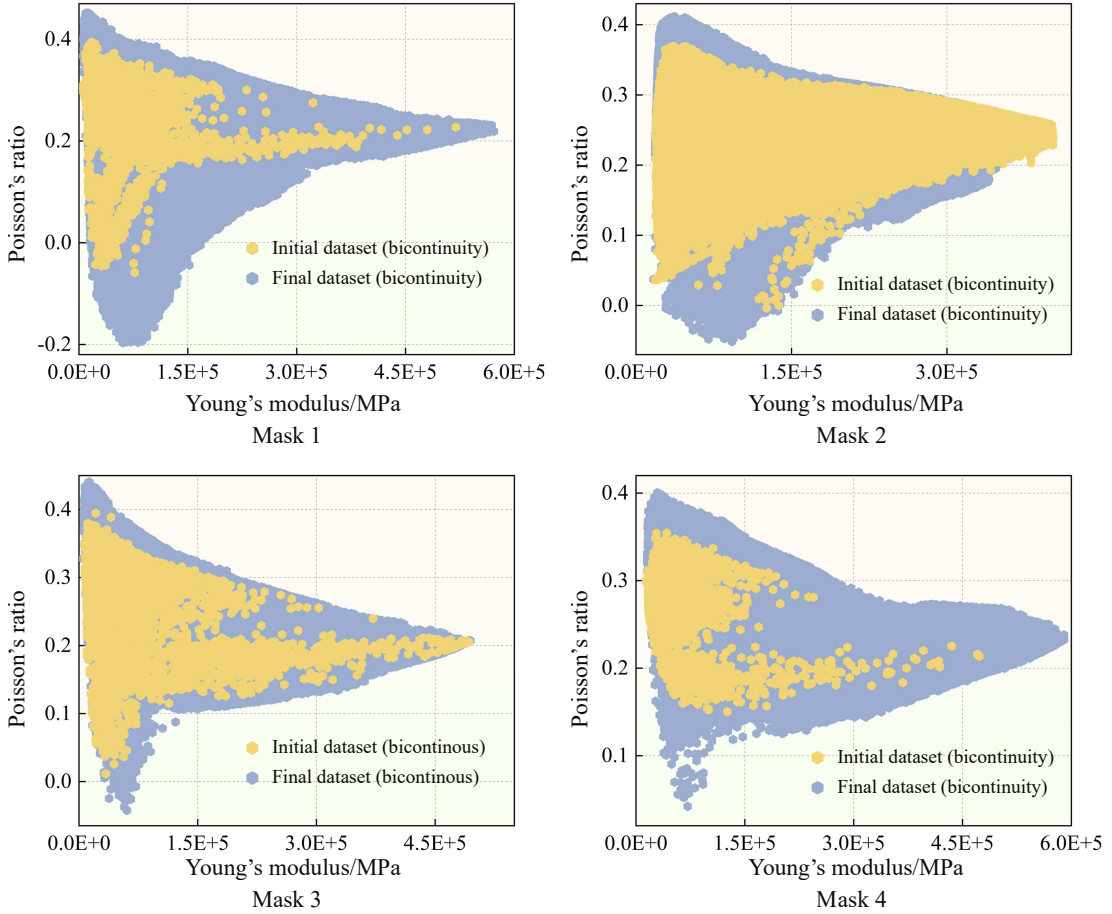


Figure R21: Comparison of the attribute coverage range of the dataset before and after active learning.

- **Reviewer #2 Comment #3:** Include automated metrics for validating bicontinuity and boundary alignment during dataset generation, such as a) Fourier transform-based spatial analysis for structural periodicity, and b) Stress-testing using finite element analysis on randomly sampled outputs.

Response: We sincerely appreciate your valuable feedback. In the dataset construction process, we employ algorithms to determine the bicontinuity of microstructures and utilize metrics to evaluate boundary matching quality, thereby eliminating non-bicontinuous structures and those with mismatched boundaries generated by the network. The methodology for verifying bicontinuity is as follows: We apply a connected component labeling algorithm to independently assess the number of connected components in both the solid and void regions of a microstructure. A microstructure is considered bicontinuous if and only if both its solid and void parts exhibit exactly one connected component each; otherwise, it is deemed non-bicontinuous. Details of the connected component labeling algorithm are provided below:

(1) First scan

For each element p at coordinate (i, j, k) , assign a label $L(i, j, k)$ to the output through the following procedure:

$$L(i, j, k) = \begin{cases} \text{a new label,} & \text{if neighboring elements } N(p) \text{ are unlabeled;} \\ \min(N(p)), & \text{if neighboring elements } N(p) \text{ are labeled;} \end{cases}$$

where $N(p)$ denotes the neighboring elements of p . When multiple labels exist in $N(p)$, select the minimum label and record these labels as equivalence relationships;

(2) Second scan

Traverse each element p again and update labels to unify all equivalent labels into a single label:

$$L(i, j, k) = \text{find}(L(i, j, k)),$$

where the find function retrieves the minimum equivalent label associated with $L(i, j, k)$, thereby achieving label consolidation.

The methodology for evaluating boundary matching is as follows: We employ the Degree of Match (DoM) between the boundary mask of the network-generated microstructures and the target boundary mask to quantify their alignment. This metric measures the spatial correspondence between the generated and predefined boundaries, ensuring structural compatibility during dataset construction. Specifically, microstructures exhibiting insufficient DoM values are systematically excluded to maintain geometric consistency with design constraints.

The degree of match is calculated as:

$$\text{DoM}(\mathbf{b}, \mathbf{b}') = 1 - \frac{\|\mathbf{b} - \mathbf{b}'\|_2}{\|\mathbf{b}\|_2},$$

where $\mathbf{b}$ represents the target boundary mask, and $\mathbf{b}'$ is the boundary mask of the generated microstructure.

- **Reviewer #2 Comment #4:** Reducing the degrees of freedom from 21 to 3 could oversimplify certain material behaviors. The paper could explore whether this reduction impacts the fidelity of the generated microstructures for applications requiring anisotropic properties.

Response: Thank you for raising these questions. We make simplifications to the material model, and these simplifications in material behavior do limit the material’s performance. We prioritize increasing the degrees of freedom in the elastic tensor to achieve richer microstructures in future work. These simplifications are primarily driven by considerations of computational resources and complexity, but they do not imply that our microstructures have limited application potential. We demonstrate this through multiscale designs across various scenarios. Furthermore, while the structures we employ exhibit cubic symmetry, cubic symmetry does not equate to isotropy, and our dataset contains numerous anisotropic microstructures. Finally, our multiscale design focuses on macroscopic properties of the multiscale structures, such as overall stiffness and Young’s modulus. Although our design approach does not enforce anisotropy requirements for microstructures, many anisotropic microstructures are naturally utilized in our design outcomes. A more detailed explanation follows:

- (1) We reduce the degrees of freedom in the elastic tensor from 21 to 3 due to the impact of dimensionality on both model complexity and dataset scalability. First, our generative model conditions on elastic tensor properties—increasing the degrees of freedom escalates the difficulty of the generation task. This requires more sophisticated model parameters, advanced network architectures, and effective conditional encoding methods to capture the complex mapping between elastic tensors and microstructural geometries accurately. Second, expanding the degrees of freedom in the elastic tensor exponentially increases the dimensionality of the property space, which necessitates a proportional expansion of the dataset size. These two factors impose significant challenges in model architecture design, training optimization, dataset construction, and storage, making them key targets for future improvements.
- (2) Our microstructure dataset contains a large number of anisotropic structures. Additionally, our multiscale design also incorporates many anisotropic microstructures. For instance, as shown in Figure R22 - R23, some of the anisotropic microstructures used in compact bone design are presented.

- **Reviewer #2 Comment #5:** Embedding physical constraints (e.g., Navier-Stokes equations for permeability or heat transfer equations for thermally conductive structures) directly into the model could improve performance on application-specific tasks.

Response: Thank you for your valuable feedback. The incorporation of diverse physical constraints into generative models could indeed significantly enhance their performance in specific scenarios, thereby enabling a more comprehensive utilization of generative models’ capabilities. This constitutes a critical component worthy of systematic exploration in our future research endeavors. We add the following sentence to the discussion part.

While the LBBM datasets demonstrate advantageous properties, there remain unexplored opportunities in expanding toward more multifunctional capabilities and asymmetric microstructure datasets. To explore multifunctional properties, integrating physical constraints such as the Navier–Stokes equations for permeability or heat transfer equations for thermally conductive structures into the model can enhance performance in application-specific tasks.

- **Reviewer #2 Comment #6:** Use latent space analysis to identify how different latent dimensions correlate with specific structural properties, aiding in targeted property tuning.

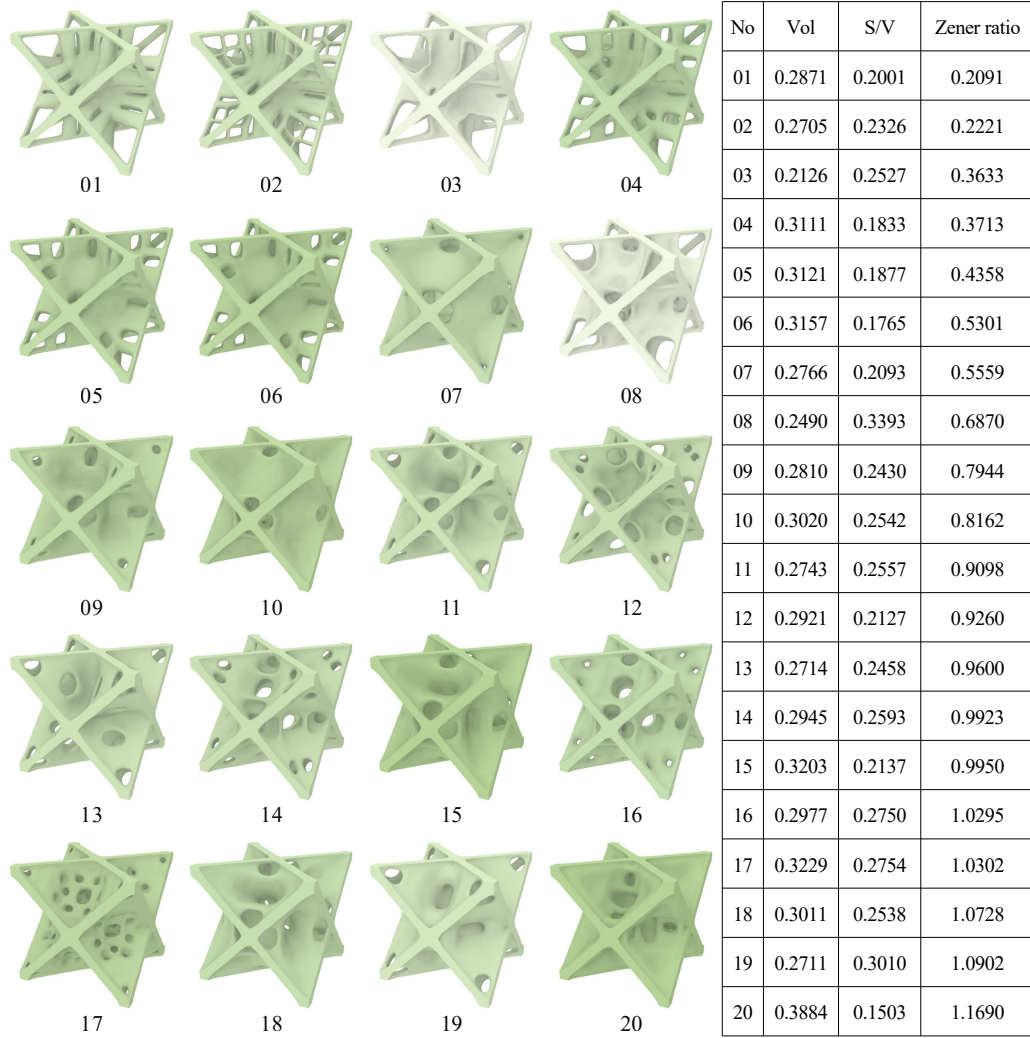


Figure R22: Some anisotropic microstructures used in compact bone design.

Response: Thank you for your valuable feedback on our methodology. The primary role of latent space analysis is to establish relationships between latent vectors and target properties, thereby enabling the regulation of generated structures by manipulating latent vectors. While latent space analysis may enhance the generative accuracy of models, based on network generation accuracy tests, we conclude that the current model architecture sufficiently fulfills the dataset generation requirements.

Specifically, our model employs classifier-free guidance for conditional generation and integrates self-regulation techniques to improve both generation accuracy and quality. To validate the precision of microstructure generation under specified elastic tensor conditions, we utilize the four masks mentioned in the paper to generate microstructures with targeted elastic properties. The R^2 -score is adopted to quantify the discrepancy between the target properties and the properties of the generated microstructures. Experimental results are summarized in Table 1.

- **Reviewer #2 Comment #7:** [Instead of static boundary masks, incorporate adaptive masks that evolve during training to explore broader structural designs.](#)

Response: Thank you for your suggestion. The exploration of structural design through adap-

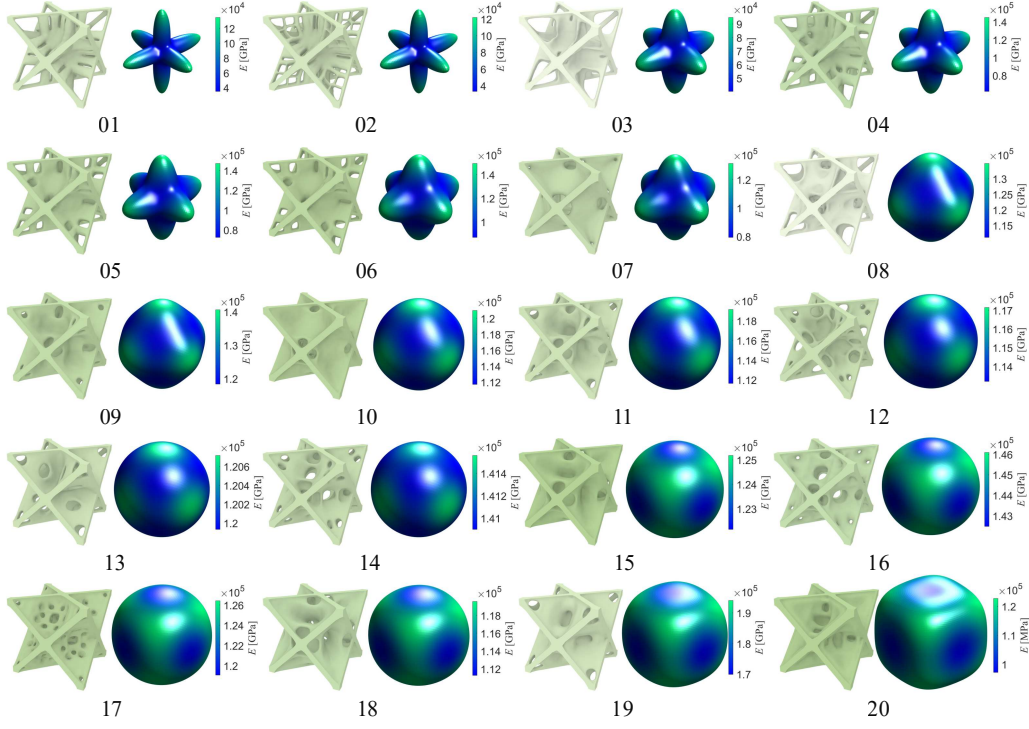


Figure R23: Some anisotropic microstructures used in compact bone design and their corresponding Young's modulus representations.

tive masks is indeed a promising direction. However, based on the following considerations, we believe this approach remains impractical at present.

First, for 3D microstructures, boundary masks can be represented as binary images. At a resolution of $128 \times 128 \times 128$ elements, the corresponding 2D boundary mask reaches 128×128 pixels, leading to an astronomical number of possible variations. Since deep generative models approximate the distribution of training data, a comprehensive dataset would be required to capture the diversity of both boundary masks and their associated elastic tensors. Constructing such a dataset poses substantial challenges in terms of computational cost and generation strategy optimization.

Second, developing an effective adaptive mask strategy is technically demanding. The vast design space necessitates systematic evaluation to guide the evolutionary trajectory of mask modifications. However, the scarcity of training data complicates this process, resulting in unreliable evaluation metrics and potentially misleading optimization directions.

- **Reviewer #2 Remarks on code availability:** [The github repository link provided by the authors does not contain the main code.](#)

Response: Thank you for pointing out this issue. We highly value your feedback and sincerely apologize for the inconvenience caused. After receiving your comment, we promptly updated and supplemented the relevant content. All related code, along with the training dataset for mask 1 (over 10,000 entries), has now been uploaded to our GitHub repository, which can be accessed through the following link: <https://github.com/llwang91/LBBM/>.

Response to Reviewer #3

- **Reviewer #3 General Comment:** The study investigates the machine learning (ML)-enabled design process of large-scale, boundary-identical, bicontinuous Microstructures (LBBM). While the study addresses an important research area, the current results fail to clearly demonstrate the novelty of the work. Several critical issues should be addressed to enhance its scientific contribution and overall quality.

Response: Thank you very much for your thoughtful feedback on our manuscript. For the novelty of this paper, we summarized as follows.

(1) The design of bicontinuous structures is significant but challenging [19, 20, 21].

Studying bicontinuous structures is essential for achieving both mechanical robustness and functional performance, as their dual-phase continuity supports improved load transfer and fluid transport. Directly optimizing bicontinuous structures remains highly challenging. Central to our approach is **the key insight** that a multiscale structure preserves its bicontinuous nature if its building blocks are themselves bicontinuous and share identical boundary conditions.

(2) Novelty

We have reorganized the manuscript and summarized the key innovations of our work as follows:

- **Rapid generation of bicontinuous multiscale structures.** We propose an efficient framework for constructing multiscale structures using large-scale, boundary-consistent bicontinuous microstructure (LBBM) datasets, overcoming the limitation of direct optimization. Compared to existing machine learning-based methods [3], our framework achieves a 120-fold acceleration in structure generation time (from 10 hours to 5 min). Additionally, this method [3] cannot guarantee structural bicontinuity.
- **Development of four LBBM datasets.** We construct four datasets featuring bicontinuous and identical boundaries, offering broader coverage than previously published datasets [7]. Although external constraints such as identical boundary, cubic symmetry, and bicontinuity have been added, the final datasets still have large property space. These datasets enhance applicability across a wider range of practical design scenarios.

We have carefully considered your comments and suggestions and made the necessary revisions to address and clarify the critical issues raised. Below, we provide detailed responses to each of the points you have highlighted.

- **Reviewer #3 Comment #1:** The manuscript shows no significant advantages in active learning or microstructure generation compared to their prior studies (reference 56<https://doi.org/10.1007/s00158-023-03657-y> and <https://doi.org/10.1002/advs.202410428>). If the novelty lies in adding boundary conditions to achieve large-scale structure assembly, the authors must clarify how their approach improves computational efficiency or structure performance. Such as directly large-scale topology optimization methods (<https://doi.org/10.1038/nature23911>) or other ML-based methods (<https://www.nature.com/articles/s41467-024-47831-2>, <https://www.nature.com/articles/s41467-023-42415-y>)

Response: We sincerely thank the reviewer for pointing out these issues. We have carefully reviewed the related literature mentioned by the reviewer, including the innovation comparing with previous studies (reference <https://doi.org/10.1007/s00158-023-03657-y> and <https://doi.org/10.1002/advs.202410428>), as well as the differences and advantages compared to existing large-scale topology optimization methods <https://doi.org/10.1038/nature23911>) or

other ML-based methods (<https://www.nature.com/articles/s41467-024-47831-2>, <https://www.nature.com/articles/s41467-023-42415-y>).

(1) Generation of bicontinuous microstructures

The innovation of our work lies not only in the extension of existing methods but more importantly in the generation of bicontinuous microstructures with a dedicated focus on addressing key challenges such as inverse design, computational efficiency and manufacturability.

It is important to emphasize that bicontinuous structures, due to their unique interpenetrating topology and continuous channels, exhibit excellent transmission, mechanical, and electrochemical properties in various material systems, and have strong printability and manufacturability. As early as 1976, Striven [19] predicted that such structures could be widely present in liquid crystal mesophases and called for the development of experimental methods capable of clearly identifying their structures, while predicting that bicontinuous structures might also appear in fluid systems. Subsequently, Lee et al. [20] proposed that “bicontinuous structures could find important applications in nanocasting composites, tissue engineering, separations, catalysis, fuel cells, sensors, and fundamental studies of transport through porous media. Bicontinuous porous morphologies present a unique paradigm in which the solid and void phases each form a convoluted percolating path throughout the sample volume. Due to the non-sequestered nature of the material phases, the bicontinuous framework can offer advanced transport, mechanical, and electrochemical properties for the abovementioned applications. **However, at the length scales pertinent to these systems, direct fabrication of a three-dimensional (3D) bicontinuous structure is difficult and expensive.**”

Carla Fernández-Rico et al. [21] further emphasized that “Bicontinuous materials feature fascinating interpenetrating structures and are found across scales in the natural world. The macroscopic bicontinuous architecture of marine corals enables an optimal balance between connectivity and surface area for nutrient absorption. In sea urchins, the smoothness of bicontinuous microstructures leads to excellent mechanical properties. At the nanoscale, bicontinuous photonic structures in bird feathers produce beautiful structural colors. The unique topology, smooth morphology, and large surface area of these complex materials have inspired the development of synthetic mimics for applications spanning catalysis, energy storage, and optical and mechanical metamaterials. **Nonetheless, precise control of bicontinuous microstructures over large volumes presents fundamental challenges.**”

Even at the single unit cell scale, the design of bicontinuous structures faces challenges such as limited topological space, significant structural stability variations, and difficulty in property prediction. As the complexity of the design task increases, particularly in the case of multiscale inverse design with macro-micro interactivity, how to maintain the bicontinuous topological features while ensuring the manufacturability of the final structure and achieving efficient computation becomes an especially daunting task. This not only requires the design method to ensure bicontinuity at the microscopic level but also necessitates maintaining overall bicontinuity of the structure at the macroscopic level to achieve manufacturability. Our research specifically addresses these challenges by proposing a multiscale inverse design method that integrates performance prediction, structural generation, and seamless connectivity between unit cells, aiming to overcome the bottlenecks in existing technologies and achieve efficient, bicontinuous, and manufacturable multiscale inverse design from the micro to macro scale.

(2) Comparisons

To clearly highlight the advantages of our approach compared to existing research, we summarize the main characteristics of the five related papers mentioned by the reviewer in Table 2, with

Work	Goal	Motivation	Method	Representation	Comparison with Ours
Zhang et al. [22]	High-performance computation of unit cell mechanics	GPU acceleration to improve efficiency	Multigrid	Element	Not suitable for multiscale design
Zhao et al. [23]	Limit structure of continuous sequence plates	Exploring mechanical limit properties	Optimization + Fitting	Implicit neural representation	Not printable; connectivity issues at boundaries in multiscale design
Aage et al. [24]	High-resolution macroscopic structures	CPU cluster parallelism	CPU parallelization	Element	Low efficiency; one billion element optimization takes 1–5 days on 8000 CPUs
Peng et al. [7]	Bone implants	Improve Young’s modulus and yield strength	Active learning loop (GAD-MALL)	Spinodal	Low efficiency; takes about one week to complete
Jia et al. [4]	Bone repair	Reduce stress shielding	Macro topology optimization + ML	Predefined blocks	Limited data range; weak generalization and complexity

Table 2: Comparisons of related works with our approach.

a particular focus on innovations and improvements in computational efficiency, data coverage, and manufacturability.

- Problem

First, the works [22, 23, 24] mentioned by the reviewer are not specifically designed for bicontinuous (double-connected) structures and therefore do not address the core challenge of bicontinuous structure design.

Second, although works [7, 4] focus on bone structure optimization, they do not incorporate topological control. As a result, they cannot regulate key structural features such as porosity and pore size across different bone regions (e.g., cancellous vs. cortical bone).

Finally, enabled by our large and diverse dataset, the proposed method supports macro-level control across a wide range of scenarios, including tunable porosity, pore size, surface-to-volume ratio, and mechanical stiffness, thus offering significantly enhanced design flexibility.

- Computational Efficiency

Zhang et al. [22] developed a GPU-based high-performance solver, which significantly accelerated the inverse generation process of high-resolution microstructures. However, the method still faces performance bottlenecks in optimizing extra high-resolution structures. For example, using the MMA optimizer, generating a 128^3 structure takes an average of 1.3 minutes, which is more than three times slower than the guided diffusion method proposed by Yang et al. [3].

In large scale topology optimization, Aage et al. [24] point out that solving a full-scale problem with over one billion elements requires massive computational resources, taking 1–5 days even on a cluster with 8000 CPUs. In contrast, multiscale design methods demonstrate tremendous potential in reducing computational cost. For example, Yang et al. [3] solve a stealth optimization problem involving approximately 1.678 billion elements ($20 \times 20 \times 20 \times 128^3$) within 11 hours on

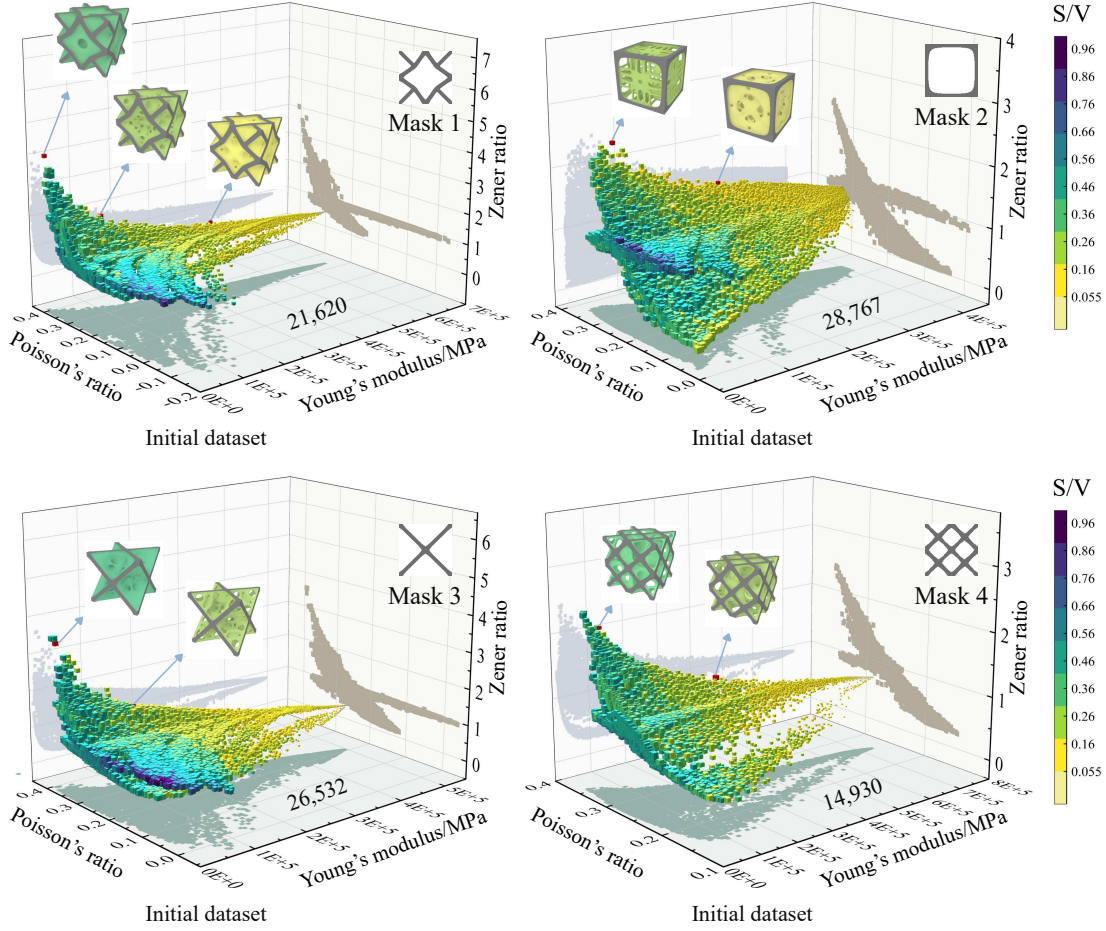


Figure R24: The optimized datasets.

an individual CPU. By comparison, using our constructed LBBM dataset, we solve the same-scale optimization problem in less than 5 minutes while achieving comparable or superior stealth performance (Figure R11). This improvement mainly stems from resolving the microstructural boundary connectivity issue.

For work proposed by Jia et al. [7], it is fast to generate by predetermined building blocks, but the application is limited, and the porosity, pore size, surface-to-volume ratio, and other properties cannot be regulated.

Learning-based optimization methods also receive increasing attention. Peng et al. [4] propose the GAD-MALL framework, which integrates generative models, 3D convolutional neural networks, and numerical simulation and applies an active learning strategy to optimize both Young's modulus and yield strength. The entire process completes within one week using standard hardware.

- Dataset Coverage

Zhang et al. [22] rely solely on optimization-based methods, resulting in sparsely distributed data points within the design space and failing to construct a dense dataset with broad coverage (Figure R24).

Similarly, the methods of Peng et al. [4] and Jia et al. [7] perform well in specific applications but are limited by a narrow data range, leading to insufficient generalization ability and complexity. Our method, by integrating performance prediction, structural reconstruction, and multiscale

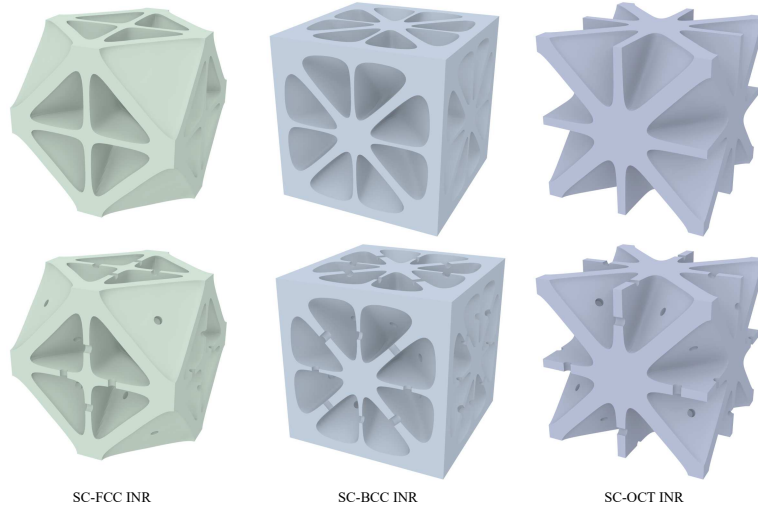


Figure R25: Near-isotropic, extreme-stiffness, 3D mechanical metamaterial and perforation results.

coupling, significantly enhances the data coverage and practical application potential.

- Manufacturability

Zhao et al. [23] designed three nearly isotropic 3D mechanical metamaterials, which, although exhibiting excellent mechanical properties, require additional manual perforation due to the closed pore issue (Figure R25). Additionally, the data points generated by their optimization method [22] are sparsely distributed in the design space, making it impossible to construct a dense dataset with broad coverage.

In summary, our method demonstrates clear advantages in computational efficiency, dataset coverage, and manufacturability. **Additionally, we provide a more detailed discussion of the computational efficiency and structural performance in our response to Reviewer #1, Comment #1.**

- **Reviewer #3 Comment #2:** The two examples of bone implants (segmental implant and fusion cage) differ from actual requirements, and the performance description is insufficient.
 - (a) The base material for constructing the structures is unclear. As load-bearing bone implants, materials such as PEEK or Ti are typically used, and optimization objectives differ significantly depending on the base material.
 - (b) For example, metal implants often require reduced stiffness to avoid stress shielding, while polymer implants face strength limitations, making strength more critical than stiffness. Additionally, base material selection affects porosity, curvature, and overall structural properties.
 - (c) What is the difference between assembling the final implant by selecting different structures within a defined range and repeatedly constructing it using a single structure optimized for the target performance?
 - (d) The authors optimized the microstructures, but do the assembled large-scale structures still meet the target performance? In other words, the final porosity, mechanical properties, and other performance metrics of the large-scale structures should be clarified and compared. A good example would be the permeability test in this paper.

Response: We sincerely thank the reviewer for pointing out the limitations in our bone implant examples regarding material assumptions, performance descriptions, and structural assembly strategies. These comments are highly valuable in improving the engineering applicability

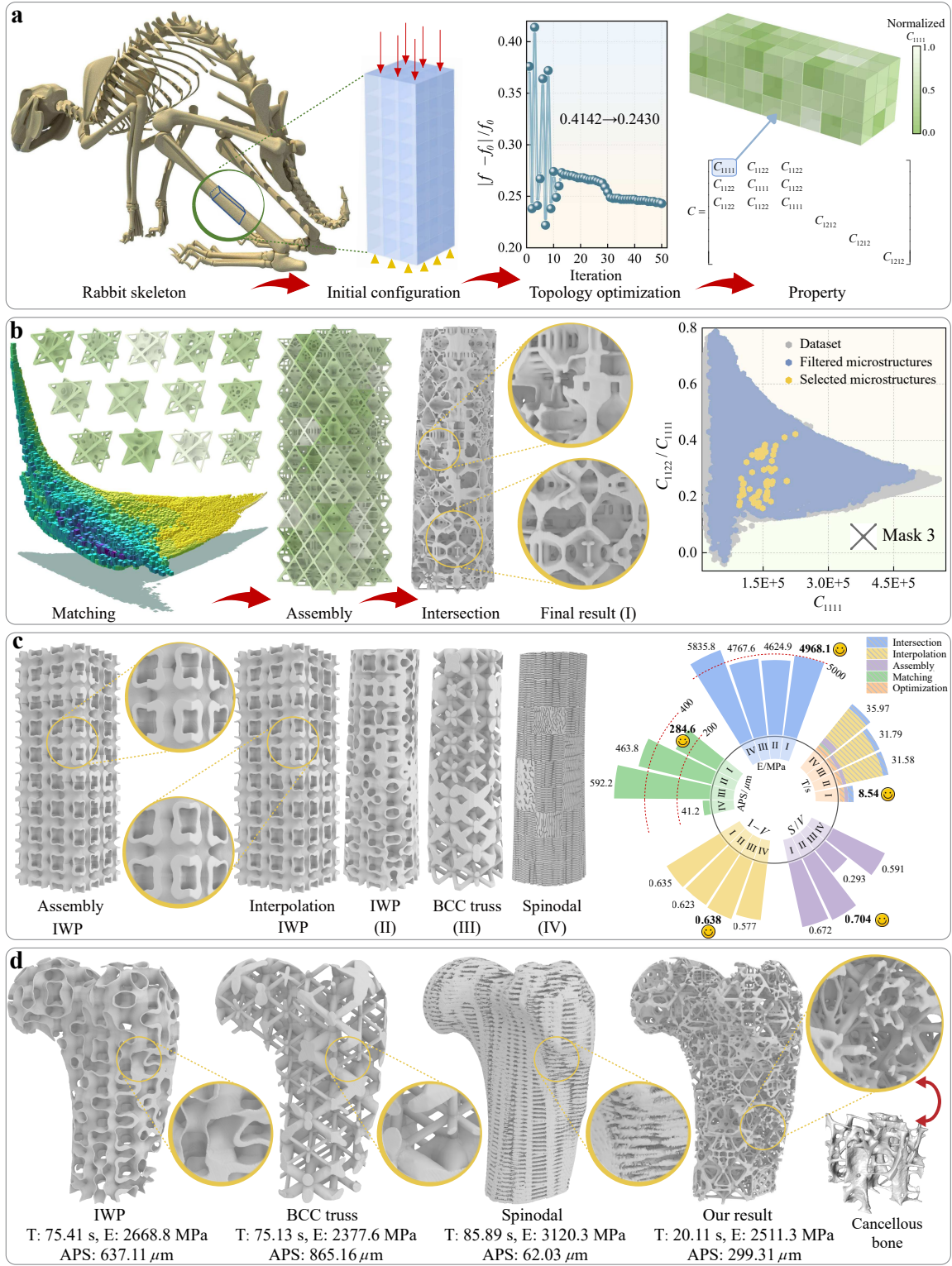


Figure R26: **Compact bone and cancellous bone implant multiscale design.** **a** The multiscale design process involves defining boundary conditions, applying forces within the design domain ($3 \times 3 \times 9$ units), and performing inverse optimization. **b** Microstructure matching, assembled multiscale structure, femur intersection results, and the corresponding data positions within the third dataset. **c** Compact bone results based on Schoen's I-graph-wrapped package (IWP), body-centered cubic symmetry (BCC) truss, and spinodal structures, along with a statistical comparison of the total computation time and the final bone structure's Young's modulus. **d** Computation time (T) and Young's modulus (E) of IWP, BCC truss, and spinodal structures are presented, along with our optimization results, which are compared in detail with cancellous bone.

and scientific rigor of our study. We have carefully revised the corresponding sections in the manuscript and clarified the optimization objectives. The detailed revisions are as follows:

1. Regarding the base material used for constructing the microstructures, we acknowledge that the original manuscript lacks explicit clarification, which may lead to misunderstanding. In the revised version, we now clearly state that the assumed base material is titanium (Ti), which possesses medium elastic modulus and density, and is commonly employed in clinical load-bearing implants. Based on this assumption, we set the optimization objective to minimize the relative error between the equivalent stiffness of the implant and the target stiffness of cancellous bone, aiming to achieve improved mechanical compatibility. Details are provided in the response to **Reviewer #1 Comment #7** and in Figure R26 of the revised manuscript, which illustrates the multiscale optimization process and results.
2. In terms of performance metrics, we convert the Young’s modulus of both cancellous and cortical bone into target equivalent stiffness values. We also consider key geometric and physical parameters such as pore size, porosity, and S/V , in order to enable a more targeted and comprehensive performance optimization.
3. With regard to the difference between assembling the final implant using varying microstructures within a predefined range and constructing it by repeating a single structure, we refer to the GAD-MALL framework proposed by Peng et al [4]. In their study, scaffolds with target stiffness values of 2500 MPa and 5000 MPa are designed. Experimental results demonstrate that the machine learning-designed diverse structures (A1–A4) significantly outperform the uniformly designed scaffolds (H1 and H2) in terms of key indicators such as yield strength (Figure R27). This result supports the strategy adopted in our study.
4. On the question of whether the assembled large-scale structure still meets the target performance, we provide further clarification in the revised manuscript. First, we evaluate the equivalent mechanical properties of the microstructures using homogenization methods and use them to guide the construction of large-scale architectures. Furthermore, we refer to the study by Garner et al. [25], which discusses how microstructural connectivity in the context of additive manufacturing affects global continuity and mechanical performance. Their results indicate that good boundary connectivity facilitates reliable mechanical properties in assembled structures. The constructed LBBM dataset follows a strict boundary-consistency design principle, which effectively avoids performance mismatch problems that often arise from poor connectivity in conventional approaches. This ensures that the assembled macrostructures better achieve the intended design targets.

Once again, we sincerely thank the reviewer for these insightful comments, which have significantly guided our improvements in material selection, performance evaluation, and structural integration strategies under realistic application scenarios.

To achieve variable permeability [26, 27, 28], we design a $4 \times 4 \times 1$ bicontinuous multiscale structure (Figure R28a, Supplementary Section 6.6 and Figures S10-S13). To comprehensively verify the broad permeability range of our design, we conducted a three-stage study comprising computational analysis, simulation validation, and experimental testing. In the computational analysis stage, we calculate the permeability and S/V for four datasets and TPMS structures. Take the second dataset as an example, computational results indicate that compared to TPMS structures, our designed multiscale structure exhibits a broader range of permeability and S/V variations (Figure R28b left). In the simulation validation stage, we further verify the computational results through fluid simulations. We fix the porosity of the structures at 0.5, 0.6, 0.7, and 0.8, and select the corresponding number of structures from the datasets. By comparing the permeability with Gyroid, Diamond, and IWP structures, we chose the five microstructures with larger S/V for in-depth analysis and present their porosity and S/V box plots (Figure R28b right). Subsequently, COMSOL simulations are performed (Figure R28c), and the results show

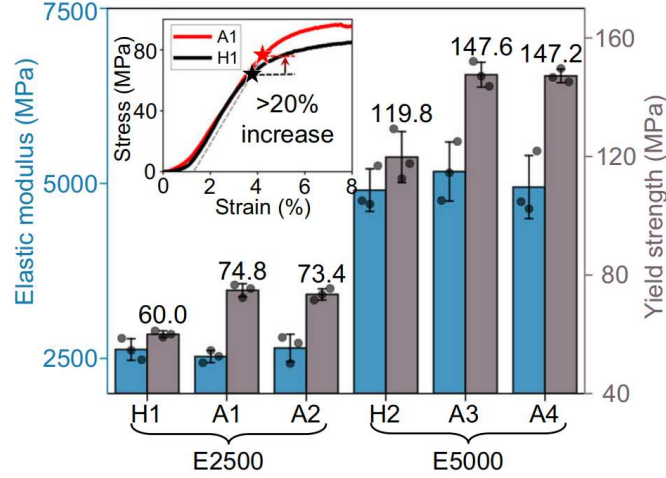


Figure R27: Comparison of the experimental Young's modulus (E) and yield strength (Y) between machine-learning (ML)-designed scaffolds (A1, A2 for $E = 2500$ MPa and A3, A4 for $E = 5000$ MPa) and uniformly designed scaffolds (H1 for $E = 2500$ MPa, H2 for $E = 5000$ MPa). The inset shows the experimental stress-strain curves of the A1 and H1 scaffolds. The dashed line in the inset was obtained by horizontally shifting the linear portion of the stress-strain curve by a 0.2% strain offset and was used to determine the yield points. The Y values of the ML-designed scaffolds were significantly higher than those of the uniform designs. Data are presented as mean $\pm$ standard deviation (SD), $n = 3$ [4].

that our designed multiscale structure exhibited a wider range of changes in porosity and S/V compared to TPMS structures (Figure R28d). In the experimental testing stage, we design an experimental setup (Figure R28e left and Supplementary Material Figure S13) to test the permeability of different structures, using water flow velocity as the testing indicator. To demonstrate the broad permeability of our structures at different porosities, we select three structures with a porosity of 0.8 (M16, M19, and M20, representing high, medium, and low permeability), and compare them with existing Gyroid, Diamond, and IWP structures. The experimental results show that the permeability behavior exhibited by the water flow velocity was consistent with the computational and simulation results, thereby verifying the effectiveness of our design across different structures (Figure R28e middle and right.)

- **Reviewer #3 Comment #3:** How do the principles of microstructure arrangement enhance or control properties such as permeability? Such summaries or discussions should be provided to support the advancement of the field.

Response: Thank you for the comments. In our previous manuscript version, we designed 10 sets of 40 multiscale structures by maximizing stiffness and obtained the permeability of these structures using COMSOL simulations. These efforts represent a forward calculation process.

Based on your valuable suggestions, we explore more physical properties based on the existing dataset. Therefore, we have redesigned the experiment, specifically by performing computational analysis, simulation validation, and experimental testing to further explore more physical properties in the dataset, particularly permeability and other key attributes. Through this experimental process, we aim not only to enhance the inverse design capability for controlling permeability but also to provide richer insights and methods for metamaterial design.

Furthermore, for inverse design, we can refer to Reviewer 1's suggestion in Question 9. We can introduce other constraint properties, such as heat transfer, conductivity, permeability, and others, into the diffusion model. This would guide the model to generate designs that are more

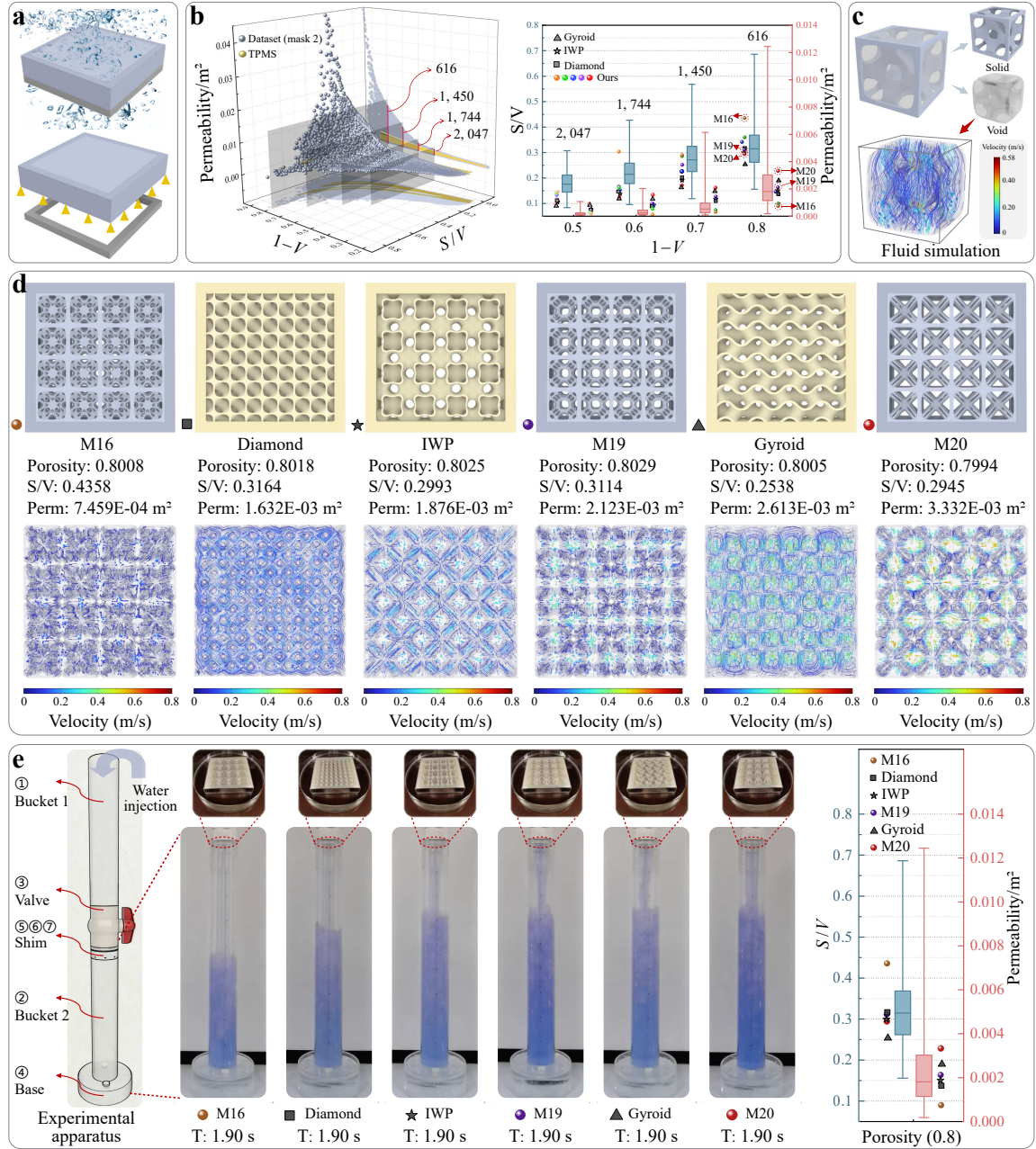


Figure R28: **Multiscale structures design for the filtering device.** **a** The initial setting of the filtering device ($4 \times 4 \times 1$ units). **b** The relationship between the microstructures in mask2 and TPMS structures (Gyroid, Diamond, and IWP) in terms of porosity, S/V , and permeability. Additionally, five representative structures selected from each porosity range of 0.5, 0.6, 0.7, and 0.8 are compared with the corresponding Gyroid, Diamond, and IWP structures in terms of their S/V and permeability. **c** The solid (gray) and void (semi-transparent) phases of the bicontinuous structure, along with fluid simulation results obtained from COMSOL. **d** A comparison of structures with a porosity of 0.8 with Gyroid, Diamond, and IWP structures, along with the presentation of their fluid simulation results. **e** Experiment on the permeability of six structures, which are IWP, Diamond, Gyroid, and optimized multiscale design (M16, M19, M20).

adaptable to a wide range of applications, even enabling exploration in multiple physical fields. In fact, this is one of the key directions for our future work. By extending the physical dimensions of the database through numerical computation and introducing permeability as a design objective or constraint in the optimization process, we can make the generated microstructures more aligned with practical engineering application needs, especially in fields such as filtration and biological tissue engineering.

The specific supplementary content is added into the discussion part as follows:

To explore multifunctional properties, integrating physical constraints such as the Navier–Stokes equations for permeability or heat transfer equations for thermally conductive structures into the model can enhance performance in application-specific tasks.

- **Reviewer #3 Comment #4:** The transitions between units with the preset boundary conditions are good. The internal structures appear to have rounded transitions near the boundaries. How were these transitions considered and achieved?

Response: We sincerely thank the reviewers for their attention. In this study, we effectively achieve the continuity and smooth transition between structural units through optimization strategies, specifically in the following two aspects.

(1) Boundary masking and density initialization strategy. During the topology optimization process, we introduce a masking mechanism to clearly distinguish the designable region from the boundary (non-designable) region. For elements located at the boundary, we impose a fixed density constraint, assigning them a density close to that of solid material (approximately 1), based on their structural role. This approach ensures seamless connectivity between structural units and effectively prevents mechanical performance degradation caused by abrupt density transitions.

(2) Density field filtering and interpolation smoothing. After generating the density field, we apply a radial convolution kernel-based filtering method to smooth the results. This approach effectively eliminates common checkerboard artifacts in topology optimization and naturally produces smooth transitions at the boundaries of the structural units.

- **Reviewer #3 Comment #5:** On Page 7, the authors claim that smaller pores contribute to faster cell seeding and that high curvature improves nutrient flow, cell attachment, and tissue regeneration. These statements are inaccurate. Accurate discussions of these can be referred to <https://doi.org/10.1016/j.matt.2022.06.003> and <https://doi.org/10.1038/s42254-024-00700-9> for accurate discussions of these phenomena.

Response: We sincerely thank the Reviewer for pointing out the inaccuracy in our discussion regarding the effects of pore size and curvature on cell behavior on Page 7 and for providing valuable references. Following the Reviewer’s suggestions, we have carefully reviewed the recommended literature [29, 30] and re-examined the relevant statements in our manuscript.

In the revised version, we have modified the original claims about “smaller pore sizes accelerating cell seeding” and “high curvature enhancing nutrient flow and cell attachment” to better reflect the current consensus in the literature. We have also cited the Reviewer-recommended references on scaffolds for bone tissue engineering to strengthen the scientific accuracy and rigor of our discussion. The revised content can be found in the updated paragraph on Page 7 of the manuscript.

The design of femoral implants entails balancing multiple objectives such as Young’s modulus, pore size, S/V , and weight constituting a prototypical multifunctional optimization problem.

Young’s modulus is pivotal for replicating the mechanical behavior of native bone, enabling effective load transmission while minimizing stress shielding[31, 32, 33, 4]. Compact and cancellous bone exhibit Young’s moduli of approximately 5,000 MPa and 2,500 MPa, respectively[4]. Pore sizes in the range of 200–400 μm have been shown to support cellular proliferation, nutrient diffusion, and vascular infiltration[34, 35, 36, 37]. A higher S/V promotes bone ingrowth[38], while sufficient permeability facilitates nutrient transport and metabolic waste clearance[39]. Finally, lightweight architectures reduce physiological loading, thereby improving postoperative comfort and implant longevity [32].

- **Reviewer #3 Remarks on code availability:** Code is not yet updated.

Response: Thank you for the valuable feedback. We sincerely apologize for the issue you raised regarding the absence of the main code in the GitHub repository, and we regret any inconvenience this may have caused. Following receiving your feedback, we have promptly updated and added the relevant content. All related code, along with the training dataset for mask 1 (comprising over 10,000 entries), has now been uploaded to our GitHub repository. You can access it via the following link: <https://github.com/llwang91/LBBM/>.

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Revision summary “NCOMMS-24-80671B”
“Data-driven Inverse Design of Multifunctional Bicontinuous
Multiscale Structures”

Lili Wang, Jingxuan Feng, Xiaoya Zhai, Jiacheng Han, Kai Chen,
Winston Wai Shing Ma, Ligang Liu, Xiao-Ming Fu

September 15, 2025

REVIEWER COMMENTS

Reviewer #1:

Remarks to the Author:

The authors have thoroughly addressed all of my previous comments and concerns. The revised manuscript is significantly improved and is now suitable for publication in Nature Communications.

Remarks on code availability:

I briefly reviewed the code without installing or running it locally. The repository seems to have clear instructions for installation and execution.

Reviewer #3:

Remarks to the Author:

The authors have made substantial revisions that address most major concerns. I think this paper can be accepted after addressing some issues remained below:

The reply to their novelty is reasonably thorough and includes performance comparisons, e.g., in mechanical cloak design (5 minutes vs. 10 hours). Still, a more explicitly contrast the new boundary-aware generation strategy with their previous “boundary-free” designs should be clarified.

About the discussion part, the author experimentally compared the permeability of two LBBM structures and four TPMS structures, achieving a wide range of permeability results. And the addition of application such as thermal conductivity to the permeability discussion is good. However, the author still have not addressed my previous question: Does this contribute to some theoretical understanding of the relationship between structural design and permeability, rather than merely comparing different results? For example, among parameters such as porosity, pore size, pore shape, and orientation, how do they rank in terms of influence on permeability? The authors do not need to experimentally or numerically verify each factor, but should at least provide a theoretical discussion.

Remarks on code availability:

The code is uploaded, and the README file has enough instructions.

Reviewer #4:

Remarks to the Author:

Comment 1: In general this is a quality piece of work. The manuscript and figures are well constructed. Most, but not all prior reviewer concerns appear to have been addressed.

Comment 2: I am confused by the need to resolve connectivity in conventional periodic lattices. This must stem from the discretization of the design domain, but why this is necessary for conventional

lattice design is not explained. Continuous fields can be used to efficiently drive periodic lattice design variable such as cell size/shape, density, and tiling.

Comment 3: There are still some concerns over novelty. If the term “open cell” is substituted (quite appropriately) for bi-continuous, much of the implications of this work can be more readily understood.

Comment 4: There are too many complex multi-panel figures. To be fair these figures are executed extremely well, and are visually pleasing, but many features become too small to see, making interpretation of results difficult at times. A more straightforward quantitative presentation of results may help make direct comparisons, and remove any obfuscation.

Comment 5: I am also curious about the choice of boundary masks. Can the authors provide more detail on how they were selected and enforced. What order connectivity is enforced at the boundary, geometric, tangent, continuous (C^0 , C^1 , C^2)? Can the authors comment more about the impact of boundary mask on properties? Is it useful to construct 100,000 internally different iterations of 4 boundary configurations, or would more performance gains be made by constructing 1000 different boundary masks with 100 internal designs each? The re-entrant boundary mask showing such wide spread in poissons ratio is telling that this initial constraint is significantly blocking/unlocking property spaces. Until the boundary conditions can be fully understood and modified where possible by machine design, human designs will often remain superior.

General Response

We thank all three reviewers for their constructive and insightful comments. In response, we have thoroughly revised the main manuscript and the Supplementary Information. The key changes are as follows:

- **Importance of connectivity.** We expanded the discussion of connectivity, detailing its implications for both mechanics and manufacturing. We clarify how connectivity governs effective properties and directly affects printability and practical feasibility.
- **Fabrication.** We report additive manufacturing of both single-cell and multiscale structures and now include the fabricated samples.
- **Simplified analytical framework.** We analyze permeability within the Kozeny–Carman framework—highlighting the roles of porosity, pore size, shape/tortuosity, and orientation—and complement it with a maximum-flow surrogate that captures connectivity and bottlenecks.
- **Definitions of bicontinuity and open-cell.** We sharpen these definitions and revise the title and main text to ensure terminological precision and consistency throughout.
- **Language and figures.** We streamline the prose and simplify figures to improve clarity, readability, and the intuitive presentation of key results.

We believe these revisions substantially strengthen the clarity, rigor, and impact of the work.

Please see below for a point-by-point response to the reviewers’ comments and concerns. All page/figure/table/line numbers refer to the revised manuscript file with tracked changes. All paragraphs that appear in the revised manuscript or supplementary are marked in **red**.

Response to Reviewer #1

- **Reviewer #1 Remarks to the Author:** The authors have thoroughly addressed all of my previous comments and concerns. The revised manuscript is significantly improved and is now suitable for publication in Nature Communications.

Response: We sincerely thank the reviewer for the insightful comments and are pleased that our revisions have addressed the concerns and improved the manuscript. It is an honor that our work is considered suitable for publication in Nature Communications. Your thoughtful guidance has not only strengthened this study but will also continue to inspire our future research.

- **Reviewer #1 Remarks on code availability:** I briefly reviewed the code without installing or running it locally. The repository seems to have clear instructions for installation and execution.

Response: We greatly appreciate the reviewer’s positive feedback on our code availability. In line with the commitment to open science and reproducibility, the repository has been thoroughly audited in this revision to ensure completeness, clarity, and ease of use. It now includes full source code, detailed installation and dependency guides, standardized scripts, over 10,000 microstructures, and a comprehensive README facilitating quick setup and independent reproduction of results. To further ensure usability, installation tests have also been successfully performed by non-expert users.

Response to Reviewer #3

- **Reviewer #3 Remarks to the Author:** The authors have made substantial revisions that address most major concerns. I think this paper can be accepted after addressing some issues remained blow.
- **Response:** Thank you very much for your positive feedback. The comments have prompted deeper reflection on both methodology and presentation, and the remaining concerns have been addressed thoroughly in the revised manuscript. These revisions serve to clarify our contributions and enhance the overall impact of the study.
- **Reviewer #3 Comment #1:** The reply to their novelty is reasonably thorough and includes performance comparisons, e.g., in mechanical cloak design (5 minutes vs. 10 hours). Still, a more explicit contrast between the boundary-aware generation strategy with their previous “boundary-free” designs should be clarified.

Response: We greatly appreciate your recognition of our previous comparative experiments and the insightful questions you have raised. Regarding a more detailed comparison between *the boundary-aware generation strategy* and the *boundary-free design*, the differences can be elaborated from the following aspects:

- **Physical properties:** The boundary connectivity between microstructures plays a critical role in determining the physical properties of the resulting composite structures.
- **Manufacturability:** Boundary connectivity also strongly influences manufacturability by reducing interfacial defects and enabling smooth resin drainage.

A more detailed explanation is provided below:

Physical properties The connectivity between microstructures has a pronounced impact on the physical properties of the resulting composite structures. Our study demonstrates this effect through the following observations shown in Figure R1 (a):

Composite structures assembled from microstructures with poor boundary connectivity show inferior mechanical performance compared to the boundary-identical microstructural composites.

To verify this, we conduct a comparative experiment on the relative bulk modulus of composite structures following the steps below. The target of the experiment is to compare whether the bulk modulus of two types of composite structures—those composed of microstructures with the same boundaries and those composed of microstructures with different boundaries—are close to the average of the bulk modulus of the original microstructures.

- (a) Ten microstructures are predefined and marked as $\mathcal{M}^* = \{M_i^*, i = 1, 2, \dots, 10\}$ as illustrated in Figure R1 (b);
- (b) Fifty Microstructures are selected from the same identical-boundary dataset (Mask 1) marked as $\mathcal{M}^S = \{M_j^S, j = 1, 2, \dots, 50\}$ and fifty Microstructures are selected from the random-boundary dataset marked as $\mathcal{M}^R = \{M_j^R, j = 1, 2, \dots, 50\}$. For fairness, microstructures from the random-boundary dataset are chosen to match the bulk modulus of their identical-boundary counterparts. That is, $f(M_j^S) = f(M_j^R)$ ($j = 1, 2, \dots, 50$) where f is the bulk modulus;
- (c) The pre-defined microstructure $\mathcal{M}^*$ is combined with each of the two sets ($\mathcal{M}^S$ and $\mathcal{M}^R$) to form composite units ($[\mathcal{M}^*, \mathcal{M}^S]$ and $[\mathcal{M}^*, \mathcal{M}^R]$). The bulk modulus of the composite microstructures ($f([\mathcal{M}^*, \mathcal{M}^S])$ and $f([\mathcal{M}^*, \mathcal{M}^R])$) are then analyzed using homogenization.

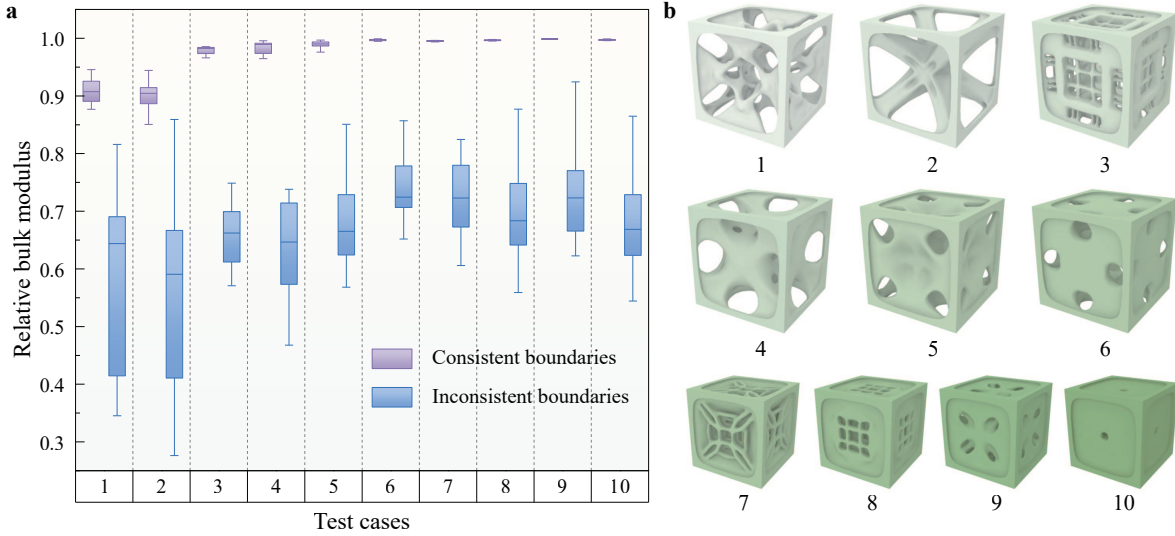


Figure R1: (a) Statistics of relative bulk modulus of composite structures under 10 test cases. (b) Predefined microstructures (1-10).

- (d) The analysis focuses on the relative bulk modulus, which is uniformly defined as follows: for any composite microstructure formed by two microstructures X and Y , let f_X and f_Y denote the bulk modulus of X and Y , respectively, and f_{XY} denote the bulk modulus of the composite $[X, Y]$; the relative bulk modulus r_{XY} of the composite is then given by

$$r_{XY} = \frac{f_{XY}}{\frac{f_X + f_Y}{2}}$$

This definition applies to both groups of composites in the analysis: for composites $[M_i^*, M_j^S]$, $r_{ij}^S = \frac{f_{ij}^{*S}}{\frac{f_i^* + f_j^S}{2}}$; for composites $[M_i^*, M_j^R]$ (where $M_j^R \in \mathcal{M}^R$), $r_{ij}^R = \frac{f_{ij}^{*R}}{\frac{f_i^* + f_j^R}{2}}$, where f_i^* , f_j^S , f_j^R are the bulk modulus of M_i^* , M_j^S , M_j^R , and f_{ij}^{*S} , f_{ij}^{*R} are the bulk modulus of the composites.

The results confirm our observations: composite microstructures with consistent boundaries have a higher relative bulk modulus than those with inconsistent boundaries. Moreover, in 10 sets of experiments, the average value of the former (composite microstructures with consistent boundaries) exceeded 90% in all cases, demonstrating the potential of microstructures with consistent boundaries in multiscale design.

Manufacturability The connectivity of microstructures critically influences the manufacturability of the composite structures.

- **Reduce interfacial defects:** Boundary-identical microstructures promote seamless joining between neighboring units, thereby minimizing interfacial gaps, weak joints, or misalignments that may cause cracks, fractures, or premature failure under load.
- **Enable smooth resin drainage:** In stereolithography (SLA) and other additive manufacturing processes, sufficient connectivity ensures that uncured resin can flow out of enclosed regions. This prevents material entrapment, facilitates complete curing, and enhances both structural integrity and surface quality.

We assessed manufacturability by conducting 3D printing tests on composite microstructures with either identical or inconsistent boundary connections. Figure R2 shows the printing results

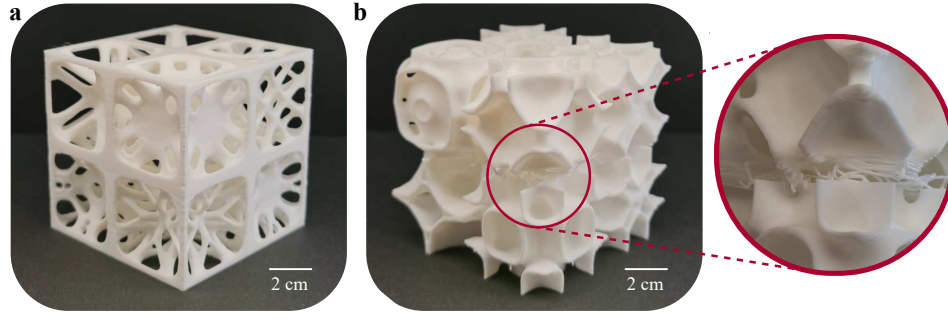


Figure R2: **2×2×2 3D-printed multiscale structures.** **a** 3D-printed multiscale structure composed of microstructures with Mask 1. **b** 3D-printed multiscale structure composed of microstructures with different boundaries.

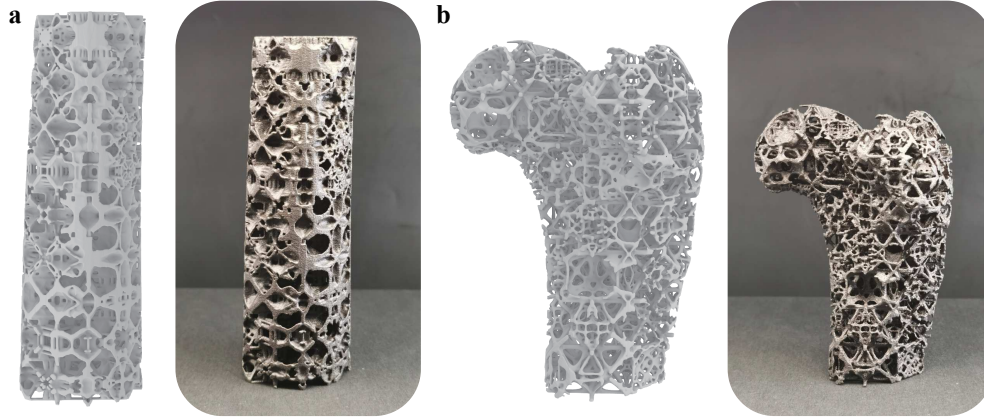


Figure R3: Optimized results and fabricated compact and cancellous bone design.

of the 2×2×2 multiscale structure. In Figure R2a, the structure is assembled from microstructures with identical boundaries and can be fabricated without post-processing. Figure R2b shows a structure containing microstructures with partially incompatible boundaries: two adjacent units fail to fuse smoothly, the splice interfaces exhibit poor quality, and redundant features remain that require post-processing. Such deficiencies make these designs difficult to translate into practical applications. Moreover, to verify bicontinuity, we fabricated multiscale bone implants, as shown in Figure R3.

Overall, microstructural connectivity is critical for both performance and manufacturability. Composites with matched boundaries exhibit higher bulk modulus, whereas those with disconnected boundaries fail during fabrication. Ensuring connectivity minimizes defects, facilitates resin drainage, and is essential for achieving robust, application-ready designs. The detailed discussion has been added to the supplementary materials. Revisions have also been made to the main text. The specific changes to the main text are as follows:

“This boundary-aware generation ensures effective structural properties while improving manufacturability by reducing interfacial defects and enabling smooth resin drainage.”

- **Reviewer #3 Comment #2:** About the discussion part, the author experimentally compared the permeability of two LBBM structures and four TPMS structures, achieving a wide range of permeability results. And the addition of application such as thermal conductivity to the permeability discussion is good. However, the author still have not addressed my previous question:

Does this contribute to some theoretical understanding of the relationship between structural design and permeability, rather than merely comparing different results? For example, among parameters such as porosity, pore size, pore shape, and orientation, how do they rank in terms of influence on permeability? The authors do not need to experimentally or numerically verify each factor, but should at least provide a theoretical discussion.

Response: We thank the reviewer for this insightful comment. To extend the discussion beyond a comparison of results and contribute to a theoretical understanding of how structural parameters govern permeability, we proceed in two steps:

- We examined the key influencing factors, i.e., **porosity**, **pore size**, **pore shape**, and **orientation**, and provided theoretical explanations for their roles. The Kozeny-Carman (KC) framework [1, 2] shows that porosity is the dominant control, pore size is the next most significant enhancer, pore shape/tortuosity acts as a secondary suppressor, and orientation mainly governs tensorial anisotropy.
- We also model pore-scale permeability using a maximum-flow network surrogate that explicitly encodes connectivity and bottlenecks. The surrogate correlates strongly with the reference permeability (linear $R^2 = 0.801$, Spearman $\rho = 0.948$). It complements the KC framework by capturing connectivity effects that are not resolved by porosity ϕ and surface-to-volume ratio S/V alone.

In porous media theory, **porosity** is typically the dominant factor, as it defines the fraction of void space available for flow. However, porosity alone is not sufficient: materials with identical porosity can exhibit orders-of-magnitude differences in permeability due to microstructural variations [3]. Larger average **pore size** generally enhances permeability by creating wider flow channels, while improved connectivity reduces dead-ends and facilitates transport. Conversely, irregular **pore shapes** or unfavorable **orientations** increase tortuosity, thereby reducing permeability even at high porosity [4].

Thus, these quantities interact in nontrivial ways, and their combined influence on permeability cannot be easily generalized. To gain insight, we proceed under KC-type assumptions (homogenized RVE and laminar/Stokes flow) and first analyze canonical idealized geometries to decouple the effects of porosity, S/V , shape/tortuosity, and orientation, employing theoretical analysis to clarify the underlying mechanisms.

(1) A theoretical perspective

The KC framework provides a compact organizing relation linking permeability k to porosity $\phi = 1 - V$ (where V denotes the solid volume fraction), the surface-to-volume ratio S/V (interfacial area per sample volume), and tortuosity τ . The proportionality constant c (Kozeny constant) subsumes geometric details not captured explicitly.

Step 1. Starting from Poiseuille flow in capillaries and modeling a porous medium as an effective capillary bundle, with microstructures parameterized by the surface-to-volume S/V , and incorporating tortuosity τ into a proportionality constant, the KC relation reads

$$k = \frac{1}{c} \frac{\phi^3}{(1 - \phi)^2} \frac{1}{(S/V)^2} \frac{1}{\tau^2}. \quad (1)$$

Step 2. Take the logarithm of both sides of Eq. (30) simultaneously, we have

$$\ln k = (-\ln c) + 3 \ln \phi - 2 \ln(1 - \phi) - 2 \ln(S/V) - 2 \ln \tau. \quad (2)$$

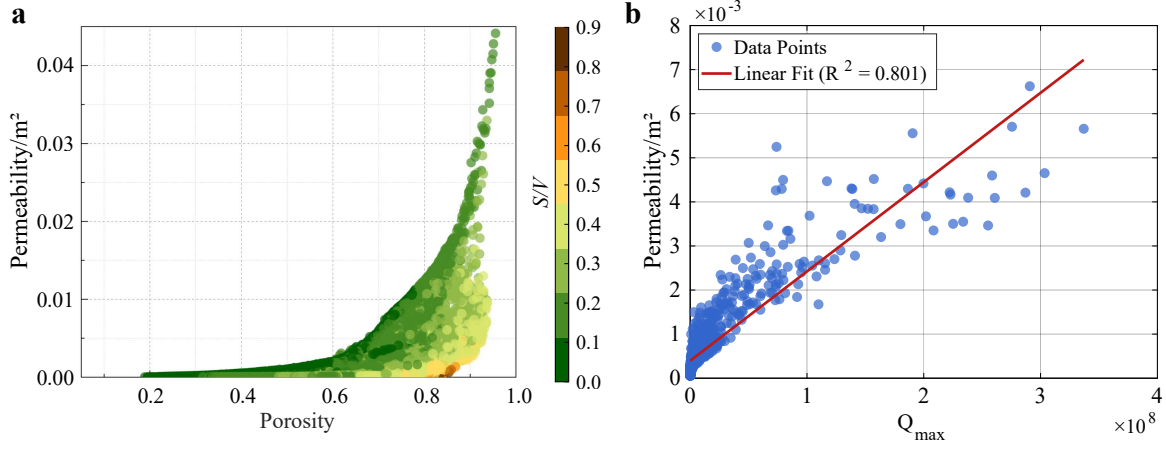


Figure R4: **a** Permeability k versus porosity ϕ ; point color encodes S/V (colorbar at right). **b** Permeability k versus the graph-based maximum flow $Q_{\max}$, with a least-squares linear fit (red) yielding $R^2 = 0.801$.

Define the log-derivative $E_X \equiv \frac{\partial \ln k}{\partial \ln X}$ ($X = \phi, S/V, \tau, d$):

$$E_\phi = 3 + \frac{2\phi}{1-\phi}, \quad E_{S/V} = -2, \quad E_\tau = -2. \quad (3)$$

Using an effective pore size $d \propto 1/(S/V)$ gives $E_d = +2$. Thus, a 1% change in X produces approximately $E_X\%$ change in k . A small perturbation form is

$$\frac{\Delta k}{k} \approx \left(3 + \frac{2\phi}{1-\phi}\right) \frac{\Delta\phi}{\phi} - 2 \frac{\Delta(S/V)}{S/V} - 2 \frac{\Delta\tau}{\tau}, \quad (4)$$

Within the KC framework for scalar k , the log-derivative implies the ranking

$$|E_\phi| = 3 + \frac{2\phi}{1-\phi} > |E_d| = 2 \approx |E_\tau| = 2, \quad (5)$$

where $d \propto 1/(S/V)$. This indicates that porosity is the dominant control, pore size is the next most significant enhancer, and tortuosity acts as a secondary suppressor. Orientation does not enter explicitly in the scalar KC relation but mainly governs tensorial anisotropy. This hierarchy holds within the validity range of the KC framework, but may break down near the high-porosity limit ($\phi \rightarrow 1$).

Step 3. To test the sensitivity analysis implied by the KC framework, we plotted permeability (k) versus porosity (ϕ), with data points color-mapped by the surface-to-volume S/V (Figure R4a). This reveals several key trends:

- **Nonlinear porosity effect:** Permeability increases strongly and nonlinearly with porosity.
- **Role of S/V at fixed ϕ :** For a given porosity, the spread in permeability is modulated by S/V . Higher S/V (more complex pore geometries with rough surfaces or narrow throats) increases flow resistance and lowers k , while lower S/V (smoother flow paths, larger hydraulic radii) yields higher k .
- **Upper envelope:** The distribution exhibits a distinct upper bound defined by low- S/V samples, representing the theoretical permeability maximum achievable for a given porosity.

To quantitatively compare the global influence of porosity and pore-size proxy on permeability, we apply a **binned smoothing** procedure [5]. Let $X \in \{\phi, S/V\}$. We partition the range of X

into K consecutive bins $\{B_j\}_{j=1}^K$ using equal-count (quantile) edges. For each bin we compute the bin-level median permeability

$$m_j = \text{median}(k \mid X \in B_j). \quad (6)$$

We summarize the total variation in k attributable to X by the amplitude of this median trend,

$$R_X = \max_j m_j - \min_j m_j. \quad (7)$$

Side-by-side R_ϕ and $R_{S/V}$ provide a global, marginal comparison of their influences on k , with the quantitative summary from quantile-binned smoothing ($K = 25$) being:

- $R_{S/V} = 7.88 \times 10^{-4}$;
- $R_\phi = 1.11 \times 10^{-2}$.

This result confirms that **porosity (ϕ) is the dominant factor controlling the global variation of permeability (k)**, and its influence significantly outweighs that of the surface-to-volume S/V . The negligible fluctuation range for the S/V -smoothed trend indicates that its role within the KC framework is primarily microscopic: it acts as a key modulating factor that determines the specific permeability value at a given porosity, rather than driving its macroscopic variation.

In conclusion, both theoretical and empirical analyses converge to demonstrate that: Porosity is the primary control on permeability, determining its macroscopic scaling behavior, whereas S/V acts as a secondary control, constraining the microscopic efficiency attainable within a given pore structure. This conclusion is entirely consistent with the sensitivity ranking ($|E_\phi| > |E_{S/V}|$) derived from the KC equation.

While our quantitative insight in this work is explicitly framed within the KC paradigm, prior studies e.g., Rödning et al. (2020)[6] show that a model considering only porosity and specific surface is not a general predictor of permeability. Microstructures sharing ϕ and S/V may still yield widely different k . Motivated by this gap, we next introduce a connectivity-aware maximum-flow surrogate model to complement KC framework.

(2) Modeling Pore-Scale Permeability via a Maximum Flow Network

To explicitly capture connectivity and bottleneck effects that are not resolved by $\{\phi, S/V\}$ alone, we therefore introduce a graph-theoretic maximum-flow surrogate of the pore space. The core mathematical framework is as follows: Given a binarized 3D pore structure matrix $V \in \{0, 1\}^{n_x \times n_y \times n_z}$ (where 0 denotes pore space and 1 denotes solid matrix), the equivalent hydraulic radius R for each pore voxel is first calculated via the Euclidean distance transform (EDT), which assigns to each pore voxel its Euclidean distance to the nearest solid voxel:

$$R(x, y, z) = \min_{(x_0, y_0, z_0) : V(x_0, y_0, z_0) = 1} \sqrt{(x - x_0)^2 + (y - y_0)^2 + (z - z_0)^2}. \quad (8)$$

In other words, (x_0, y_0, z_0) only needs to satisfy $V(x_0, y_0, z_0) = 1$; no additional conditions are required.

Subsequently, a directed graph network $G = (V_G, E_G)$ is constructed, where V_G and E_G denote the node set and the edge set, respectively. The node set V_G comprises all pore voxels along with

source and sink nodes $\{s, t\}$. The edge set E_G is defined as

$$E_G = \{(i, j) \mid i, j \text{ are face-adjacent (6-neighbor) pore voxels}\} \cup \{(s, i) \mid i \in \Gamma_{\text{in}}\} \cup \{(j, t) \mid j \in \Gamma_{\text{out}}\}, \quad (9)$$

where Γ_{in} and Γ_{out} represent the sets of pore nodes on two opposite boundary faces of the sample (chosen as inlet and outlet, respectively). The edge capacity function, based on Poiseuille’s law, is defined as:

$$c(i, j) = [\min(R(i), R(j))]^4. \quad (10)$$

The prediction of permeability is ultimately transformed into solving an s - t maximum flow problem:

$$\begin{aligned} \max_{\{f_{uv}\}} \quad & Q = \sum_{(s,u) \in E_G} f_{su} \\ \text{s.t.} \quad & \sum_{(u,v) \in E_G} f_{uv} - \sum_{(w,u) \in E_G} f_{wu} = 0, \quad \forall u \in V_G \setminus \{s, t\}; \\ & 0 \leq f_{uv} \leq c(u, v), \quad \forall (u, v) \in E_G; \end{aligned} \quad (11)$$

Denote by Q_{max} the optimal objective value of the above problem, i.e., the maximum feasible net flux from s to t .

Computations on $N = 1000$ randomly selected pore structures show a strong association between the graph-based maximum flow Q_{max} and the reference permeability. A simple linear regression explains $R^2 = 0.801$; Spearman’s rank correlation is $\rho = 0.948$, confirming an almost monotonic relationship (Figure R4b). The rank correlation notably exceeds the linear correlation, indicating a nearly monotonic yet mildly nonlinear relationship, consistent with interpreting Q_{max} as a bottleneck-dominated geometric surrogate rather than an exact hydraulic response under a prescribed pressure drop.

Although the surrogate captures key pore-space features through a hydraulic-radius map and global connectivity, it oversimplifies the physics of fluid transport. Permeability arises from viscous dissipation, inertial effects, tortuosity, connectivity, and anisotropy, so even small geometric variations can cause large changes under Stokes flow. Thus, while geometric proxies such as Q_{max} provide structural insight and strong discriminatory power, accurate prediction ultimately requires solving the full pressure-driven flow (e.g., hydraulic-conductance networks or Stokes/Navier–Stokes simulations). These results clarify the scope and limitations of simplified graph-based models and highlight the high-fidelity simulations for quantitative accuracy.

(3) Potential future direction

A promising future direction is hybrid AI–physics approaches, which can link learned features to pore characteristics and capture subtle geometric effects that strongly influence permeability. Such methods, especially when combined with high-fidelity flow simulations, may overcome the limitations of simplified proxies and yield more accurate and interpretable predictions [7, 8]. While beyond the scope of this work, we view this as an important avenue for future research.

The corresponding revised manuscript is added to Section 8 of the supplementary materials. The following sentences are added to the main text:

“A simplified analytical framework links channel connectivity and tortuosity to permeability,

offering theoretical insight into governing structural parameters (Supplementary Section 8, Fig. S17).”

- **Reviewer #3 Remarks on code availability:** The code is uploaded, and the README file has enough instructions.

Response: We thank the reviewer for the positive feedback on code availability. In this revision, we thoroughly audited the repository to ensure completeness, clarity, and usability. It now includes full source code, detailed installation guides, standardized scripts, over 10,000 microstructure data, and a comprehensive README, with installation tests by non-expert users confirming reproducibility.

Response to Reviewer #4

- **Reviewer #4 Comment #1:** In general this is a quality piece of work. The manuscript and figures are well constructed. Most, but not all prior reviewer concerns appear to have been addressed.

Response: We thank the reviewer for the positive assessment of our study and for recognizing the improvements made in this revision. It is acknowledged that some concerns remain unresolved. In response, these points were carefully re-evaluated, the manuscript was revised in accordance with the overall framework and objectives, and a clear point-by-point account of the changes with their scientific rationale is provided below to further strengthen the clarity and impact of the work.

- **Reviewer #4 Comment #2:** I am confused by the need to resolve connectivity in conventional periodic lattices. This must stem from the discretization of the design domain, but why this is necessary for conventional lattice design is not explained. Continuous fields can be used to efficiently drive periodic lattice design variable such as cell size/shape, density, and tiling.

Response: Thank you very much for your valuable comments. We structure our response around five aspects:

- The definition of connectivity;
- The importance of connectivity and its challenge;
- The connectivity in traditional periodic unit cells;
- The contrast between continuous-field and discrete-variable design approaches;
- The effectiveness of discrete voxel-based microstructure design with identical boundaries.

(1) The definition of connectivity

Here, by “connectivity” we refer to the geometric compatibility of boundaries when different types of unit cells are joined together. Although the unit cells in this paper belong to periodically tiling lattices, the scenario we consider is not the traditional design with a single type of lattice. Instead, it involves combining unit cells from different lattices to form the final multiscale structures. Given that these unit cells from different lattices vary in shape, issues may arise where two unit cells fail to fuse well at their boundary junctions during assembly.

(2) The importance of connectivity and its challenge

Importance of connectivity Microstructures with identical boundaries exhibit excellent connectivity, conferring significant advantages for both physical performance and manufacturability. Please refer to the response to “Reviewer #3 Comment #1”. Therefore, resolving connectivity between neighboring micro-architectures is essential when macrostructures incorporate heterogeneous units, as this ensures manufacturable designs capable of bearing loads efficiently [9, 10, 11].

Challenge In prior studies, many design approaches have been proposed to resolve the connectivity issue between neighboring micro-architectures. For instance, a virtual scalar field method (VSFM) was developed for describing and enforcing desired connectivity constraint in the SIMP-based topology optimization framework [12]. For the level set-based topology optimization, a VCUT method was proposed, which utilized a variable and continuous cutting function by interpolating with a set of height variables to devise functionally graded lattice structures, guaranteeing the connectivity between adjacent unit cells directly [13]. Besides, based on the parameterized

level set model, different orders of connectivity (C^0 , C^1 , and C^2) can be ensured by imposing constraints on the control coefficients [14]. The connectivity issue of adjacent micro-architectures can also be resolved by incorporating a kinematical connective constraint [15], introducing additional intermediate cells to connect each pair of adjacent cells [16], and other approaches [9]. Current research typically constructs composite microstructures by imposing compatibility constraints. However, this optimization process is highly time-consuming, and the additional task of dataset generation further increases the computational burden. The associated challenges and difficulties are discussed in detail at the end of the third paragraph of the main text.

(3) The connectivity in traditional periodic unit cells

Traditional periodic unit cells are typically constructed by tiling a single cell periodically to generate the final multi-scale structure. However, such an approach imposes significant restrictions on the design space. In contrast, the present work assembles multi-scale structures from multiple distinct microstructures. Although this introduces the challenge of ensuring connectivity, it substantially enlarges the design space and enables the discovery of superior multi-scale structures.

It is important to clarify a potential misconception in the comment regarding the statement *“This must stem from the discretization of the design domain.”* The connectivity issue does not arise from discretization itself, but rather from the independent treatment of unit cells during the design process. When constructing multiscale structures, different microstructures are combined in pursuit of enhanced performance, and this independent design approach inherently introduces the risk of poor connectivity. However, if a single microstructure is arranged periodically, the same limitations described above. It greatly restricts the design space and results in multiscale structures with inherently limited performance.

(4) The contrast between continuous-field and discrete-variable design approaches

From the perspective of continuous fields, we identify three approaches to designing multiscale structures.

- The first approach treats the entire multiscale structure as a continuous field and directly optimizes the field. However, this incurs prohibitive computational costs—contradicting the fundamental intent of multiscale design, which is to simplify the process by decomposing the design of complex structures into the assembly of diverse, complex unit cells.
- The second approach uses continuous fields to represent unit cells and applies smoothing operations to the field at unit cell junctions when composing the multiscale structure. This makes the performance of the designed structure difficult to regulate: the altered morphology of each unit cell leads to severely uncontrollable performance.
- The third approach focuses on designing mutually compatible unit cells. The core challenge here, however, lies in ensuring boundary compatibility between unit cells—and there is no fundamental difference in this regard between using continuous fields and discrete voxels.

In our method, we opt for discrete voxel-based modeling, and its effectiveness has been validated experimentally.

(5) The effectiveness of discrete voxel-based microstructure design with identical boundaries

In this study, we focus on the data-driven design of multifunctional bicontinuous multiscale structures based on the 3D Large-range, Boundary-identical, Bicontinuous, Open-cell Microstructure (L-BOM) datasets, which possess the following key advantages, including addressing the connectivity issue effectively. First, the boundaries of the micro-architectures in each dataset are identical, which can ensure the seamless connectivity between adjacent cells straightforwardly.

Besides, the identical boundaries can also simplify the assembly process and accelerate the multiscale design/optimization process. Moreover, the datasets feature a larger design space, thus enabling a large range of tailorable properties for the designed structures. The advantages and potentials of the proposed design framework are further demonstrated by the design of bone implants, chair components, and multifunctional materials with tunable elasticity and permeability in this study.

To elaborate the necessity of resolving the connectivity issue of periodic lattices, we have added the following explanations at the end of the second paragraph of the “Introduction” part:

“The inadequate connectivity leads to structural failures leaving lattices unable to bear loads effectively and complicates the additive manufacturing process. To develop manufacturable, load-efficient designs, the connectivity issue between neighboring microstructures must be resolved when the macrostructure incorporates various microstructures [9, 10, 11].”

We have also highlighted the advantages of our proposed design framework in ensuring seamless connectivity between adjacent unit cells and other aspects in the first paragraph of the “Discussion” part:

“The boundaries of the micro-architectures in each dataset are identical, which can ensure the seamless connectivity between adjacent cells straightforwardly. The identical boundaries can also simplify the assembly process and accelerate the multiscale optimization process. Moreover, the datasets also feature a larger design space, thus enabling a large range of tailorable properties for the designed structures.”

The following references are also added in the main text of the Manuscript:

[1] V. Cool, N. Aage, O. Sigmund, A practical review on promoting connectivity in topology optimization, *Struct. Multidiscip. Optim.* 68(4) (2025) 73.

[2] J.E. Cadman, S. Zhou, Y. Chen, Q. Li, On design of multi-functional microstructural materials, *J. Mater. Sci.* 48(1) (2013) 51-66.

[3] J. Alexandersen, B.S. Lazarov, Topology optimisation of manufacturable microstructural details without length scale separation using a spectral coarse basis preconditioner, *Comput. Methods Appl. Mech. Eng.* 290 (2015) 156-182.”

- **Reviewer #4 Comment #3:** There are still some concerns over novelty. If the term “open cell” is substituted (quite appropriately) for bi-continuous, many of the implications of this work can be more readily understood.

Response: Thank you for your comment. We recognize that the term **open cell** may be confused with **bicontinuous**, and we therefore clarify the distinction as follows:

- **Open cell:** Porous materials in which the **voids** are interconnected, forming a continuous pathway for fluid or gas transport that remains open to the external environment.
- **Bicontinuous:** Materials where both the **solid phase** and the **pore phase** are continuous and interpenetrating across the entire structure.

The key difference is that open-cell structures require only the pore phase to be continuous and open-ended, whereas bicontinuous structures demand mutual continuity of both phases shown in Figure R5. It is worth noting that a bicontinuous structure can be either open or closed (Figure R5e-f).

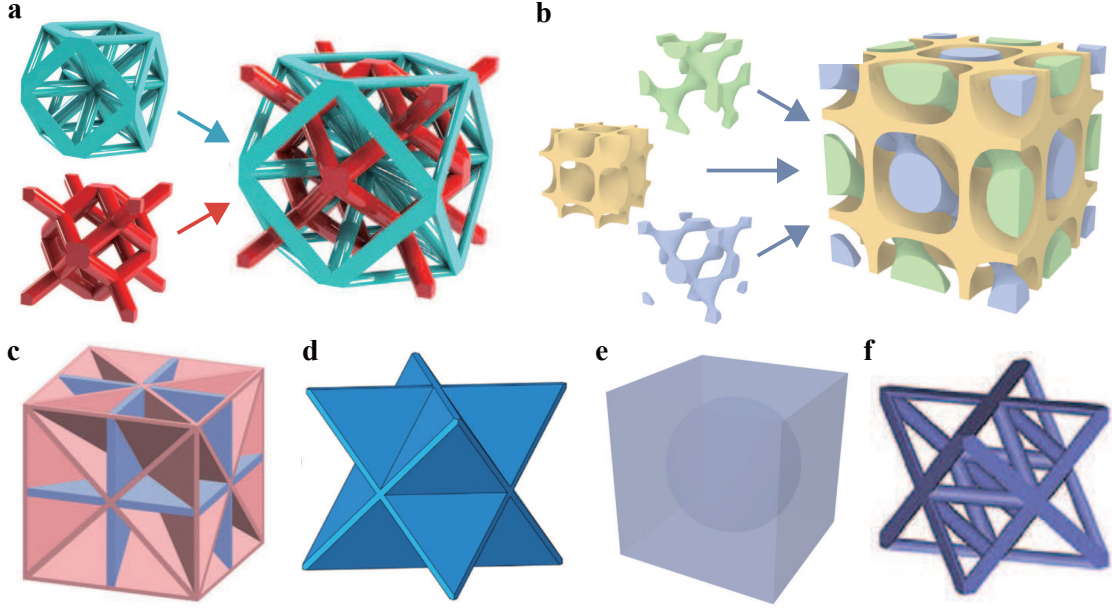


Figure R5: **Illustration of open cell (a-b), closed cell (c-d), and bicontinuous open-cell structures (e).** **a-b** Interpenetrating lattices [17, 18]: open-cell structures that are not bicontinuous. **c** Closed cell structure with sealed pores at the boundary junctions [19]. **d** Closed cell structure containing isolated internal cavities [20]. **e** Bicontinuous closed-cell structure—in which both solid and pore phases are continuous but the pores are sealed from the external environment. **f** Bicontinuous open-cell structure—in which both the solid phase and the pore phase are continuous and fully interconnected with open ends [21].

Literature background The concept of bicontinuous topology, characterized by two interpenetrating continuous phases without isolated domains, has been extensively studied across multiple disciplines, including materials science, physics, and biology. Early research primarily focused on the formation mechanisms and stability of bicontinuous structures in polymer blends [22], where such morphologies showed significant advantages in tuning material properties. Subsequently, nanoparticle-stabilized emulsions, commonly known as *bijels* (bicontinuous interfacially jammed emulsion gels), have emerged as typical examples of bicontinuous systems, realizing the coexistence of two continuous fluid phases stabilized by interfacial jamming, thereby further stimulating research interest in bicontinuous architectures [23]. Moreover, natural materials such as the skeletal structures of echinoderms exhibit naturally occurring bicontinuous features; their complex 3D networks not only provide excellent mechanical performance but also play crucial roles in fluid permeability and nutrient transport within physiological processes [24].

In this work, we observe that when each microstructure is boundary-identical and possesses an opening hole channel, the resulting multiscale structure also retains a bicontinuous topology. To improve accuracy, we have revised the terminology in the manuscript: *the phrase “bicontinuous microstructure” has been replaced with “bicontinuous open-cell microstructure,” emphasizing that the microstructure is both bicontinuous and open-ended.* Accordingly, we have revised the introduction (page 1, lines 8–10) and provided a detailed explanation of their overlap and distinctions. Specifically, we added the following:

“Bicontinuous open-cell multiscale structures are organized at multiple hierarchical levels, where each level builds upon the previous one, leading to increased complexity and enhanced functionality. These structures exhibit bicontinuous properties, characterized by two interpenetrating continuous phases that remain distinct without mixing, thereby forming a network of interconnected voids or channels. Among these, the pores are open to the external environment and maintain direct openings.”

Table R1: Detailed revisions of figures in main text.

Figure/ Table	Change type	Issue before revision	Modification applied	Expected improvement
Figure 1	Vectorization + Content refinement	The text description in panel c is imprecise; in panel d, coordinates and data labels are blurred when zoomed, labels are overcrowded, and arrows are unclear	In panel c, change <i>strong connection</i> to the more precise <i>well connection</i> ; in panel d, convert all coordinates and labels to vector format; remove redundant arrows and dense labels	The description is made more accurate; interpretation difficulties are reduced
Figure 2	Vectorization	Data labels are blurred when zoomed	Convert all coordinates and labels to vector format	The data remain clear at all scales
Figure 3	Vectorization + Simplification	Box plots in panels a–b are blurred when zoomed; panels c–h have been removed	Vectorize panels a–b; remove panels c–h; replace the original panels c–d with more intuitive statistical graphs and add explanatory text	Figure complexity is reduced; quantitative comparison is facilitated
Figure 4	Vectorization + Content refinement	Radar chart labels are blurred when zoomed; numeric labels are overcrowded	Vectorize coordinates and labels; remove redundant numeric labels	Clarity is improved; interpretation difficulties are reduced
Figure 5	Vectorization + Content refinement	Central data labels in panel a are blurred when zoomed; the lower-right text label is unclear; color contrast in panel c is insufficient	Vectorize the data labels in panel a; change the lower-right text to “optimized property”; adjust panel c colors so that Young’s modulus (E), average pore size (APS), porosity ($1-V$), and surface-to-volume S/V are more clearly distinguished from time (T)	Label clarity and color contrast are enhanced; interpretation difficulties are reduced
Figure 6	Vectorization + Content refinement	Data labels in panels b and d are blurred when zoomed; arrows are unclear	Vectorize the right side of panel b and the middle of panel d; remove unclear arrows	Annotation accuracy is improved; ambiguity is reduced
Figure 7	Vectorization + Content refinement	Labels on the left of panel b are blurred when zoomed; the box plots on the right of panel b are overcrowded; terminology in panel d is unclear; panel e is redundant with panel b; the time label in panel e is unclear	Vectorize the left-side labels in panel b; Vectorize the labels in panel b and remove redundant elements; replace porosity with $1-V$ in panel d; delete redundant content in panel e, revise the time label to show the total infiltration time, and indicate in the legend that the snapshots correspond to $t = 1.90$ s.	Figure elements are simplified; redundancy is reduced; readability is improved

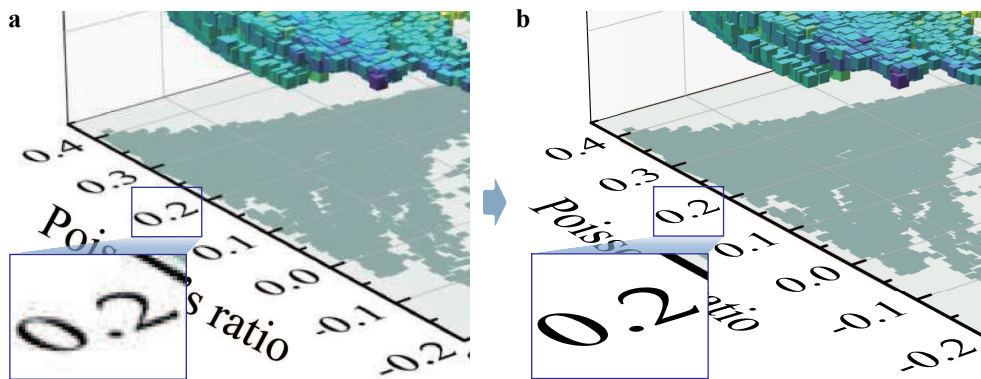


Figure R6: **Comparison of the original and vectorized images with coordinate scales.** **a** The original raster image and its magnified region. **b** The vectorized image and corresponding magnified view, showing improved clarity and scalability of the coordinate axes and labels

- **#4 Comment #4:** There are too many complex multi-panel figures. To be fair these figures are executed extremely well, and are visually pleasing, but many features become too small to see, making interpretation of results difficult at times. A more straightforward quantitative presentation of results may help make direct comparisons, and remove any obfuscation.

Response: We thank the reviewer for the constructive comments. All figures and tables have been revised to improve readability and intuitiveness while maintaining visual rigor.

The revisions are guided by three core principles:

- Simplifying complex visual layouts and removing redundant elements to enhance readability;
- Ensuring accuracy and clarity, including label precision, arrow indications, and logical sequencing avoiding misinterpretation caused by resolution limits or improper ordering;
- Enhancing the directness and transparency of information presentation by refining textual descriptions, improving color contrast, and supplementing percentage-based tables.

A review of all figures and tables (Table R1–R2) identified issues such as blurred labels, over-crowded layouts, unclear arrows, dense labeling, imprecise text, low color contrast, redundant elements, and tables showing only percentages. Improvements have been implemented accordingly. It should be noted that “**Figure X**” refers to figures in the main text, “**Figure SX**” to those in supplementary materials, and “**Figure RX**” to those provided in response text.

(1) Enhanced clarity of coordinate labels

All coordinate labels have been redrawn as high-resolution vector graphics to ensure sharpness and legibility. Figures 1 and 2 previously pixelated when zoomed are now presented in vector format with markedly improved clarity, as illustrated in Figure R6.

(2) Optimization of multi-panel layouts for improved readability

For multi-panel figures with dense information (e.g., Figure R7a–f, corresponding to Figure 3c–h in the main text), we have made the following adjustments:

- Panels c–h are removed and correspond to Figure R7a–f in the response.
- Panels c–d are replaced with simplified statistical charts that highlight key trends and improve readability (Figure R7g–h).

In Figure 7, further refinements are implemented:

Table R2: Detailed revisions of figures in supplementary materials.

Figure/ Table	Change type	Issue before revision	Modification applied	Expected improvement
Supp. Fig. S1	Vectorization	Panel a labels are blurred when zoomed	Vectorize and improve the labels in panel a	Numeric clarity is ensured
Supp. Fig. S3	Correcting image order	Images labeled 6–10 and 11–15 are misplaced	Correct the order to the proper sequence	Misleading information is avoided
Supp. Fig. S4	Vectorization	The lower-right coordinate plot is unclear	Modify and optimize the coordinate plot	The accuracy and intuitiveness of axis representation are improved
Supp. Fig. S9–S10	Vectorization + Content refinement	Data labels are blurred when zoomed; numeric labels are overcrowded	Vectorize all coordinates and labels; remove redundant numeric labels	Clarity is improved
Supp. Fig. S11	Image replacement	The upper-left of panel a uses an AI-generated image, which is of low reliability	Replace it with a non-AI, materials-based schematic	Academic rigor is improved
Supp. Fig. S12–S15	Vectorization + Content refinement	Data labels are blurred when zoomed; terminology is inconsistent	Vectorize all coordinates and labels; unify <i>Porosity</i> to $1-V$	Terminology is kept consistent and readability is improved
Supp. Fig. S16	Arrow style adjustment	Some arrows are misaligned	Replace arrows with simpler and standardized styles	Visual consistency and aesthetics are enhanced
Supp. Tables S4, S5	Numerical update	Only percentages are shown; actual values are missing	Add actual numerical values alongside percentages	Results are presented more transparently and intuitively

- The left-side data labels of panel b are vectorized to enhance clarity when zoomed in;
- Redundant elements in the right-side boxplots of panel b are removed (Figure R8a-b).
- The term *porosity* in panel d is replaced with the more intuitive $1-V$.
- Redundant content in panel e, which duplicates panel b, is deleted to avoid unnecessary repetition. The time label is revised to show the total infiltration time, and the legend is updated to indicate that the snapshots correspond to $t = 1.90$ s (Figure R8c-d).

(3) Improved color contrast and visual distinction

In the rose plot on the right side of Figure 5c (Figure R9a), insufficient color contrast hampers clear differentiation. We have therefore adjusted the color mapping scheme so that Young’s modulus (E), average pore size (APS), porosity ($1-V$), surface-to-volume S/V , and time (T) are more clearly distinguishable (Figure R9b). This refinement enhances the intuitiveness and interpretability of multivariate comparisons.

(4) Standardization of text and terminology

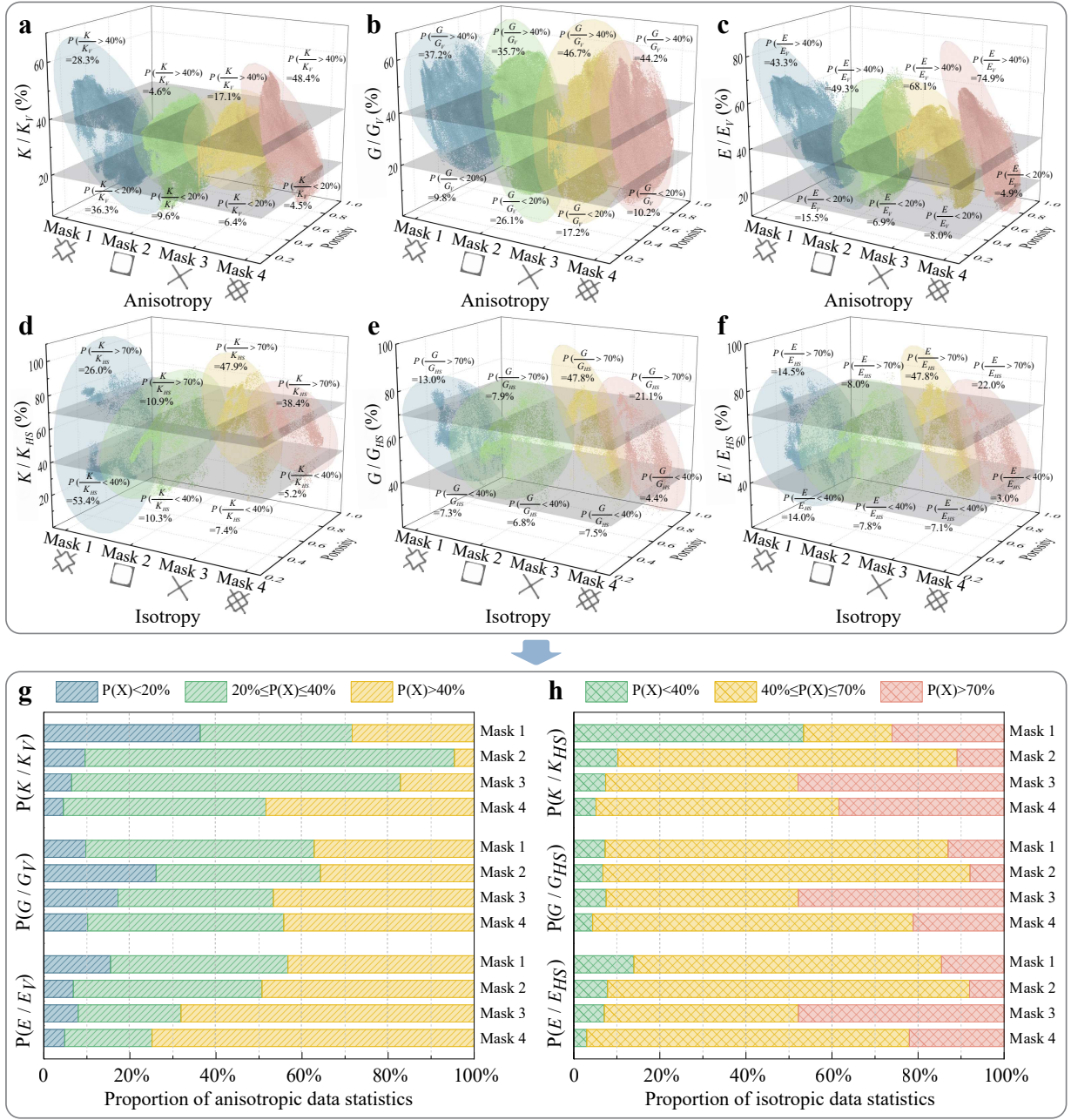


Figure R7: Figure 3c–h in the main text is changed to c–d for before-and-after comparison.

Inconsistencies in terminology and textual descriptions across figures have been corrected. For example, in Figure 7 and Supplementary Figures S12–S15, the term *porosity* has been standardized to the more intuitive $1-V$, and in Figure 1c, the phrase *strong connection* has been revised to the more accurate *well connection*. These revisions ensure greater precision and consistency, reducing potential misinterpretations by readers.

(5) Refinement of supplementary figures

Supplementary Figures S1, S3, S4, and S9–S15 have undergone vectorization and detailed content refinements. For example, in Supplementary Figure S4, the axis scaling and label clarity of the lower-right coordinate plot have been optimized; in Supplementary Figure S3, the misplacement of images labeled 6–10 and 11–15 has been corrected; in Supplementary Figure S11, the AI-

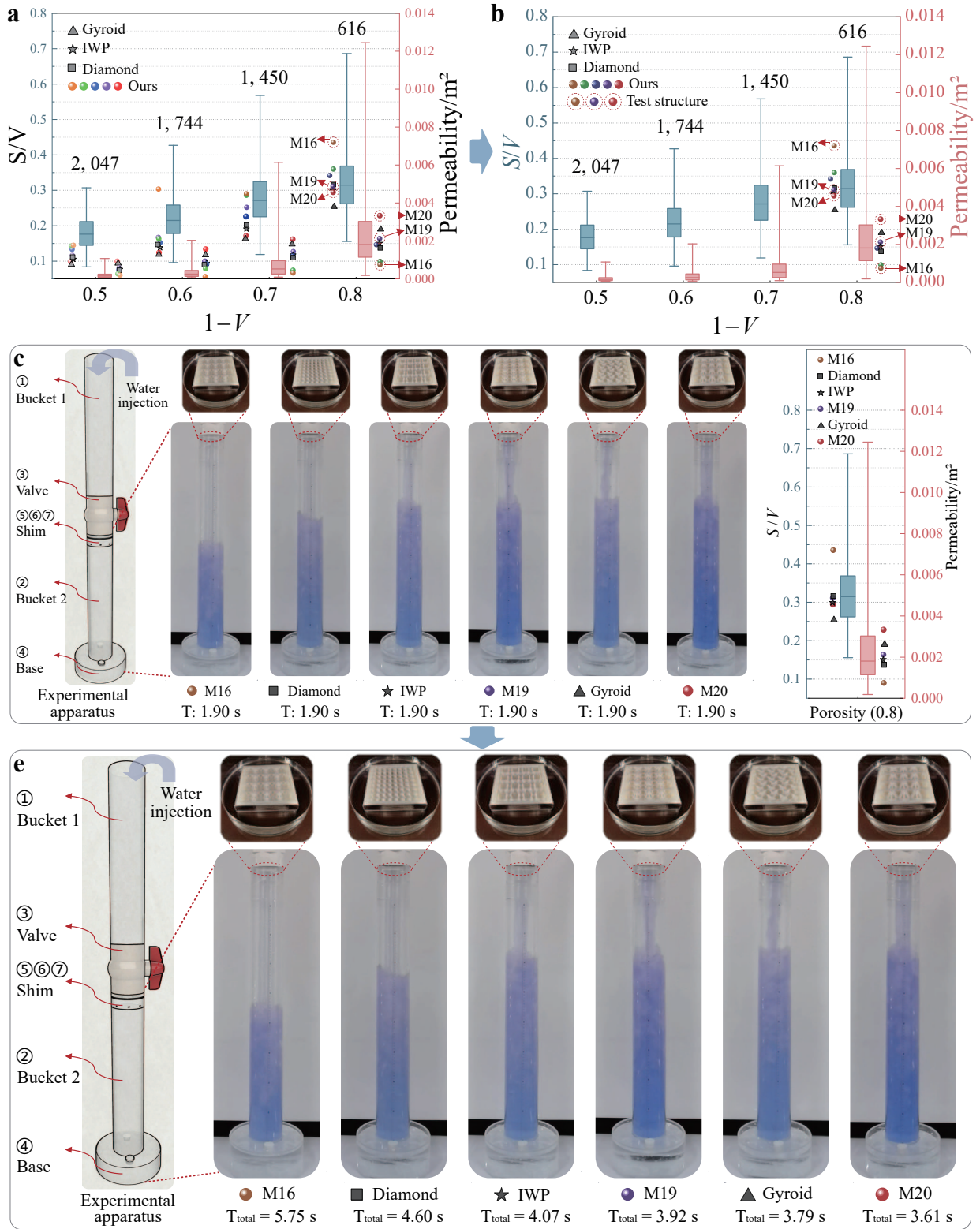


Figure R8: Comparison of modifications to Figure 7 in the main text. **a** The original Figure 7b statistical plot. **b** The statistical plot after removing redundant information. **c** The original Figure 7e. **d** The updated plot after removing duplicated information.

generated schematic has been replaced with a non-AI-generated illustration conveying the same meaning but with higher reliability (Figure S10a); and in Supplementary Figure S16, arrow styles

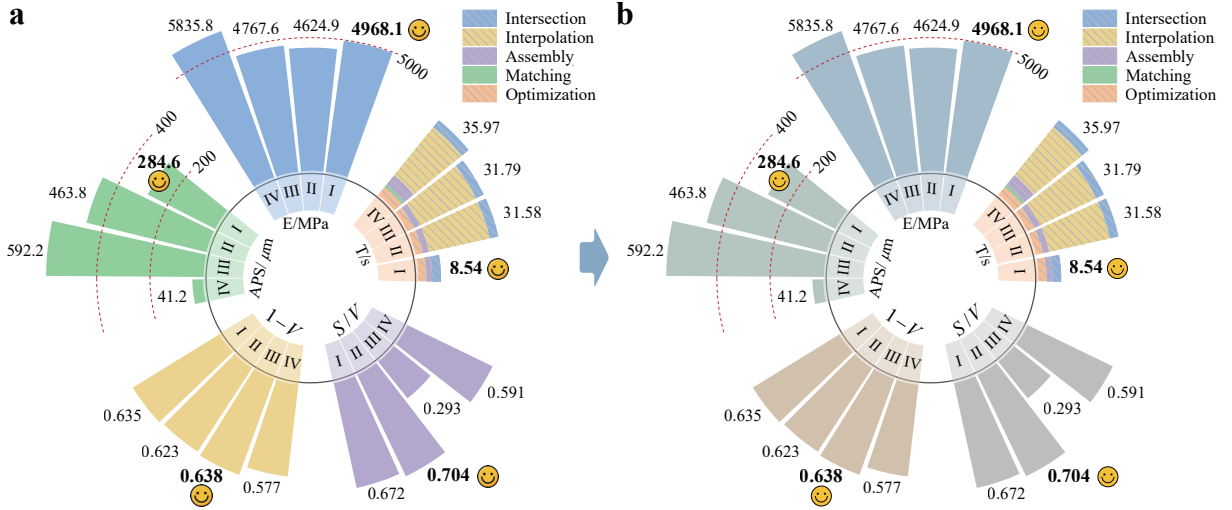


Figure R9: **Comparison of the right-side statistical plots in Figure 5c of the main text.** **a** The original plot. **b** The plot with the updated color scheme.

have been redesigned to improve directional clarity. These refinements substantially improve the readability, accuracy, and overall effectiveness of the supplementary materials.

(6) Increased quantitative transparency

In Supplementary Tables S4 and S5, actual numerical values have been added alongside percentages, enabling readers to make precise comparisons without additional calculations. This enhancement not only facilitates deeper understanding of data distributions but also strengthens the verifiability and transparency of our conclusions.

• Reviewer #4 Comment #5: I am also curious about the choice of boundary masks.

- Can the authors provide more detail on how they were selected and enforced.
- What order connectivity is enforced at the boundary, geometric, tangent, continuous (C^0 , C^1 , C^2)?
- Can the authors comment more about the impact of the boundary mask on properties?
- Is it useful to construct 100,000 internally different iterations of 4 boundary configurations, or would more performance gains be made by constructing 1000 different boundary masks with 100 internal designs each?
- The re-entrant boundary mask showing such a wide spread in Poisson's ratio tells that this initial constraint is significantly blocking/unlocking property spaces. Until the boundary conditions can be fully understood and modified where possible by machine design, human designs will often remain superior.

Response: We appreciate the reviewers' insightful comments and constructive suggestions. To ensure clarity and coherence, the response is organized into five key aspects:

1. Selection and implementation details of boundary masks;
2. Connectivity order at the boundaries;
3. Impact of boundary masks on performance;
4. Comparison of different dataset construction strategies;
5. Comparison between human and machine designs;

The following is a detailed explanation.

(1) Can the authors provide more details on how they were selected and enforced.

As illustrated in the main text, four boundary mask types (masks 1-4) are determined based on clustering, testing, and quality evaluation. The screening process is further clarified as follows.

* **Boundary mask source.**

The boundary data primarily originate from three sources: the 3D microstructure dataset [25], the 2D microstructure dataset [26], and user-designed boundaries, as shown in Figure S1a.

* **Clustering.**

We apply K-means clustering to the boundary masks. For microstructures with a low volume fraction (0.1–0.4), 15 representative cluster centers are extracted as candidate boundary mask patterns for 3D microstructure generation.

* **Quality evaluation.**

Two key metrics are considered: the proportion of open-cell structures and Poisson’s ratio coverage. Finally, the four boundaries are selected. Detailed information is shown in Supplementary Section 2, Figure S1.

(2) What order connectivity is enforced at the boundary, geometric, tangent, continuous (C^0 , C^1 , C^2)?

Our method enforces C^0 continuity, ensuring positional consistency at boundaries so that adjacent unit cells join seamlessly without gaps or overlaps. Regarding higher-order continuity, we fully agree with the reviewer on its importance. Achieving C^1 or C^2 continuity would enhance smoothness, stress transfer, and mechanical performance but this remains theoretically and computationally challenging. For example, C^1 and C^2 continuity require adding some additional smoothness constraints on material distribution during the structure generation process. In actual structure generation, it is difficult to ensure the strict satisfaction of these constraints, and exploring the property space of the structure under such constraints may require more prior theoretical knowledge to help narrow down the search space. In contrast, for the C^0 dataset, it only requires specifying the mask as a boundary condition in the diffusion model. This is easily achievable under current technical conditions, and we have demonstrated the effectiveness of the generated structures in experiments.

(3) Can the authors comment more about the impact of the boundary mask on properties?

To address this question, we first analyze the geometric features of the mask and the associated properties that may be influenced.

- **Geometric features of mask:** the volume fraction V_{mask} , the number of voids N_{void} , pore distribution, pore size, and connectivity.
- **Physical properties:** S/V , dataset similarity, isotropy, solid continuity, bicontinuity and mechanical performance.

To assess the impact of the boundary mask on the attributes of the constructed dataset, and following the suggestion in Question (4), we generated 100,000 samples comprising 1,000 boundaries, each producing 100 structures. The detailed construction procedure is provided in the [Appendix](#) in this reply.

Here, we discuss the influence of 1,000 masks with varying V_{mask} on the S/V , similarity, isotropy, and bicontinuity of the generated microstructure dataset.

- **Surface-to-volume S/V .** As shown in Figure R10a, S/V gradually decreases as V_{mask} increases.
- **Similarity.** As shown in Figure R10a, the similarity gradually increases as V_{mask} increases.
- **Bicontinuity.** As shown in Figure R10b, V_{mask} has little effect on the bicontinuous generation rate. However, the presence of small isolated pores within the mask or at its boundaries can cause a sharp decline in bicontinuity, even reducing the generation rate to zero.
- **Isotropy.** Isotropic microstructures are rarely generated when $V_{mask} > 0.7$ (Figure R10d-f).

Lower boundary volume fractions promote the generation of 3D bicontinuous open-cell structures with higher S/V , while reducing structural similarity and thereby enhancing microstructural diversity. Under these conditions, it also becomes easier to obtain isotropic bicontinuous open-cell structures, which is advantageous for achieving direction-independent mechanical performance.

Beyond the primary descriptors, we analyzed additional geometric features—including the number of voids N_{void} , pore spatial distribution, characteristic pore size, and topological connectivity—using descriptive and inferential statistics appropriate to the data. The aggregated results are reported in the Appendix. Across model specifications, effect sizes were small and, where present, did not survive standard multiple-comparison controls; accordingly, we refrain from asserting statistical significance. Although the dataset currently comprises approximately 100,000 samples, this scale remains insufficient for drawing universal conclusions. In future work, we will enlarge and diversify the dataset (e.g., by sampling broader geometry classes, manufacturing/process conditions, and boundary constraints) to enable more generalizable and statistically robust findings.

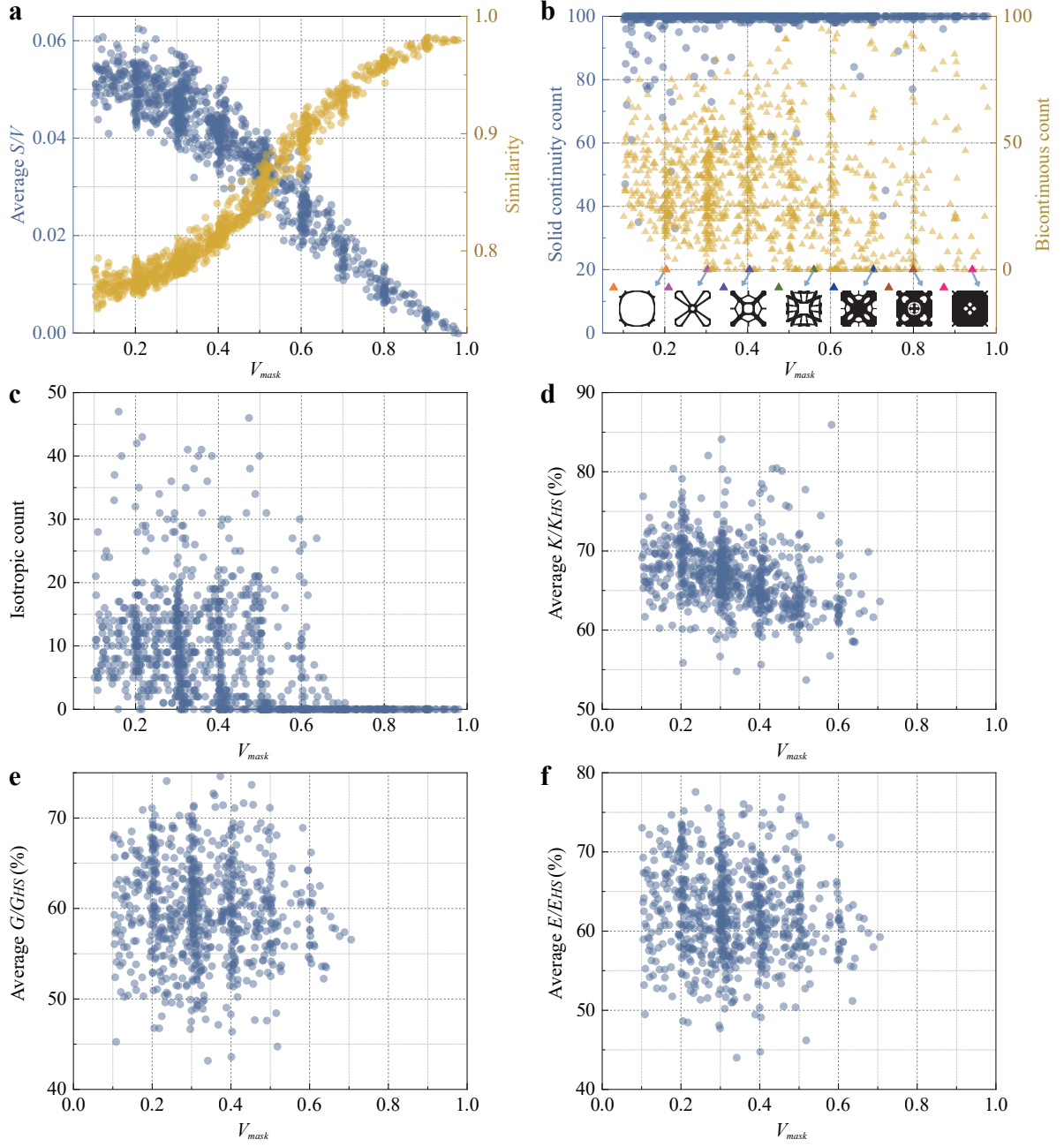


Figure R10: **Relationship between V_{mask} and structural characteristics.** **a** Average S/V and structural similarity. **b** Number of structures with a connected solid phase and bicontinuous open-cell structures. **c** Number of isotropic structures. **d-f** The average values of K/K_{HS} , G/G_{HS} , E/E_{HS} .

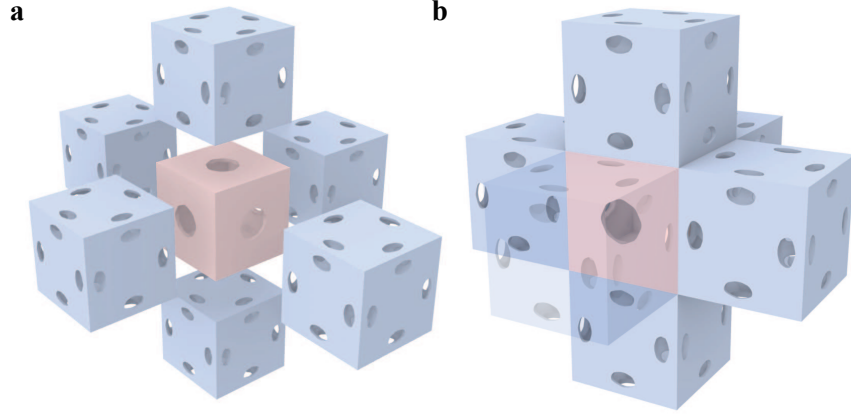


Figure R11: **Non-bicontinuous multiscale structure.** **a** The pink region is taken from structure 0289, and the blue region is taken from structure 0298. **b** After multiscale assembly, a closed cavity emerges inside the pink region, breaking the bicontinuity of the structure.

(4) Is it useful to construct 100,000 internally different iterations of 4 boundary configurations, or would more performance gains be made by constructing 1000 different boundary masks with 100 internal designs each?

We adopted four representative boundary configurations (Mask 1–Mask 4), generating approximately 100,000 microstructures per mask, with 106,445, 142,980, 75,350, and 79,580 internal realizations, respectively. This strategy ensures broad coverage of mechanical and topological properties, maintains boundary consistency and bicontinuity, and achieves substantial internal diversity.

In addition, we generated 100,000 samples from 1,075 boundaries (1,000 screened from 2D/3D microstructures and 75 manually designed), with each boundary mask producing 100 structures. The detailed construction procedure is provided in the Appendix of this reply.

It is important to note that the 100,000 microstructures generated by these two strategies are not directly comparable, for two main reasons.

- **Bicontinuity.** In our approach, 100,000 structures are generated under the same boundary mask and openings, thereby naturally forming bicontinuous open-cell architectures. However, the dataset generated from 1,000 different masks cannot be directly assembled into bicontinuous multiscale structures, which runs counter to the central objective of our study shown in Figure R11.
- **Manufacturing.** A dataset of 1,000 masks, each containing 100 structures, is difficult to fabricate directly. For specific manufacturing details, please refer to “Reviewer #3, Comment #1”.

(5) The re-entrant boundary mask showing such a wide spread in Poisson’s ratio tells that this initial constraint is significantly blocking/unlocking property spaces. Until the boundary conditions can be fully understood and modified where possible by machine design, human designs will often remain superior.

We sincerely appreciate the reviewer’s attention to the Poisson’s ratio range under the Mask 1 boundary condition and concur that the boundary effects are not yet fully understood. Although we have collected several hundred thousand data samples and performed preliminary analyses, our findings thus far only reveal certain emerging trends.

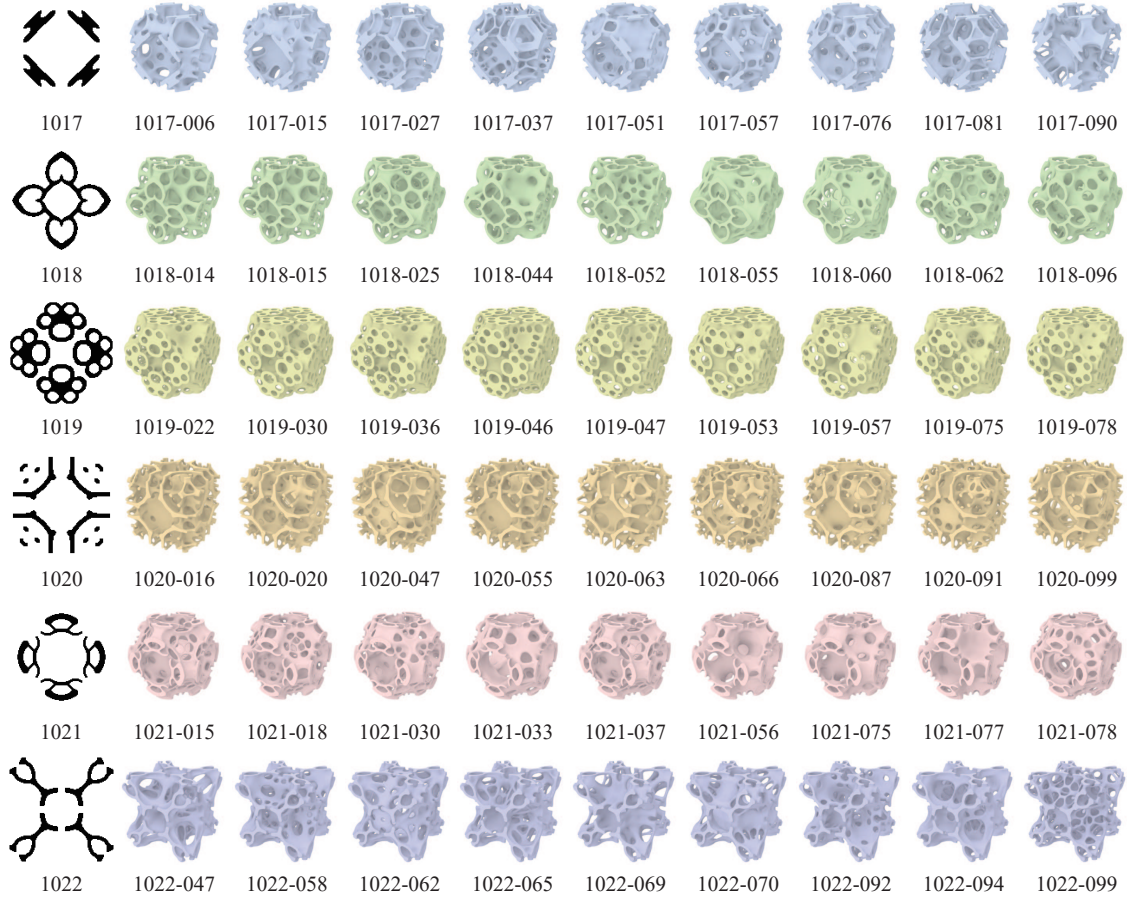


Figure R12: Customized boundaries and their corresponding structures guided by user preferences.

5.1 Difficulties in understanding the boundaries influence

We believe that fully elucidating the mechanisms by which boundaries influence 3D microstructural properties remains challenging. The primary difficulties lie in:

- Mask geometry involves numerous factors such as the number, size, and arrangement of holes, whose enumeration and interactions are difficult to analyze comprehensively.
- The analyzed data are inherently limited, and a key challenge remains how to efficiently traverse the structural design space.

We consider this an important direction for future work, where principal component analysis could be applied beginning with relatively simple parametric microstructures.

5.2 Human design exploration

Human design, guided by analytical reasoning or individual preferences, is able to explore non-traditional topologies (Figure R12), leading to innovative design solutions. In comparison, machines often struggle to effectively explore or cover such unconventional design spaces in the absence of tailored constraints or targeted training.

Appendix: Analysis of the test results for different masks

This section examines the sources of the masks used in our experiments and systematically analyzes their geometric features, 3D structural properties, and the relationships among them. Figure R13 shows a flowchart of the workflow—from sourcing and selection criteria through construction of the test masks, optimization formulations, descriptive statistics, and presentation of results.

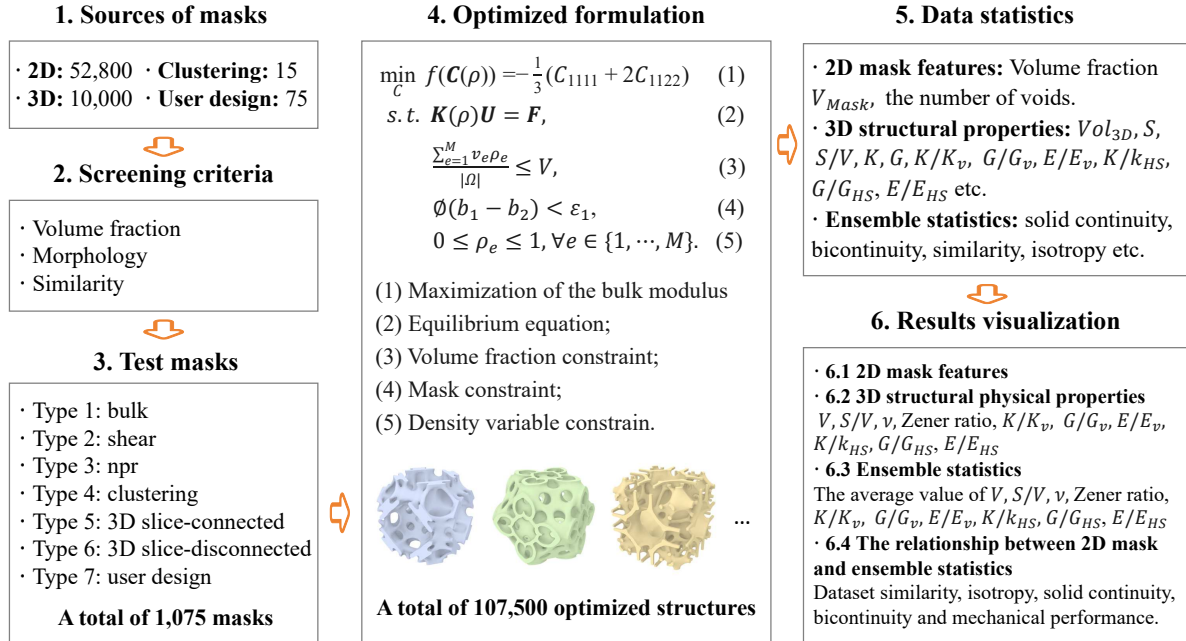


Figure R13: Flowchart of the analysis workflow.

Next, we will demonstrate the approach for each step.

1. Sources of masks

To ensure representativeness and diversity in the selected masks, the mask data are drawn from four distinct sources: a dataset comprising 52,800 2D topological structures [26], a dataset of 10,000 3D structural configurations [25], representative samples obtained through clustering analysis on the 2D data, and user-defined mask designs.

2. Screening criteria

The following criteria are employed to construct the final test mask ensemble:

- **Volume fraction constraint:** 0.1-0.95;
- **Morphological constraint:** Aperture size and member thickness constraints are applied, and morphological dilation ($\oplus$) and erosion ($\ominus$) operations are used to adjust the boundary geometry:

$$B_{\text{dilated}} = B \oplus S, \quad B_{\text{eroded}} = B \ominus S \quad (12)$$

where B is the binary matrix of the structure, and S is the structural element;

- **Topological similarity analysis:** Intersection-over-union (IoU) [26] is used to quantify similarity between structures and remove redundant boundaries.

3. Test masks

After the aforementioned screening procedure, a total of 1,075 representative masks are retained and categorized into seven distinct types as follows:

Type 1 (T1): bulk feature masks (ID 0001-0300)

Three hundred masks are selected from a dataset of 17,600 topology-optimized 2D structures (optimized for maximum bulk modulus), and the selection strictly follows the predefined screening criteria.

Type 2 (T2): shear feature masks (ID 0301-0520)

From another set of 17,600 2D structures optimized for maximum shear modulus within the same dataset, 220 representative masks are extracted through the screening process.

Type 3 (T3): negative Poisson’s ratio feature masks (ID 0521-0685)

A total of 165 masks are selected from 17,600 2D structures designed to achieve negative Poisson’s ratio, based on the established filtering criteria.

Type 4 (T4): cluster centroid masks (ID 0686–0700)

K-means clustering is applied to the 2D structural dataset, and the centroid structures of the resulting 15 clusters are included as representative masks.

Type 5 (T5): 3D Sliced masks – Connected Topologies (ID 0701-0900)

Surface slices are extracted from the 10,000 3D structural dataset. After applying the screening criteria, 200 fully connected masks are retained.

Type 6 (T6): 3D Sliced masks – Disconnected Topologies (ID 0901-1000)

Using the same slicing and filtering approach, 100 masks with disconnected structural features are selected to represent non-contiguous geometries.

Type 7 (T7): user-designed masks (ID 1001-1075)

An additional 75 masks are manually designed to further enrich the test suite:

- IDs 1001–1016: Derived from localized modifications of established canonical structures;
- IDs 1018–1022: Incorporate complex geometries or customized designs;
- IDs 1023–1075: Specifically constructed for controlled comparative experiments to evaluate the influence of particular mask configurations on mechanical performance.

The geometric shapes and numbering distribution of the various masks are shown in Figures R14-R18.

4. Optimized formulation

Next, for each boundary, we generate 100 distinct structures. For each structure, we apply the optimization framework described in the following formulation (Supplementary Equation 18):

$$\begin{aligned}
\min_{\boldsymbol{\rho}} \quad & f(\mathbf{C}(\boldsymbol{\rho})) = -\frac{1}{3}(C_{1111} + 2C_{1122}) \\
s.t. \quad & \mathbf{K}(\boldsymbol{\rho})\mathbf{U} = \mathbf{F}, \\
& \frac{\sum_{e=1}^M v_e \rho_e}{|\Omega|} \leq V, \\
& \phi(b_1 - b_2) < \epsilon, \\
& 0 \leq \rho_e \leq 1, \forall e = 1, \dots, M.
\end{aligned} \tag{13}$$

Here, the volume fraction constraint V is set to 0.2, and the number of iterations is 2000. Using this optimization model, a total of 107,500 structures are generated.

5. Data statistics

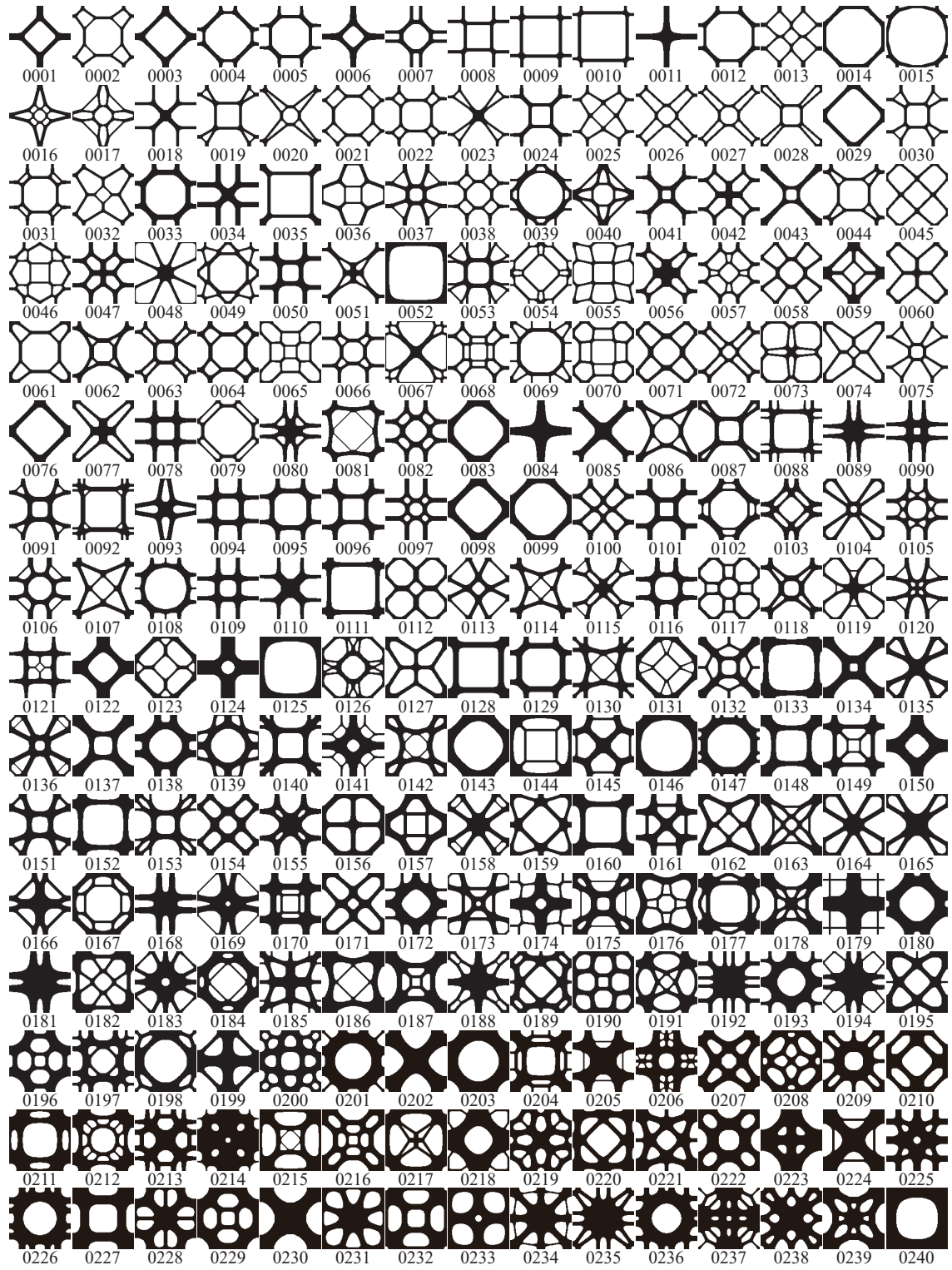


Figure R14: Identification of 2D boundary types with assigned identifiers (IDs 0241-0480).

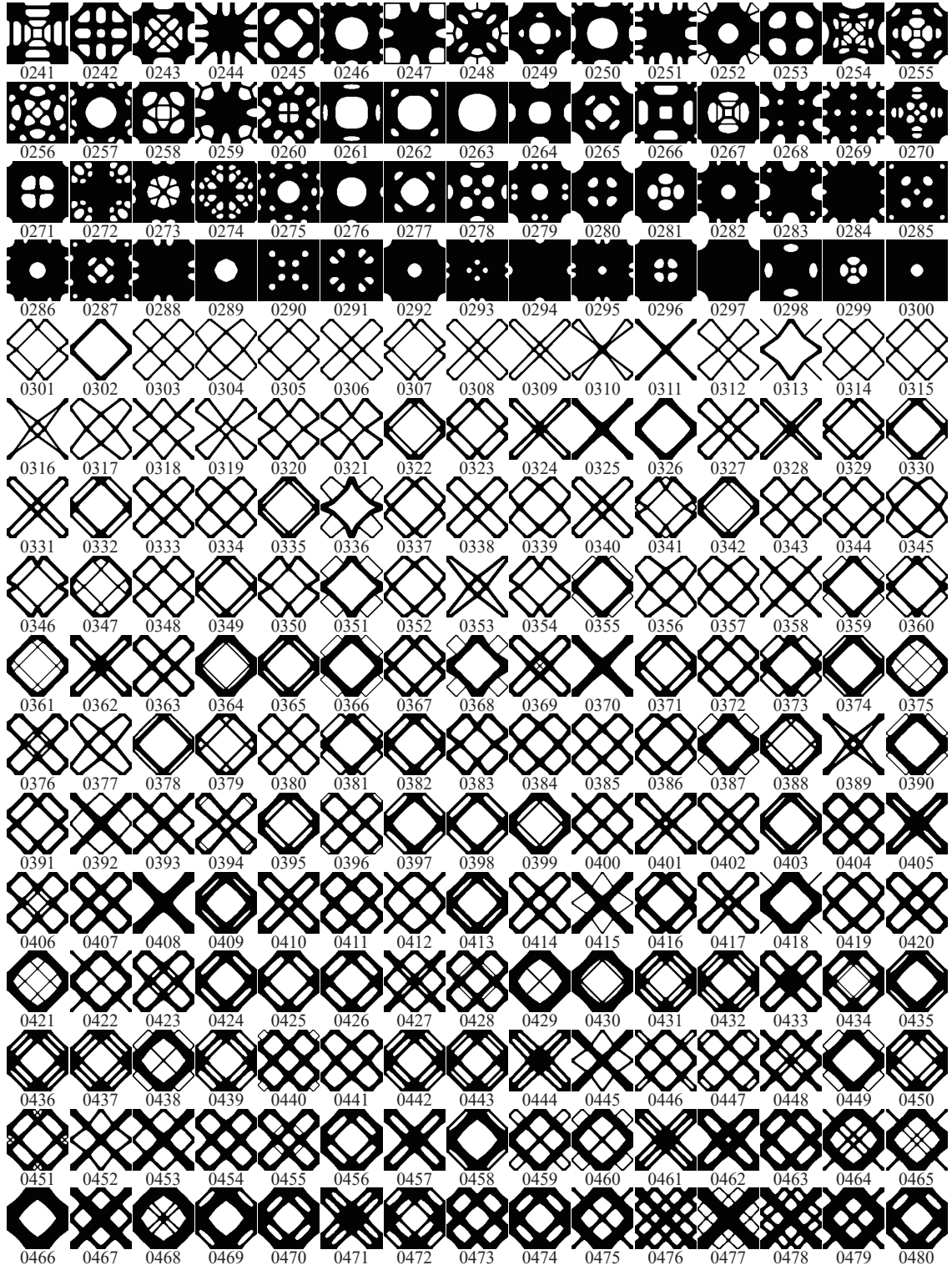


Figure R15: Identification of 2D boundary types with assigned identifiers (IDs 0241-0480).

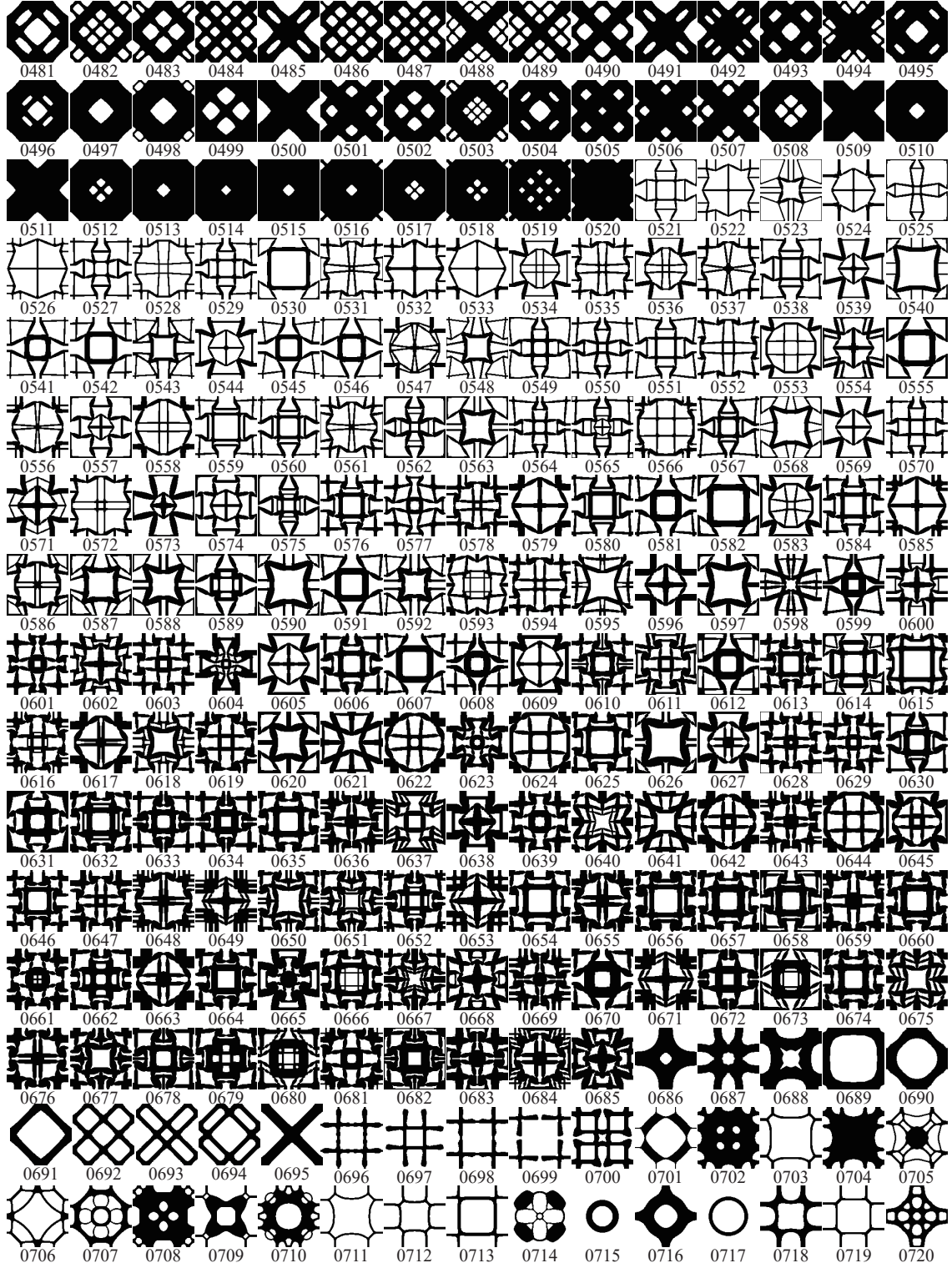


Figure R16: Identification of 2D boundary types with assigned identifiers (IDs 0481-0720).

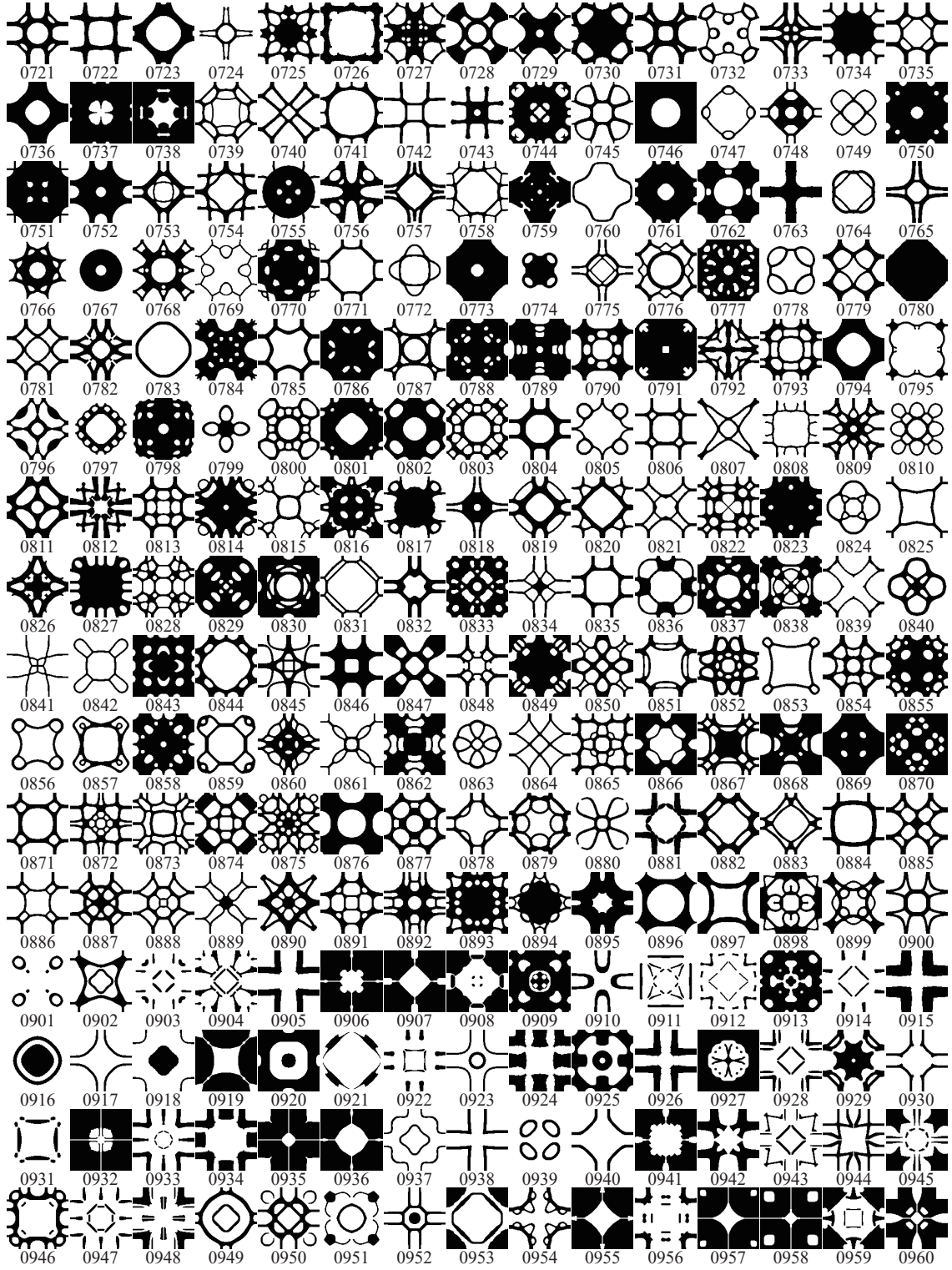


Figure R17: Identification of 2D boundary types with assigned identifiers (IDs 0721-0960).

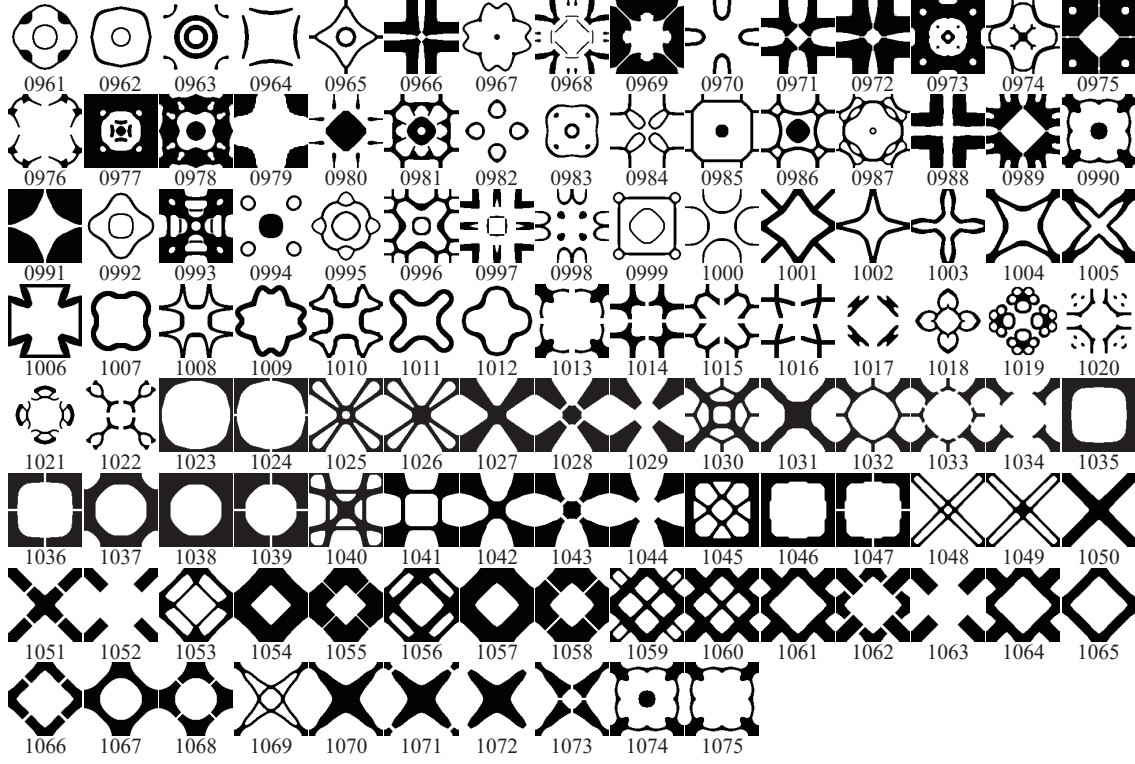


Figure R18: Identification of 2D boundary types with assigned identifiers (IDs 0961-1075).

To systematically evaluate the geometric and mechanical characteristics of the generated structures, statistical analysis is conducted at the following three levels.

5.1 2D Mask Features

For each 2D mask, the following geometric features are extracted:

- Mask volume fraction V_{mask} ;
- Number of voids, used to characterize topological complexity.

5.2 3D Structural Properties

For each optimized 3D structure, the following physical and geometric properties are computed:

- All independent components of the elastic tensor C ;
- Actual volume fraction V ;
- Surface area S and surface-to-volume ratio S/V ;
- Poisson's ratio ν and Zener ratio Z ;
- Bulk modulus K , shear modulus G , and Young's modulus E ;
- Normalized performance metrics relative to the Voigt homogenization upper bounds: K/K_v , G/G_v , E/E_v ;
- Normalized performance metrics relative to the Hashin-Shtrikman upper bounds: K/K_{HS} , G/G_{HS} , E/E_{HS} ;
- Detection results for solid connectivity and bicontinuity of the structure.

5.3 Ensemble Statistics

For each group of 100 optimized structures corresponding to a given mask type, ensemble-level statistical analysis is performed, including:

- Number of structures with connected solid phases;
- Number of structures exhibiting bicontinuous topology;
- Statistical distributions of key performance indicators across the ensemble, including mean, maximum, and minimum values of V , S , S/V , v , Z , as well as K/K_v , G/G_v , E/E_v , K/K_{HS} , G/G_{HS} , and E/E_{HS} ;
- Topological similarity among structures, quantified using metrics such as Intersection over Union (IoU) [26].

6. Visualization of results

6.1 2D Mask Features

In this subsection, we analyze the geometric features of different mask types, focusing on the volume fraction V_{mask} and the number of voids N_{void} . As shown in Figure R19a, the V_{mask} values of T1 to T3 exhibit an increasing trend. Regarding N_{void} , T3 and T5 display a wide distribution, ranging from a few to as many as 44. For the other types, N_{void} generally does not exceed 30 (Figure R19b).

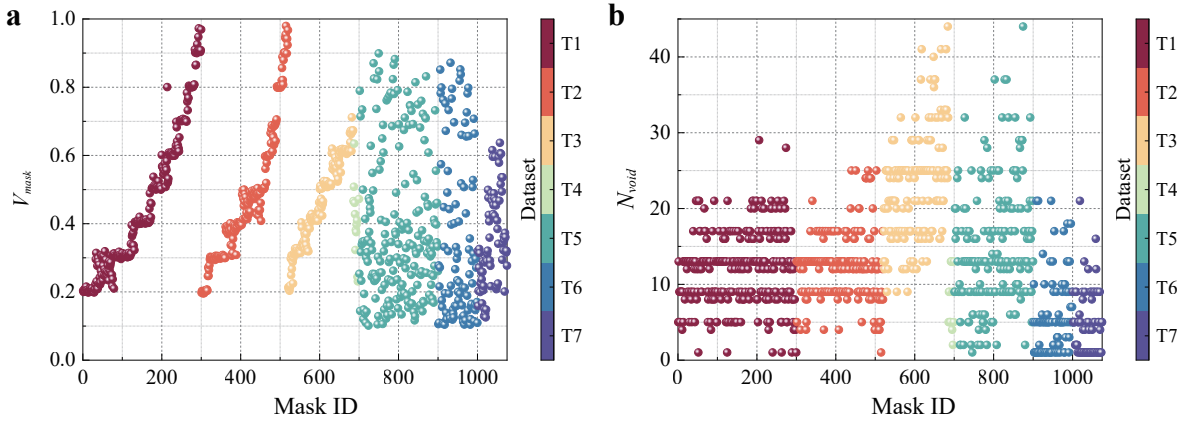


Figure R19: **Geometric features of different masks.** **a** Relationship between mask ID and V_{mask} for categories T1–T7. **b** Relationship between mask ID and N_{void} for categories T1–T7.

6.2 3D structural physical properties

We conduct a statistical analysis of the physical properties of 107,500 microstructures—100 generated from each of 1,075 distinct masks—including V , S/V , v , Z , K/K_v , G/G_v , E/E_v , K/K_{HS} , G/G_{HS} , E/E_{HS} .

As shown in Figures R20a, for certain T3 masks and some T1 masks, the optimization model imposes a volume fraction constraint of no more than 0.2, yet the generated structures still yield actual volume fractions greater than 0.2. Representative examples are provided in Figure R21.

The statistical results in Figures R20b-d indicate that as the mask type progresses from T1 to T3—with increasing volume fraction—the distributions of S/V , v , and Z gradually narrow and shift toward lower values.

Figures R22a-f present the ratio-based mechanical properties of microstructures generated by different masks, including K/K_v , G/G_v , E/E_v , K/K_{HS} , G/G_{HS} and E/E_{HS} .

6.3 Ensemble statistics

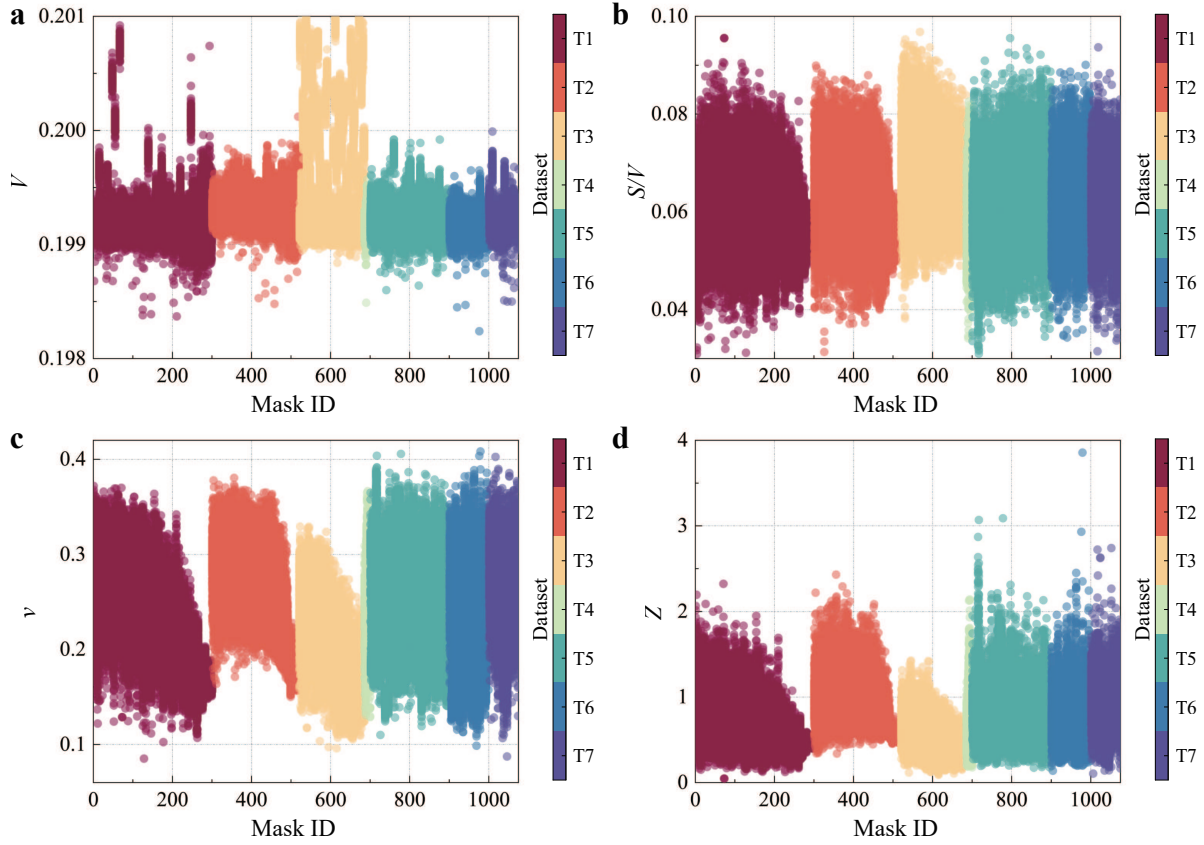


Figure R20: Statistical properties of all generated microstructures, including V , S/V , v , and Z .

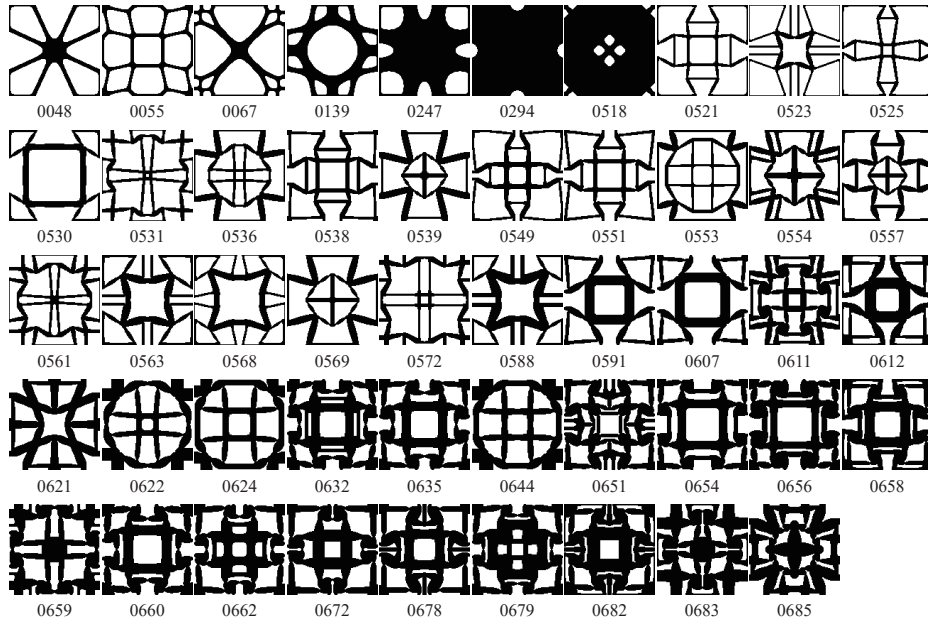


Figure R21: Representative cases of masks that partially violate the $V \leq 0.2$ constraint during optimization.

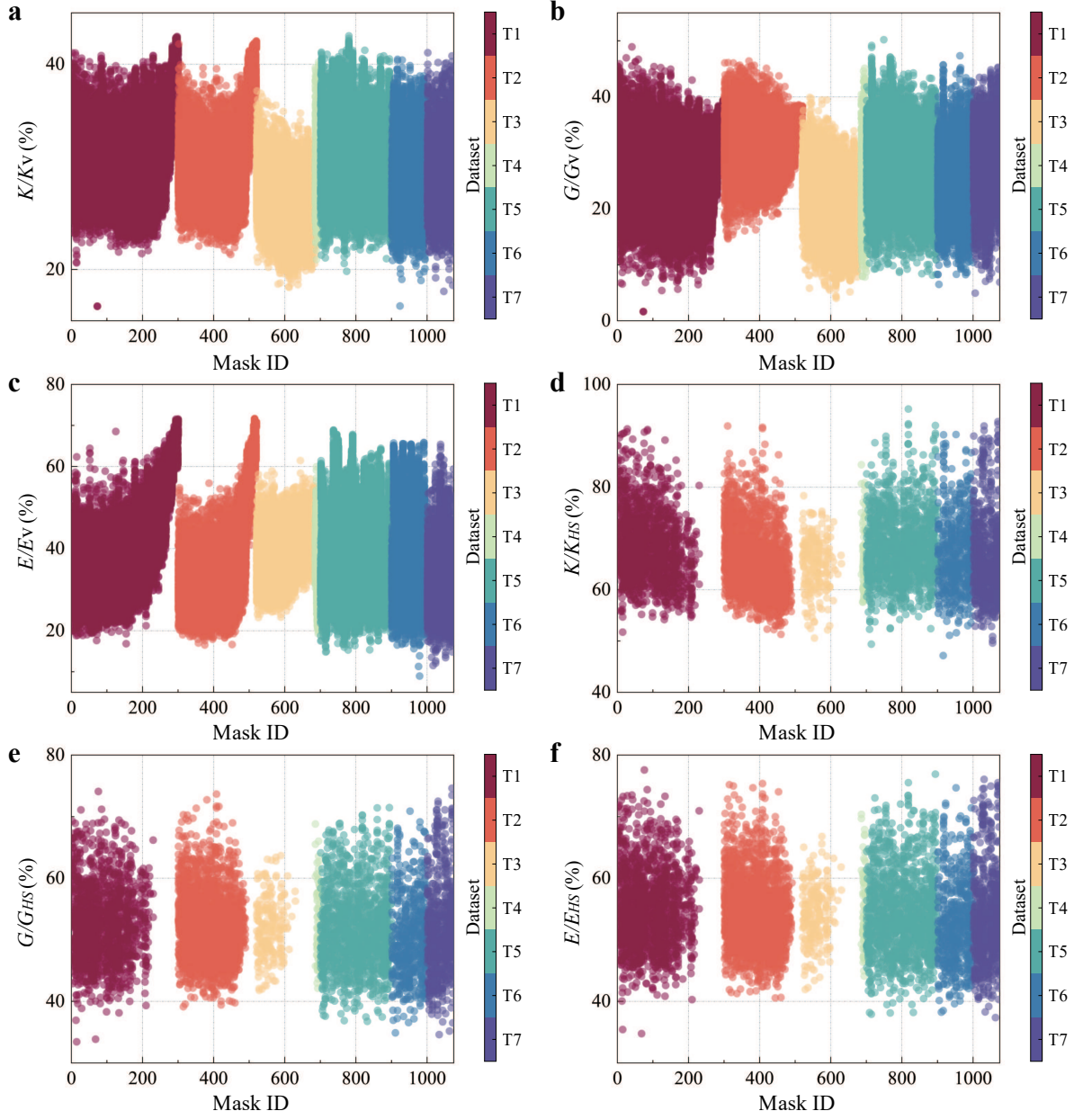


Figure R22: Statistical properties of all generated microstructures: K/K_v , G/G_v , E/E_v , K/K_{HS} , G/G_{HS} , E/E_{HS} .

Intra-group statistics are performed on the 100 microstructures generated by each mask. We analyze structural features such as the counts of solid connectivity and bicontinuity, as well as group-averaged values of V , S/V , v , Z , K/K_v , G/G_v , E/E_v , K/K_{HS} , G/G_{HS} , and E/E_{HS} . In addition, we evaluate the geometric similarity among the 100 structures within each group.

Figures R23a–b show the numbers of connected solid components and bicontinuous open-cell structures across different masks. For T6 masks, numerous disconnected cases are observed, with representative examples shown in Figure R24.

The trends in Figures R23c–f are consistent with those in Figures R20a–d, suggesting that group-averaged properties effectively capture the mechanical behavior differences across mask types and are thus representative. Figure R25 further presents the average structural similarity within each group. From T1 to T3 masks, similarity increases with mask ID, indicating that V_{mask} significantly influences topological consistency—higher volume fractions lead to more reproducible and geometrically similar outcomes. Figure R25 also compares the elastic properties across different mask groups, including K/K_v , G/G_v , E/E_v , K/K_{HS} , G/G_{HS} , and E/E_{HS} .

6.4 The relationship between 2D mask and ensemble statistics

To investigate the influence of mask geometry on microstructure generation, statistical analyses are performed on key metrics, including dataset similarity, isotropy count, solid-phase connectivity, bicontinuity, and mechanical performance.

6.4.1 Mask volume fraction (V_{mask})

As shown in Figure R10a, V_{mask} exhibits a strong negative correlation with S/V and a positive correlation with inter-group similarity. Figure R10b presents the statistical relationship between V_{mask} and the counts of solid connectivity and bicontinuity. For several masks, the generation rate of bicontinuous open-cell structures is zero (Figure R27).

Figure R10c shows the count of isotropic microstructures generated as a function of V_{mask} . The results indicate that when V_{mask} exceeds 0.7, isotropic microstructures are rarely generated.

Figures R10d–f illustrate the relationship between V_{mask} and the ensemble-averaged K/K_v , G/G_v , and E/E_v . Although emerging trends are observed, the underlying relationship requires further investigation.

6.4.2 Number of voids (N_{void})

Figure R28a shows that N_{void} has little influence on solid-phase connectivity, whereas the geometric configuration of the mask plays a dominant role. For instance, isolated features substantially reduce the likelihood of generating singly connected structures. In contrast, removing these isolated elements markedly improves connectivity, with a structural generation success rate of at least 99% (Figure R29a).

The bicontinuous generation rate, however, is strongly affected by N_{void} . As the void count increases, the rate generally decreases in a non-linear manner (Figure R28b), suggesting that other geometric factors also contribute to bicontinuous architecture formation.

To further examine this effect, masks with zero bicontinuous generation rate were selected for targeted design optimization (orange masks in Figure R27). Figure R29b shows representative examples before and after pore filling (regions enclosed by red dashed circles), demonstrating a significant increase in bicontinuous count; similar improvements are observed in other cases. Furthermore, by reducing N_{void} in addition to pore filling, the bicontinuous generation rate increases further (Figure R29b).

6.4.3 Effect of open masks on stiffness

To further enhance the bicontinuous generation rate, openings are introduced into previously enclosed masks, inspired by perforation designs in 3D structures [27]. As shown in Figure R30a, applying perforations in design transitions such as 1023 $\rightarrow$ 1024 and 1032 $\rightarrow$ 1033 significantly improved the

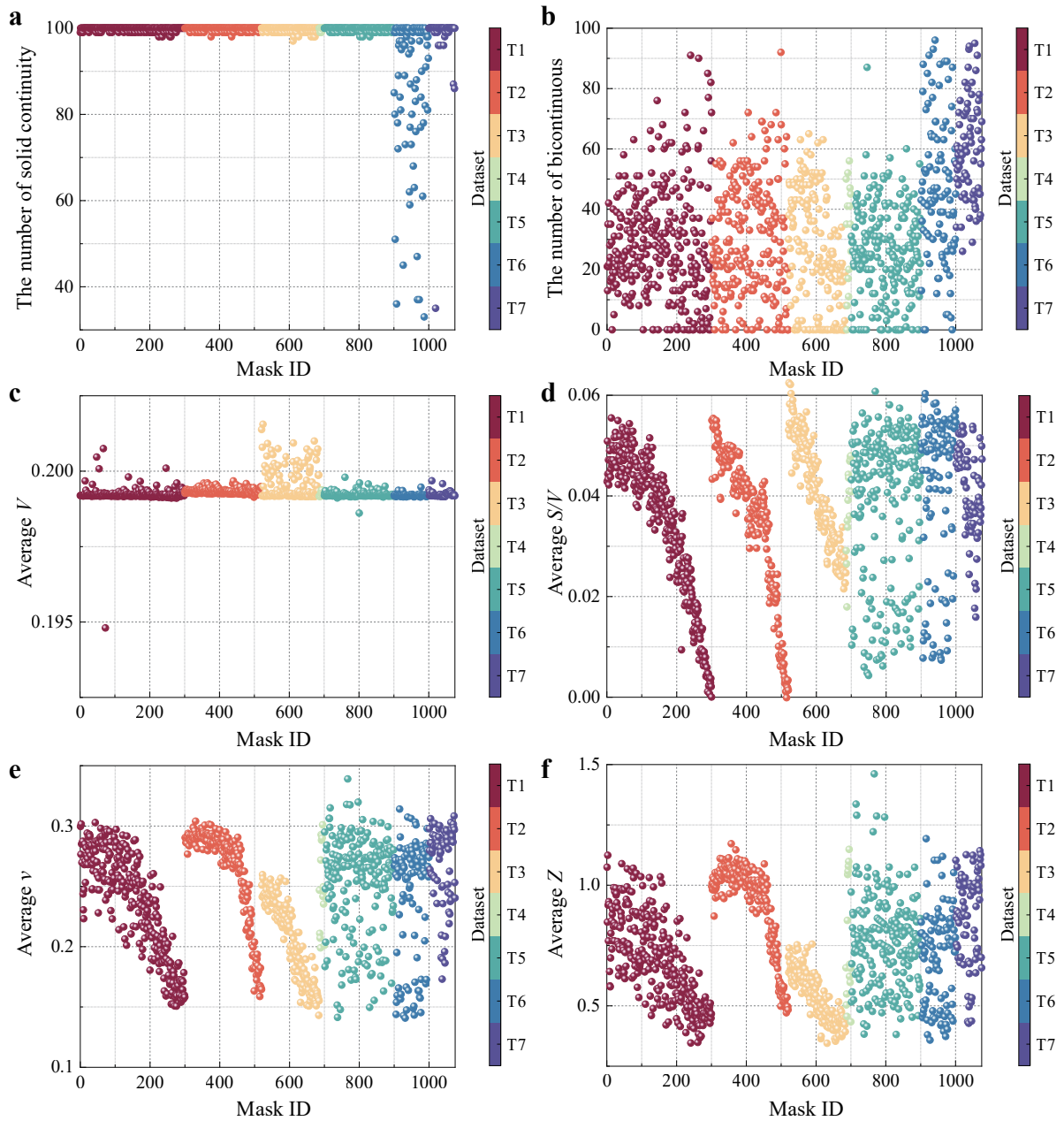


Figure R23: Inter-group statistical results, including the counts of solid connectivity and bicontinuity, and the averages of V , S/V , ν , and Z .

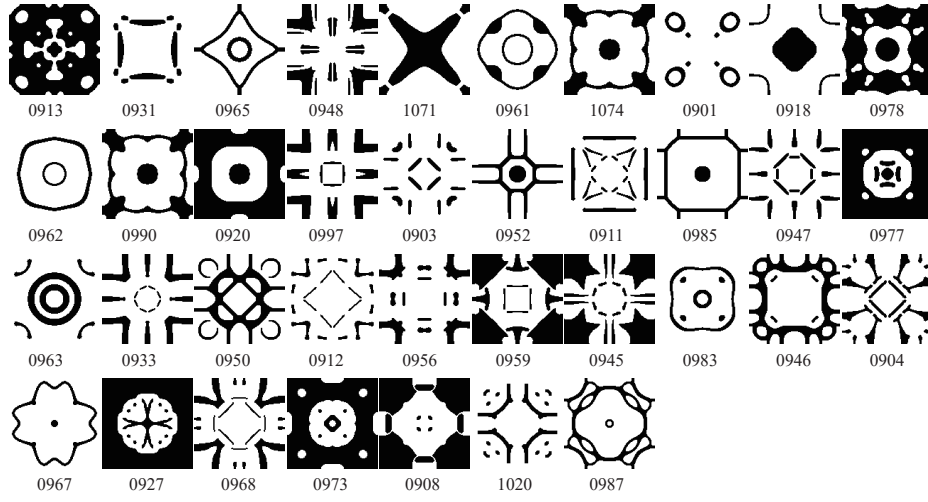


Figure R24: Masks with low solid connectivity (solid connectivity count < 10).

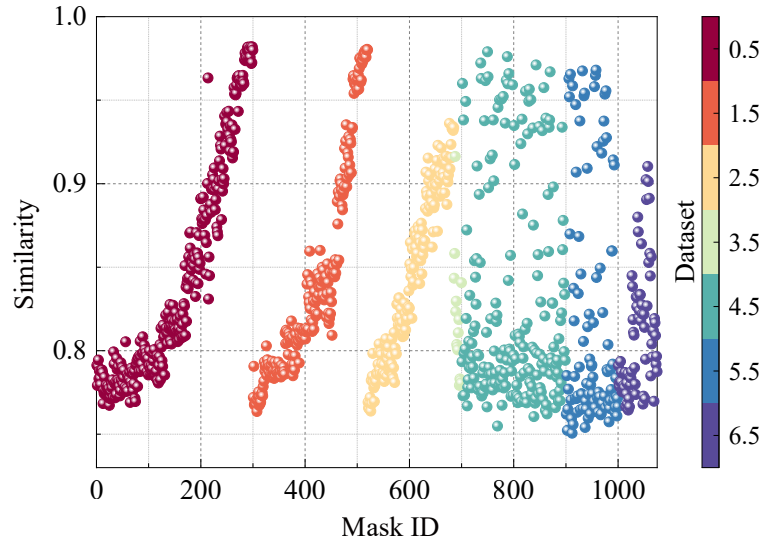


Figure R25: Inter-group Similarity Statistic.

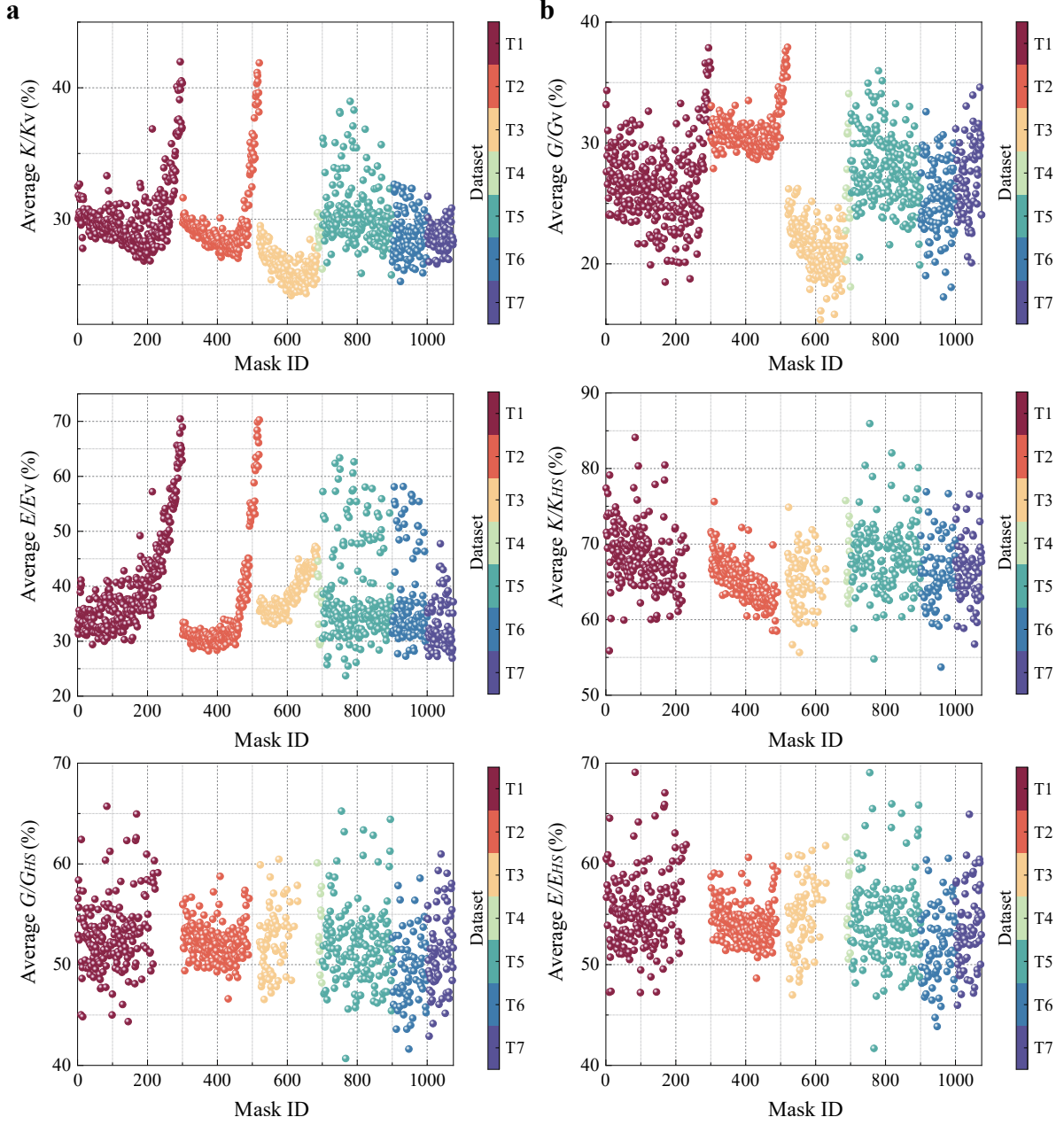


Figure R26: Statistical comparison of elastic properties across mask groups: K/K_v , G/G_v , E/E_v , K/K_{HS} , G/G_{HS} , and E/E_{HS} .

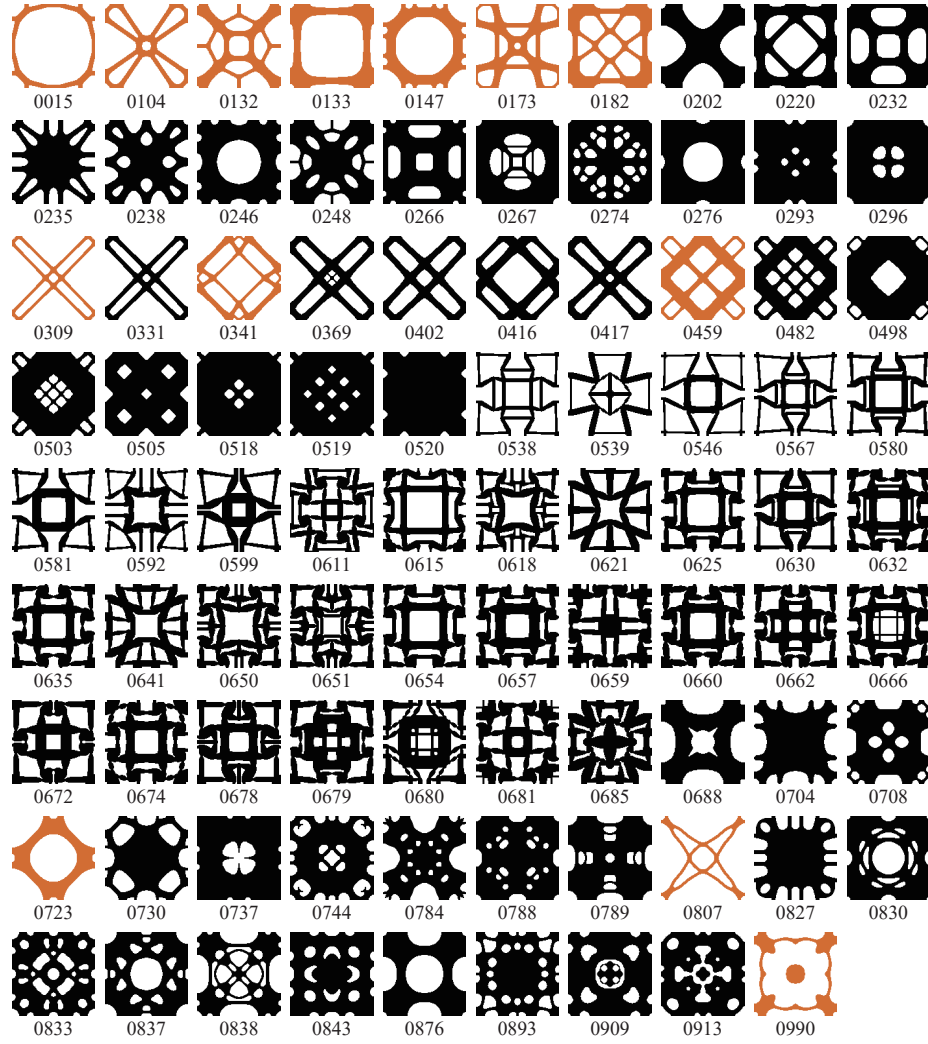


Figure R27: All masks with a bicontinuous count of zero. The 13 boundaries highlighted in orange are selected for subsequent manual design.

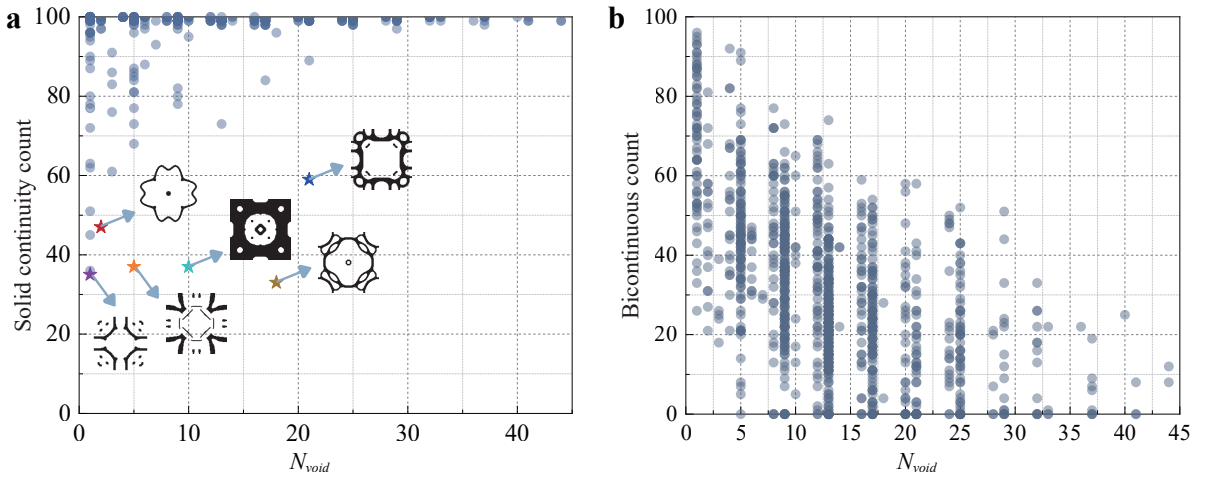


Figure R28: **Dependence of structural connectivity on N_{void} .** **a** Relationship between N_{void} and solid connectivity count. **b** Relationship between N_{void} and bicontinuity count.

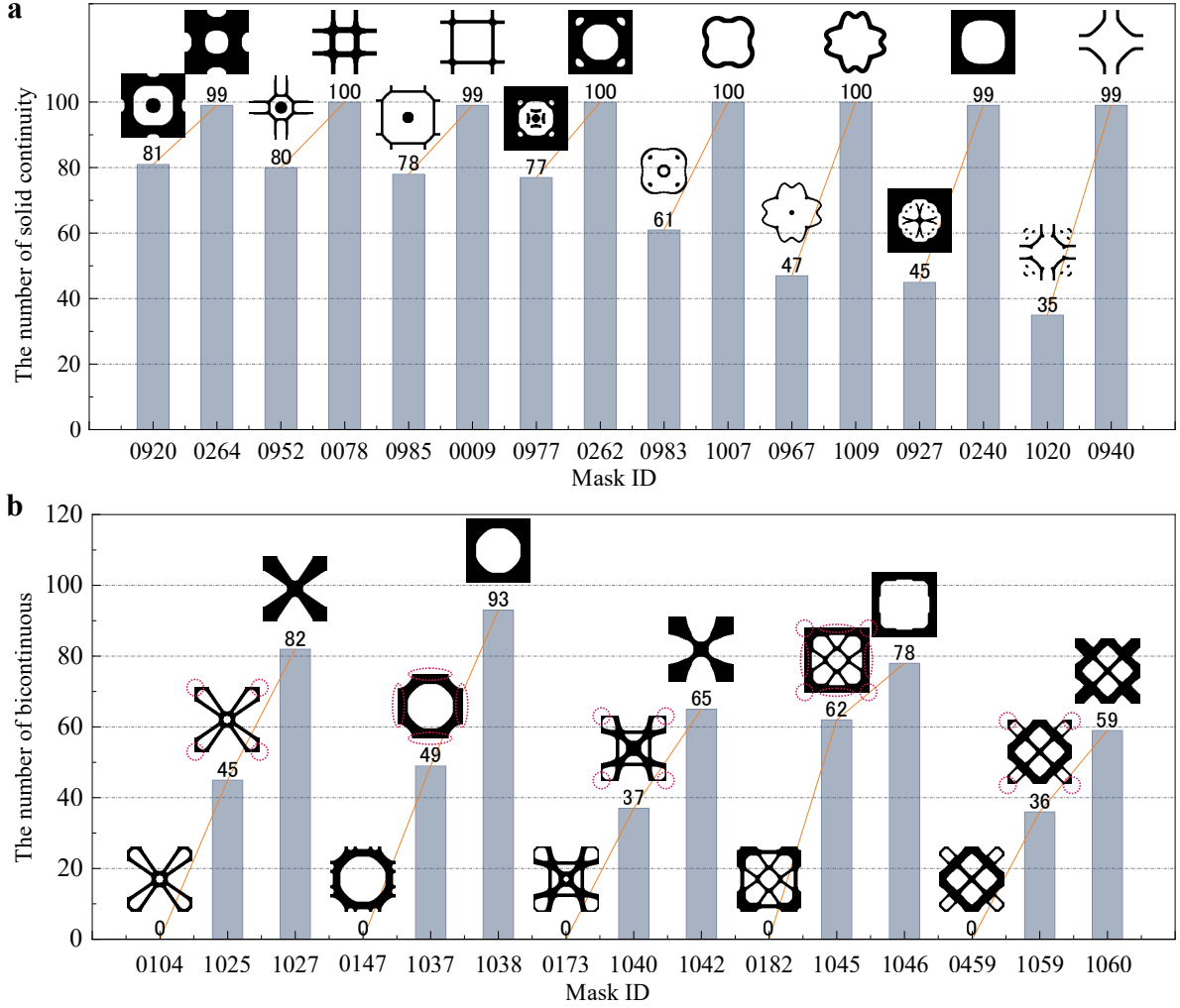


Figure R29: **Influence of boundary conditions on structural connectivity.** **a** Statistics of solid connectivity structures before and after user design. **b** Statistics of bicontinuous open-cell structures before and after user design.

bicontinuity of the generated structures.

However, numerical results indicate a consistent reduction in mechanical performance. This decline is reflected in key normalized effective property ratios, including K/K_v , G/G_v , E/E_v , K/K_{HS} , G/G_{HS} , E/E_{HS} .

Figure R30b illustrates the comparison of the K/K_v before and after perforation, and the results indicate that the values of K/K_v decrease after perforation.

This section demonstrates, through visualization and statistics, that boundary masks influence both structure and properties. Lower boundary volume fractions promote the formation of 3D bicontinuous open-cell structures with higher S/V , while reducing similarity and enhancing diversity. Under these conditions, isotropic bicontinuous structures are more likely to appear, enabling direction-independent mechanical performance. Furthermore, removing isolated pixel islands in the mask improves solid-phase connectivity; filling small holes effectively increases bicontinuous connectivity; in particular, adopting open-hole masks can further enhance bicontinuous connectivity, albeit with a concomitant decrease in certain mechanical metrics. These results highlight the critical impact of boundary masks, though larger datasets are still needed to establish universal conclusions.

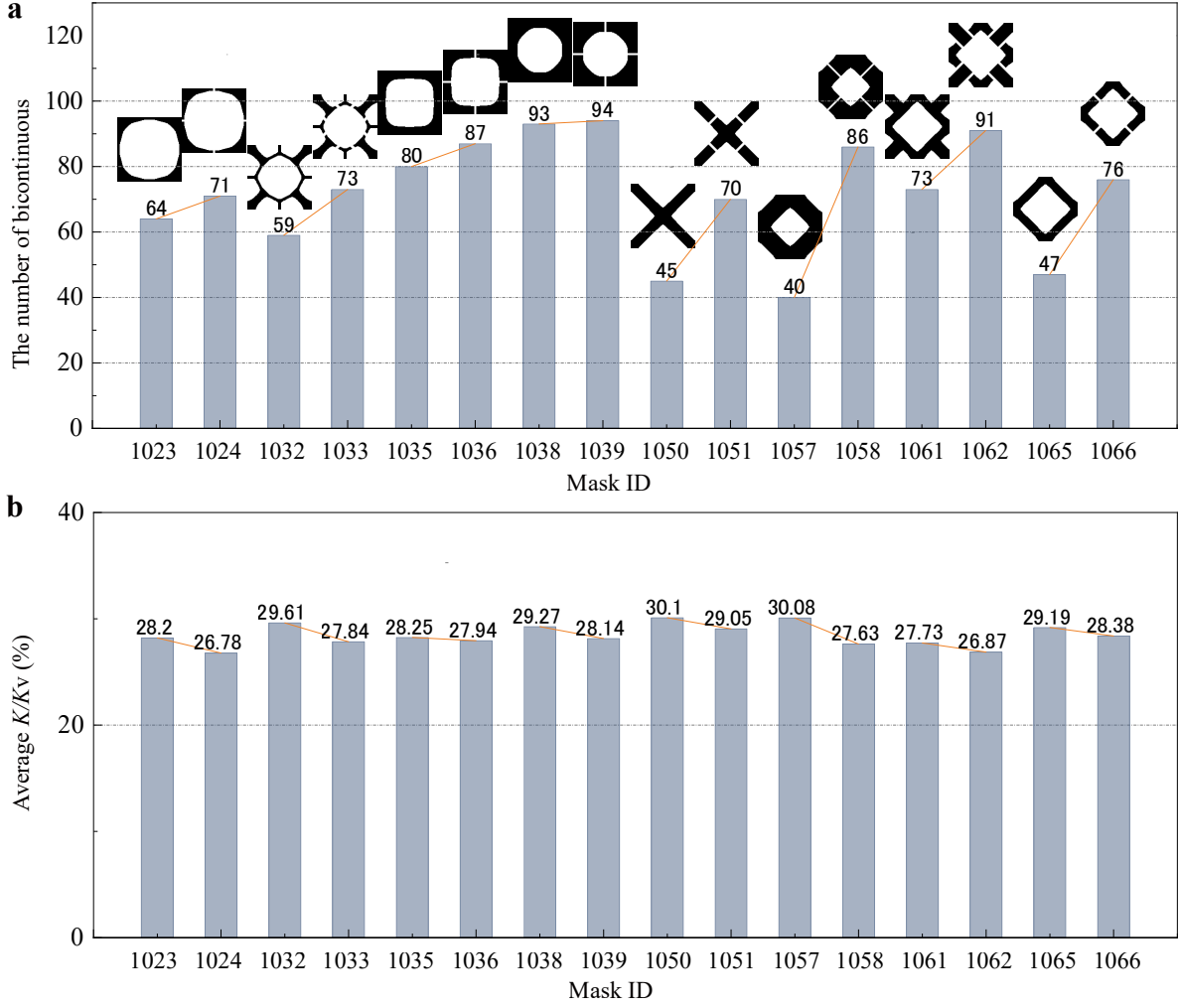


Figure R30: **Influence of boundary conditions on structural bicontinuity and stiffness.** **a** Statistics of bicontinuous open-cell structures before and after user design. **b** Relationship between mask ID and average K/K_{HS} .

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Winston Wai Shing Ma, Ligang Liu, Xiao-Ming Fu

November 5, 2025

REVIEWER COMMENTS

Reviewer #3:

Remarks to the Author:

The authors have well addressed my concerns and significantly improved the manuscript. I think it is now suitable for publication in Nature Communications.

Remarks on code availability:

The code is well structured.

Reviewer #4:

Remarks to the Author:

The modifications to this manuscript make it much better and address all the reviewer comments. It is clear the authors have done quite a bit of technical work, and work in preparation of the manuscript.

Response

We sincerely thank all the reviewers for their positive and encouraging comments and greatly appreciate the time and effort they have dedicated to reviewing our manuscript. We are pleased that the reviewers find our revisions have significantly improved the quality of the work and that the manuscript is now suitable for publication in Nature Communications.