

Reac-Discovery: an artificial intelligence–driven platform for 3D-printed continuous-flow catalytic reactor discovery and optimization

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1. Methods and Experimental details

This section provides detailed descriptions of the methodologies, computational scripts, and experimental protocols employed in the development and application of the Reac-Discovery platform. It includes additional data and resources that complement the main text, offering further insights into the parametric design of periodic open cellular structures (POCS), the fabrication and functionalization of 3D-printed reactors, and the iterative optimization of process descriptors and geometric descriptors.

1.1. Reac Gen platform

1.1.1. Structure Generation

All calculations and structure generations were performed through Python (version 3.13.0), utilizing libraries such as *NumPy* (version 2.1.0), *Trimesh* (version 4.5.1), and *Pandas* (version 2.2.3). The Python script used for this process is available on GitHub for further application and reference.

Reac-Gen generates 3D structures based on implicit mathematical surface functions to obtain Gyroids, Schwarzs, and other minimal surface geometries. Each geometry was defined by three parameters: size (S), resolution (R), and level threshold (L). These parameters determine the bounding dimensions, voxel density, and isosurface cutoff for the generated structure.

1.1.2. Parameter Definitions

Size (S): Defines the spatial boundary of the scalar field on each axis (x,y,z), which determines the bounding box dimensions in millimeters (mm).

Resolution (R): Specifies the number of sample points along each axis within the size boundary, controlling voxel density. Higher resolution values improve geometric fidelity.

Level Threshold (L): Determines the isosurface cutoff, dictating the boundary between solid and void regions within the scalar field. This parameter directly influences the structure's porosity and wall thickness.

1.1.3. Implicit Surface Function and Voxel Mesh Generation

Each geometry was generated by evaluating the chosen surface function over a 3D grid created using *np.meshgrid*. For example, the gyroid surface function was defined as:

```
def generate_gyroid(size, resolution, level):
    x = np.linspace(-size, size, resolution)
    y = np.linspace(-size, size, resolution)
    z = np.linspace(-size, size, resolution)
    X, Y, Z = np.meshgrid(x, y, z)
    gyroid = np.sin(X) * np.cos(Y) + np.sin(Y) * np.cos(Z) + np.sin(Z)
    * np.cos(X)
```

This generates a scalar field that is thresholded at level (L) to create a binary volume matrix:

```
gyroid_volume = gyroid > level
```

The binary matrix is then converted to a triangular mesh using marching cubes via the *trimesh* library:

```
gyroid_mesh = trimesh.voxel.ops.matrix_to_marching_cubes(gyroid_volume,  
pitch=2*size/resolution)
```

1.1.4. Scaling and Clipping to Cylindrical Dimensions

The generated mesh was scaled to match specific cylindrical reactor dimensions (width, depth, and height in mm). Scaling factors were calculated based on the target dimensions, and the mesh is scaled using the following script:

```
scaled_mesh = scale_mesh_to_dimensions(gyroid_mesh,  
desired_dimensions_mm)
```

To fit the mesh within a cylindrical boundary, the scaled mesh was intersected with a cylinder of the same radius and height:

```
cylindrical_mesh, _ = cut_with_cylinder(scaled_mesh,  
desired_dimensions_mm)
```

1.1.5. Continuous Structure Generation for Extended Height

To generate reactors with defined heights, the scalar field of the implicit equation is extended directly along the z-axis by adjusting the evaluation domain to span the desired length. This procedure enables the creation of vertically continuous structures without internal interfaces or discontinuities. The resolution along z is scaled proportionally to the domain extension to maintain uniform voxel density. The resulting binary volume is then processed using the marching cubes algorithm to reconstruct a three-dimensional mesh suitable for additive manufacturing.

1.1.6. Data Export and Logging

Each generated structure is exported as an STL file, named according to the geometry parameters. Metrics are logged in an Excel file for further analysis:

```
save_to_stl(stacked_mesh, geometry_name, size, resolution, level,  
dimensions_mm)  
save_metrics_to_excel(metrics)
```

The recorded parameters—geometry type, size, and level threshold—along with the STL files, ensure reproducibility and simplify data management without overcomplicating the experimental workflow.

1.1.7. Reac-Gen experimental procedure

A. Workflow for 3D Structure Generation in Reac-Gen

Figure S1 illustrates the complete workflow for 3D structure generation in the Reac-Gen module, progressing from the definition of the initial scalar field to the final geometry ready for 3D printing. The process begins with the generation of a 3D scalar field using implicit mathematical functions, such as the Gyroid or Schwarz-P. The scalar field defines regions of material presence or absence, determined by the applied threshold level.

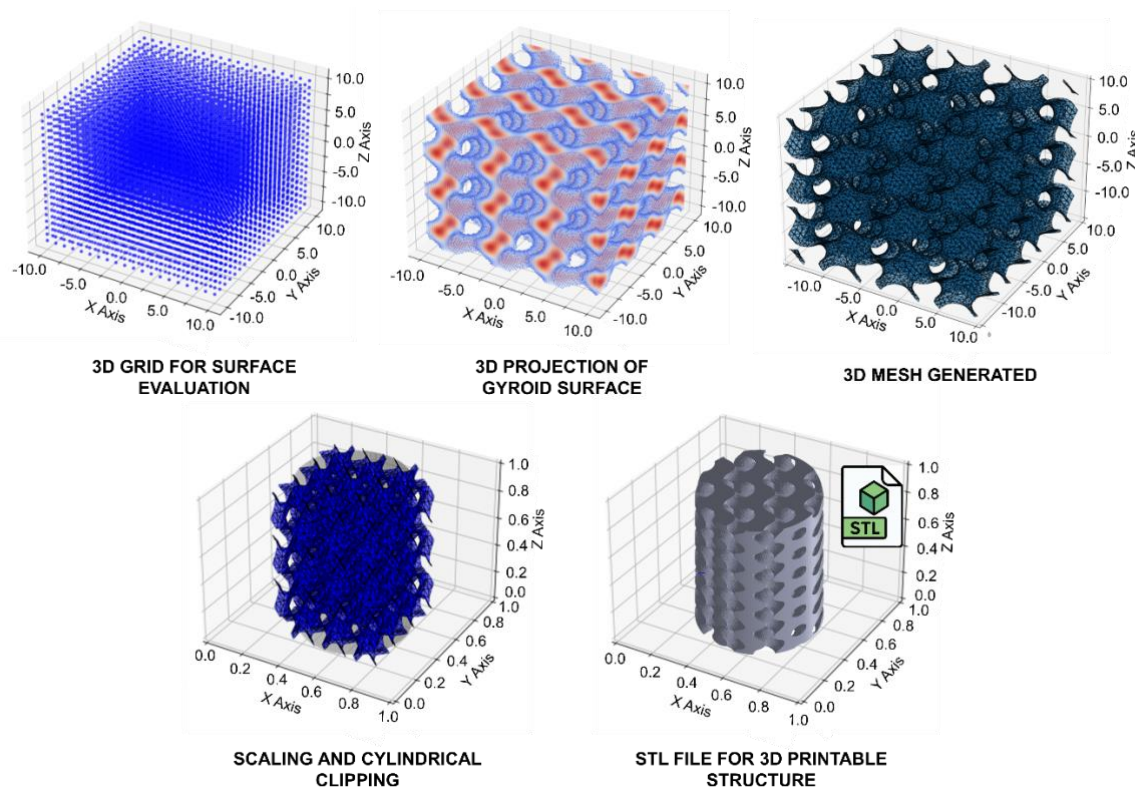


Figure S1. Workflow for 3D structure generation in Reac-Gen: (top row, left to right) scalar field definition, isosurface thresholding, and initial mesh generation; (bottom row, left to right) mesh scaling, cylindrical intersection, and final STL file preparation.

Next, the scalar field is converted into a 3D mesh using marching cubes algorithms, creating an initial representation of the structure. This mesh is further processed to conform to the specific dimensions of the reactor. The mesh is first scaled and then intersected with a cylindrical boundary to ensure compatibility with reactor design requirements. Finally, the resulting structure is exported as an STL file, ready for use in the Reac-Fab module for 3D printing and experimental evaluation.

B. Effect of the Size Descriptor on the Scalar Field Boundary

The Size descriptor in the Reac-Gen module defines the spatial boundary of the scalar field in each dimension (x, y, z), directly influencing the bounding box of the generated structure. This parameter determines the overall dimensions of the reactor geometry and scales the periodicity of the implicit surface function. A larger size value results in an

increased spatial extent of the scalar field, producing larger structures with consistent resolution and periodicity.

Figure S2 illustrates the effect of the Size parameter on the scalar field grid. The four plots show grids generated with increasing Size values: 5, 10, 15, and 20 (top left to bottom right). Each grid defines the spatial boundary within which the mathematical surface function is evaluated, demonstrating how the scalar field expands as the Size parameter increases.

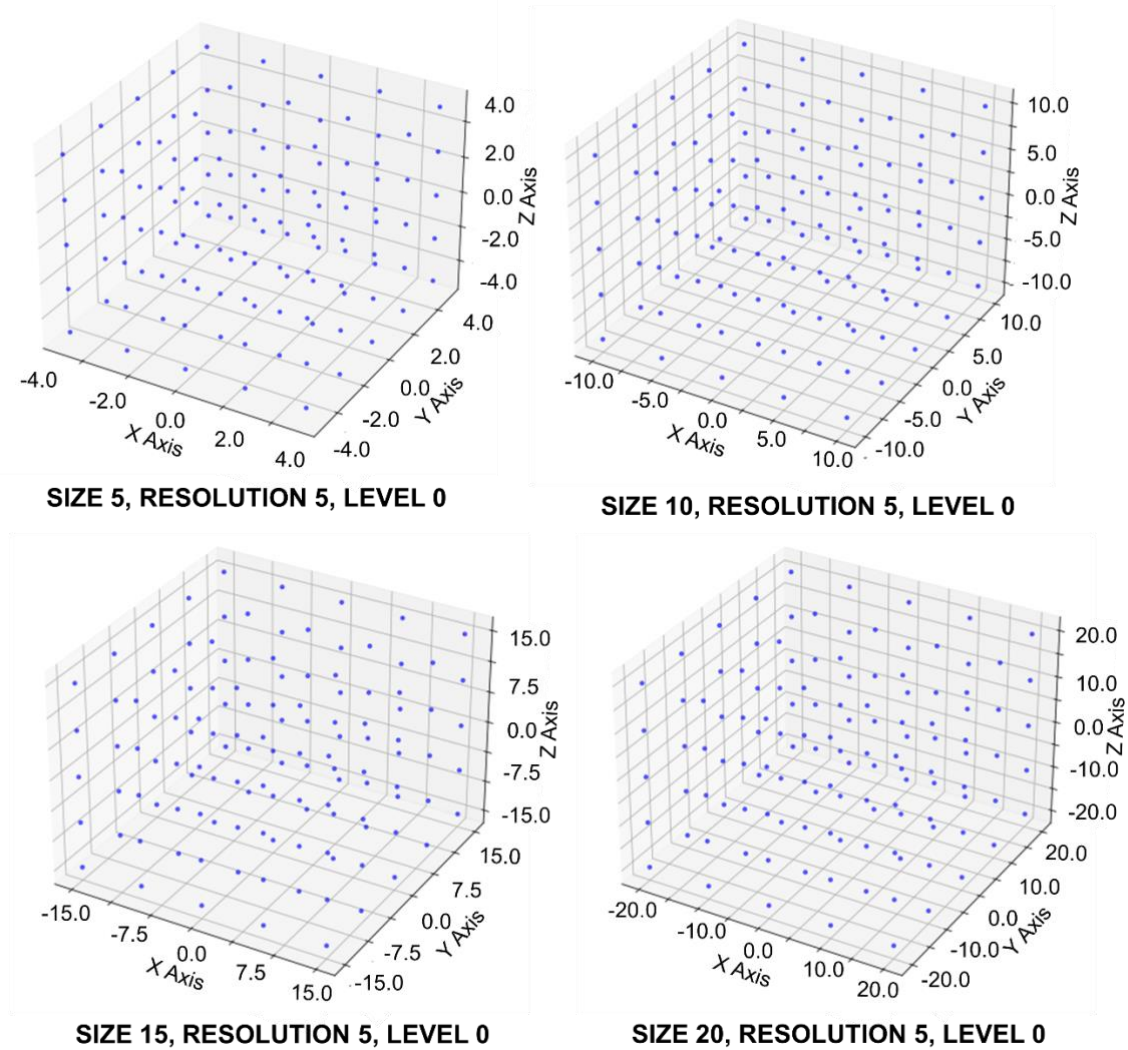
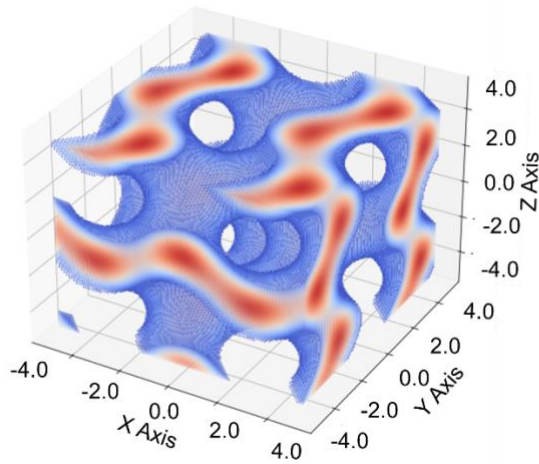


Figure S2. Effect of the Size descriptor on the scalar field boundary: (top left to bottom right) grids generated with Size values of 5, 10, 15, and 20, demonstrating the increasing spatial extent of the scalar field.

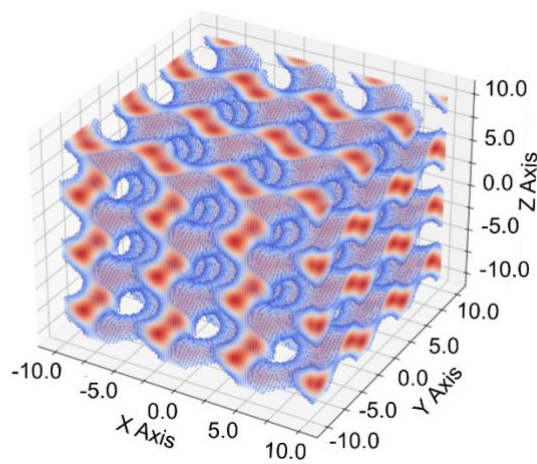
This scaling enables flexibility in the design of reactor geometries, allowing adjustment of the bounding box dimensions to fit specific experimental or functional requirements. The Size parameter is critical for controlling the physical scale of the reactor while maintaining its geometric integrity.

C. Effect of the Size Descriptor on the Projection of the Mathematical Surface Equation

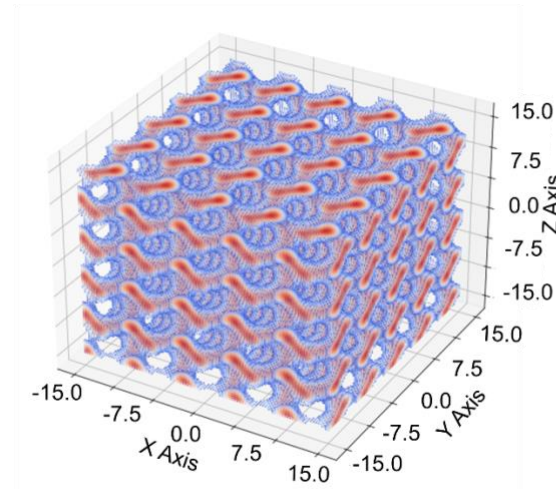
The Size descriptor in the Reac-Gen module directly influences the spatial extent of the scalar field, impacting how the mathematical surface equation is projected. By expanding the bounding dimensions along the x, y, and z axes, larger Size values increase the periodicity and spatial coverage of the implicit function, enabling the generation of larger and more complex structures while maintaining the intrinsic features of the equation.



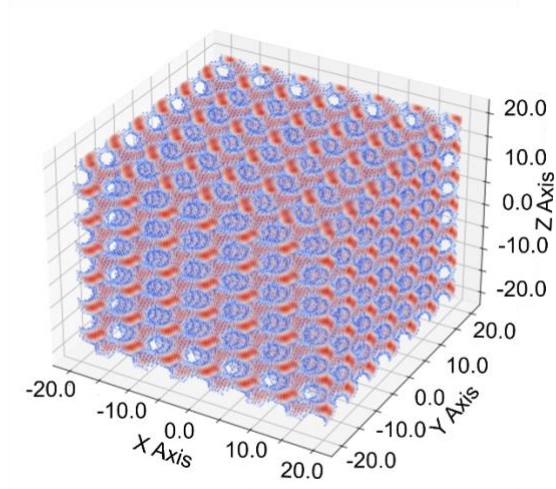
SIZE 5, RESOLUTION 100, LEVEL 0



SIZE 10, RESOLUTION 100, LEVEL 0



SIZE 15, RESOLUTION 100, LEVEL 0



SIZE 20, RESOLUTION 100, LEVEL 0

Figure S3. Effect of the Size descriptor on the projection of the mathematical surface equation: (top left to bottom right) projections generated with Size values of 4, 10, 15, and 20, demonstrating increasing spatial coverage and periodicity as the Size parameter increases.

Figure S3 illustrates the effect of the Size parameter on the projection of the mathematical surface equation. The four plots correspond to increasing Size values: 5, 10, 15, and 20 (top left to bottom right). At smaller Size values, the scalar field contains fewer repetitions of the periodic surface, resulting in a more localized projection. As the Size increases, the

projection expands to include more units of the periodic pattern, creating a larger and more detailed representation of the surface equation.

This parameter is essential for tailoring the physical dimensions of the generated structures, ensuring compatibility with experimental requirements while preserving the unique geometric features defined by the mathematical model.

D. Effect of the Resolution Descriptor on the Scalar Field Density

The Resolution descriptor in the Reac-Gen module specifies the number of sample points along each axis (x, y, z) within the spatial boundary defined by the Size parameter. Higher resolution values increase the density of points used to evaluate the implicit surface function, resulting in a more detailed and accurate representation of the geometry.

Figure S4 illustrates the effect of the Resolution parameter on the scalar field grid. The four plots show grids generated with increasing Resolution values: 5, 10, 15, and 20 (top left to bottom right). As the resolution increases, the density of sample points rises, allowing for finer geometrical details to be captured in the resulting structure.

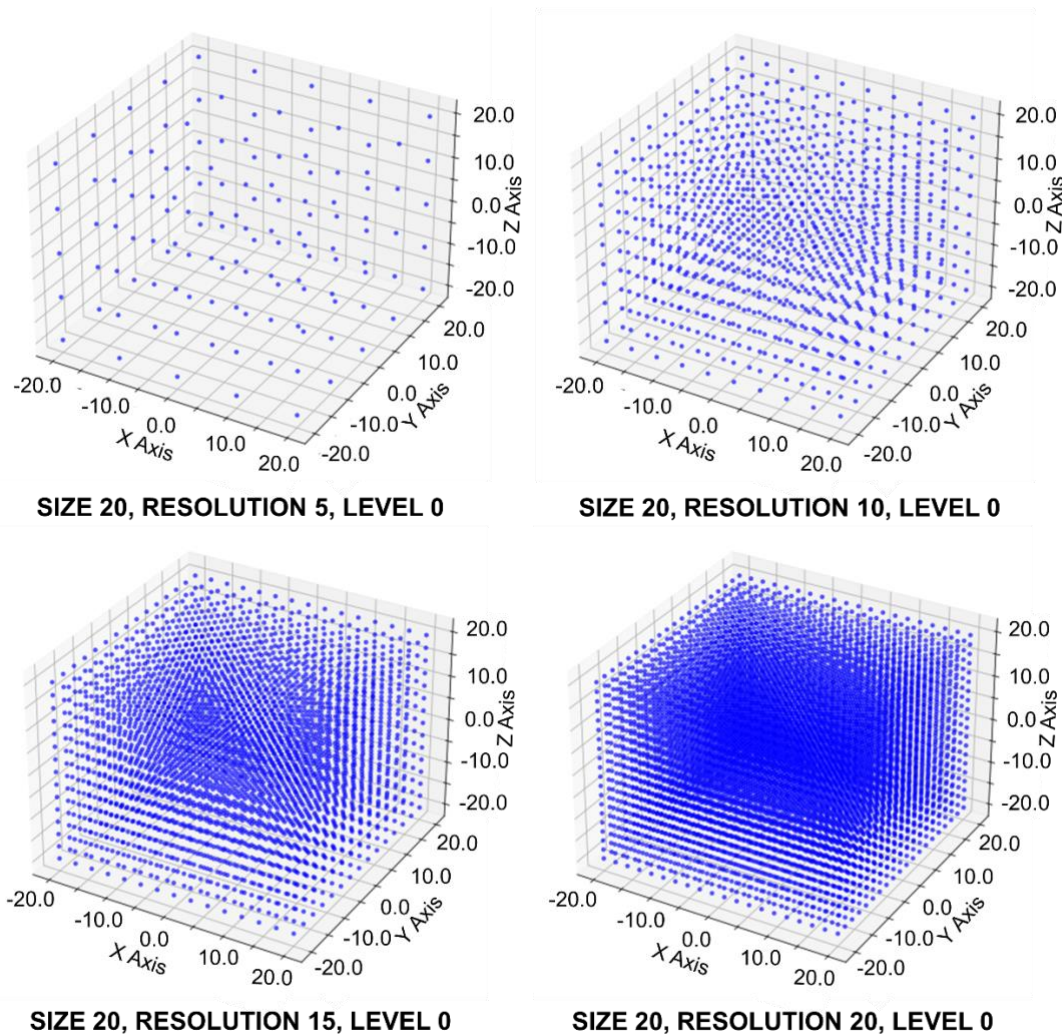


Figure S4. Effect of the Resolution descriptor on the scalar field density: (top left to bottom right) grids generated with Resolution values of 5, 10, 15, and 20, demonstrating the increasing density of sample points in the scalar field.

E. Effect of the Resolution Descriptor on the Projection of the Mathematical Surface Equation

The Resolution descriptor in the Reac-Gen module not only controls the density of sample points in the scalar field but also significantly impacts the projection of the mathematical surface equation. As the resolution increases, the surface representation becomes progressively smoother and more precise, capturing finer details of the implicit function and resulting in a geometry that more accurately reflects the theoretical model.

Figure S5 demonstrates the effect of the Resolution parameter on the projection of the mathematical equation. The four plots correspond to increasing Resolution values: 50, 100, 150, and 200 (top left to bottom right). At lower resolution values, the projection of the surface equation appears coarse, with visible grid artifacts and less defined features. As the resolution increases, these artifacts diminish, and the surfaces become smoother, showcasing the intricate patterns defined by the mathematical function.

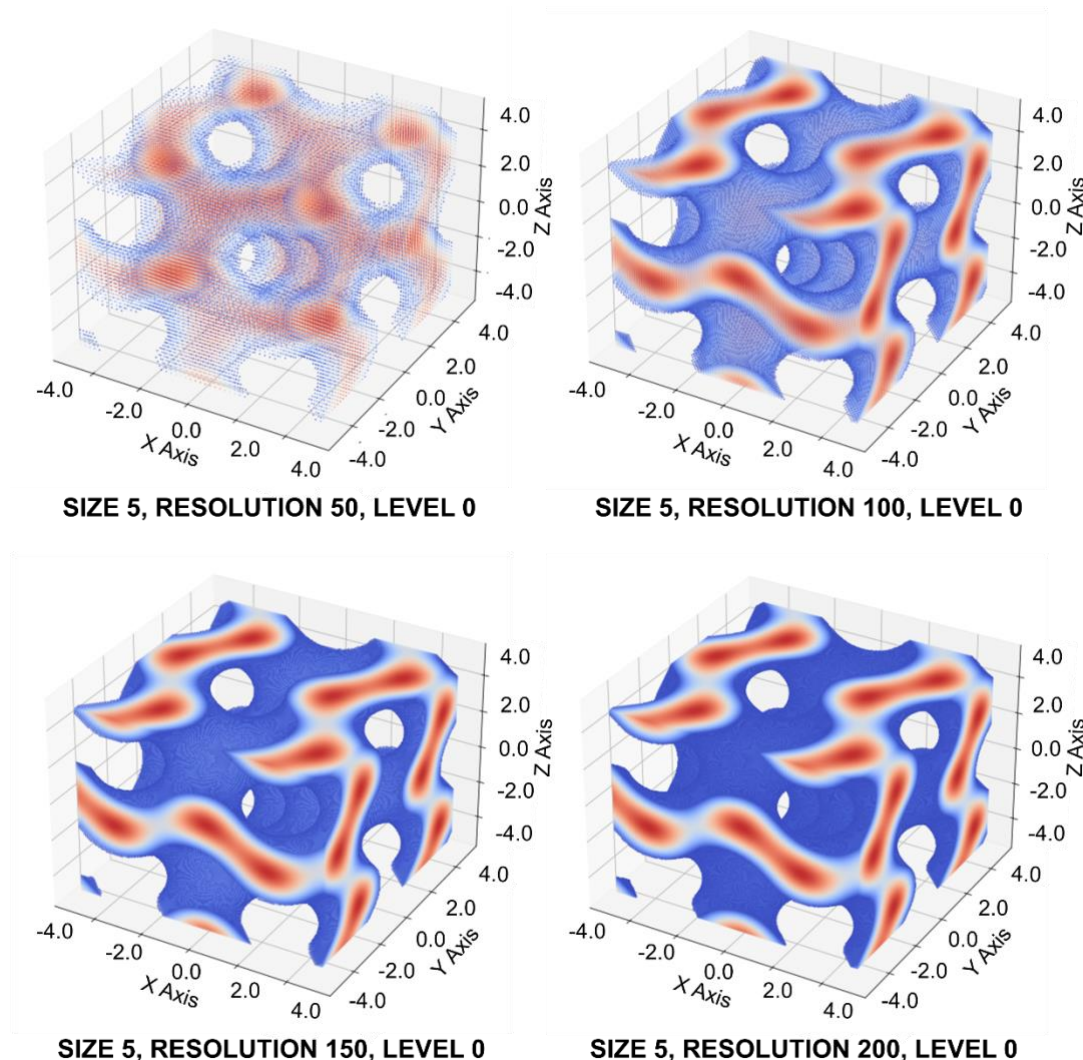


Figure S5. Effect of the Resolution descriptor on the projection of the mathematical surface equation: (top left to bottom right) surfaces generated with Resolution values of 50, 100, 150, and 200, showing progressively smoother and more refined surface projections as resolution increases.

This refinement through higher resolution enhances the accuracy of the generated geometry, which is particularly critical for applications requiring precise control over structural features, such as catalytic reactors. However, it also increases computational demand, requiring a balance between resolution and processing efficiency depending on the application.

F. Effect of the Resolution Descriptor on Mesh Refinement

The Resolution descriptor in the Reac-Gen module also directly impacts the mesh refinement of the generated structures. A higher Resolution value increases the number of triangles in the mesh, resulting in smoother and more detailed representations of the mathematical surface equation. This enhancement in mesh quality allows for better preservation of intricate geometric features and improved accuracy during subsequent fabrication processes.

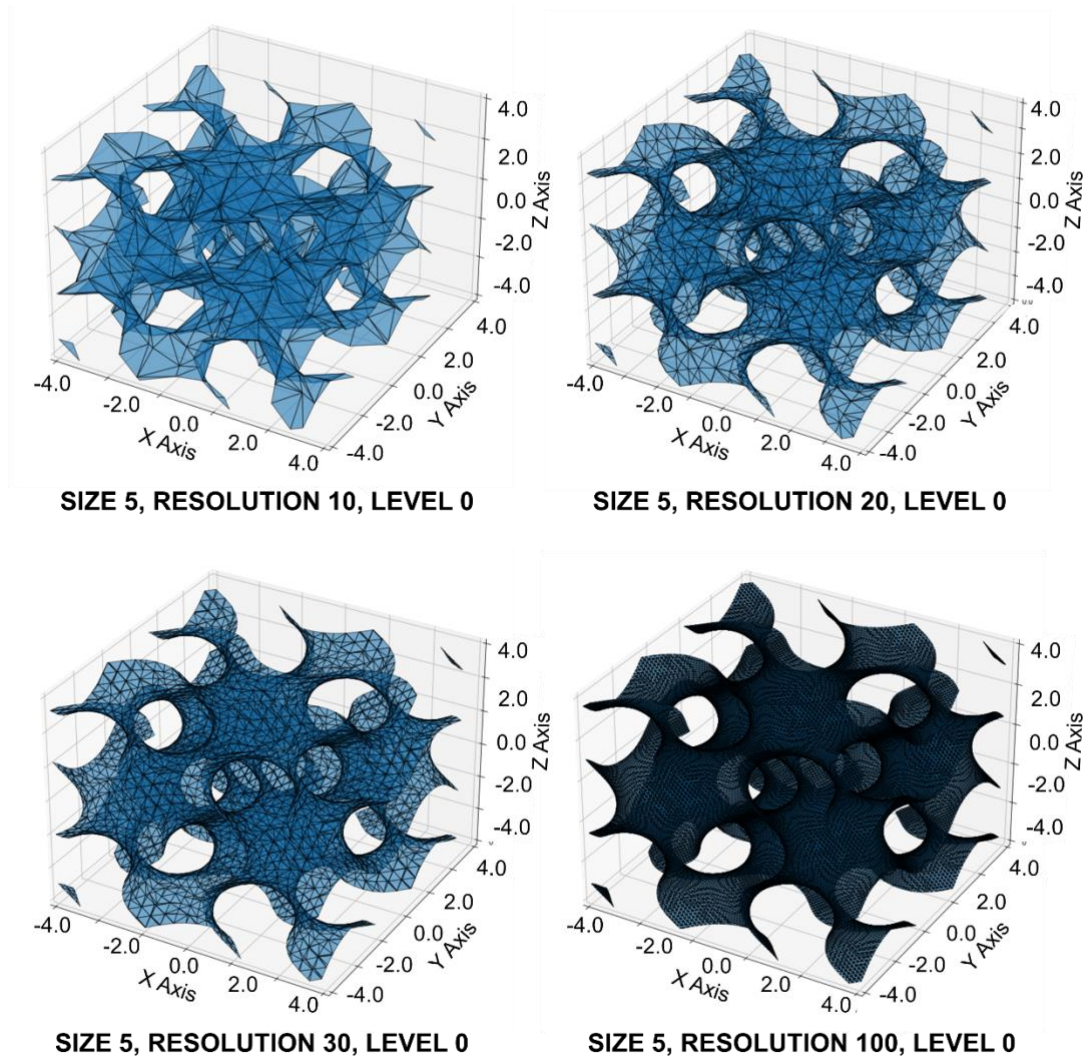


Figure S6. Effect of the Resolution descriptor on mesh density: (top left to bottom right) meshes generated with Resolution values of 10, 20, 30, and 100, showing increasing refinement and detail as the Resolution parameter increases.

Figure S6 demonstrates the effect of the Resolution parameter on the mesh density of the generated structures. The four plots correspond to increasing Resolution values: 10, 20,

30, and 100 (top left to bottom right). At lower resolutions, the mesh appears coarse, with fewer triangles and less definition in the structure's features. As the resolution increases, the number of triangles rises, creating smoother surfaces and capturing finer details of the geometry.

This parameter is crucial for balancing computational efficiency and structural fidelity. Higher resolution improves the quality of the mesh for 3D printing and functionalization but requires greater computational resources. Selecting an optimal resolution ensures that the structure meets both experimental and fabrication requirements.

G. Effect of the Level Descriptor on Structural Porosity

The Level descriptor in the Reac-Gen module plays a crucial role in determining the isosurface threshold, which defines the boundary between solid and void regions in the projected 3D geometry. Variations in the Level parameter within different ranges affect the porosity and wall thickness of the generated structures, enabling precise tuning of geometric properties to meet specific requirements.

Figures S7 and S8 illustrate the effect of the Level descriptor across two distinct ranges:

- **Figure S7 (0 to 1):** As the Level increases within this range, the void spaces expand, and the solid regions become thinner, resulting in more open and lightweight structures. This range is particularly suitable for designs requiring higher porosity and reduced material usage.
- **Figure S8 (-1 to 0):** In contrast, as the Level increases within this range, the structures transition from highly dense geometries with minimal void spaces to more balanced configurations with intermediate porosity. This range is ideal for applications requiring robust mechanical properties or higher surface area-to-volume ratios.

By adjusting the Level descriptor within these ranges, Reac-Gen allows the user to achieve tailored structural characteristics, balancing porosity, wall thickness, and material distribution to optimize reactor performance for specific catalytic or mechanical applications.

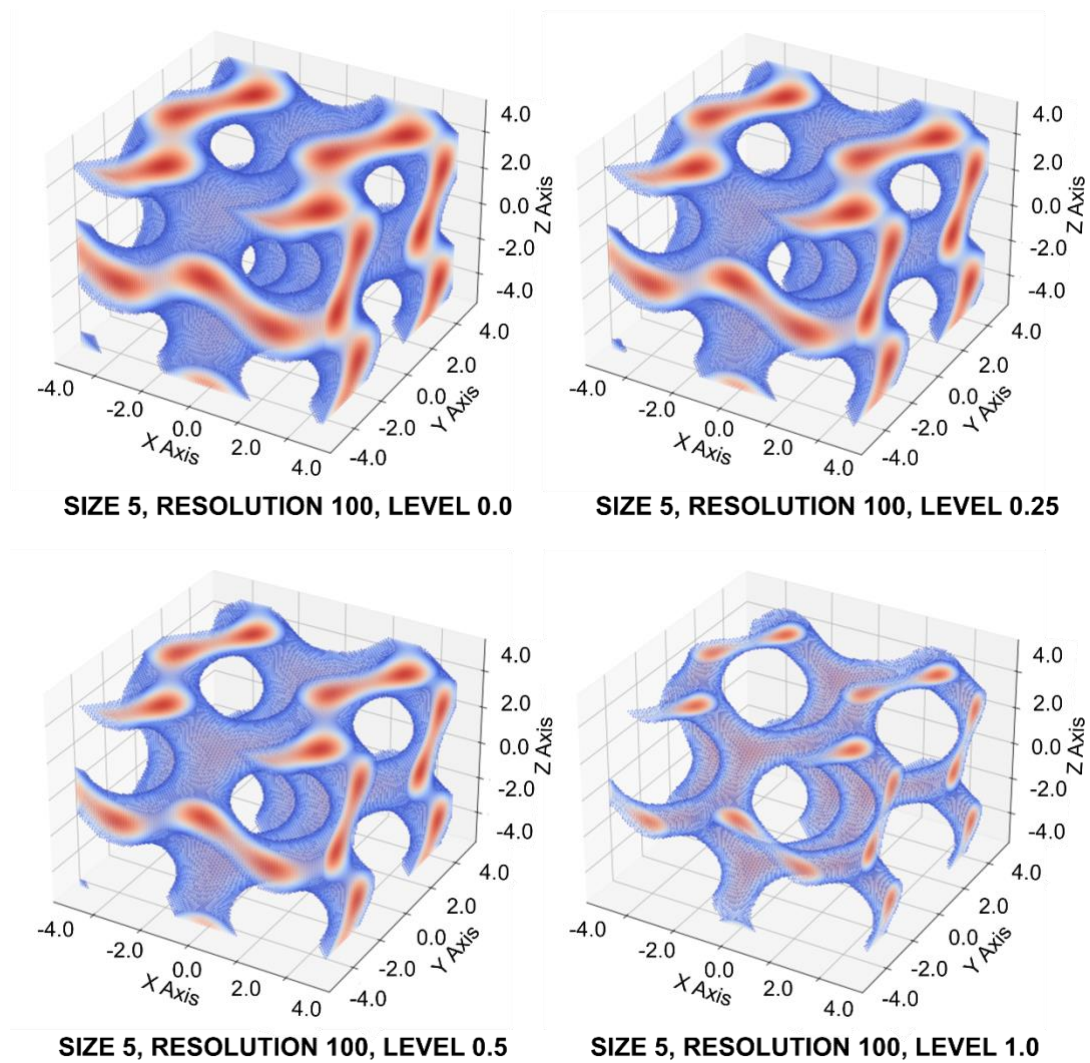


Figure S7. Effect of the Level descriptor on the projection of the mathematical surface equation within the range of 0 to 1: (top left to bottom right) structures with increasing Level values from 0 to 1, showing enhanced porosity and thinner solid regions.

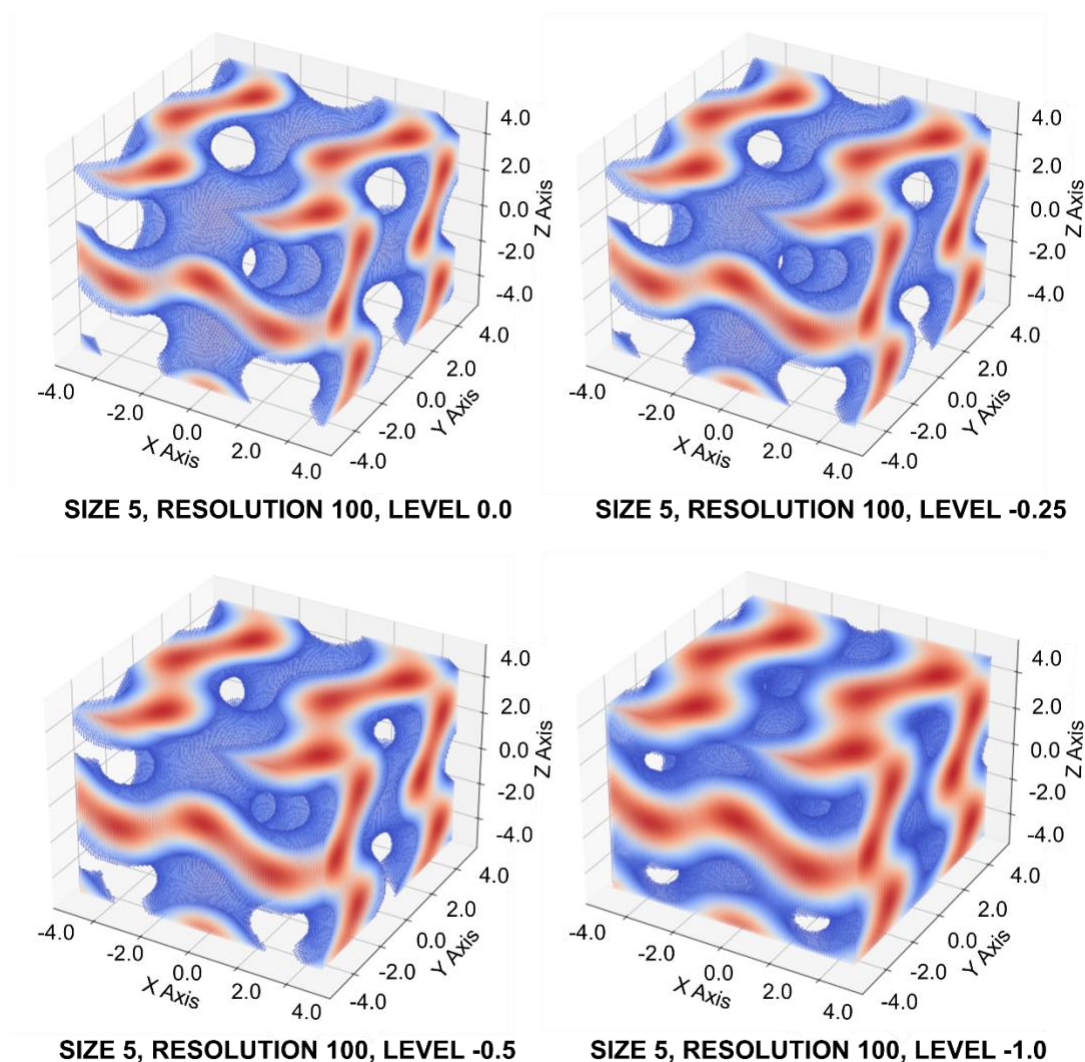


Figure S8. Effect of the Level descriptor on the projection of the mathematical surface equation within the range of -1 to 0: (top left to bottom right) structures with increasing Level values from -1 to 0, transitioning from dense geometries to intermediate porosity configurations.

I. Reactor Geometries Generated by Reac-Gen

The Reac-Gen module can generate 20 distinct reactor geometries using implicit mathematical surface equations. These designs are tailored to provide a wide range of structural properties, such as tortuosity, surface area, and free volume, making them suitable for various catalytic applications. Each geometry is visualized with different perspectives to highlight its unique features, demonstrating the versatility and flexibility of the module in generating customized reactor designs.

Figures S9 and S10 showcase the 20 reactor geometries generated by Reac-Gen. Each reactor has a diameter of 1 cm and a height of 1 cm.

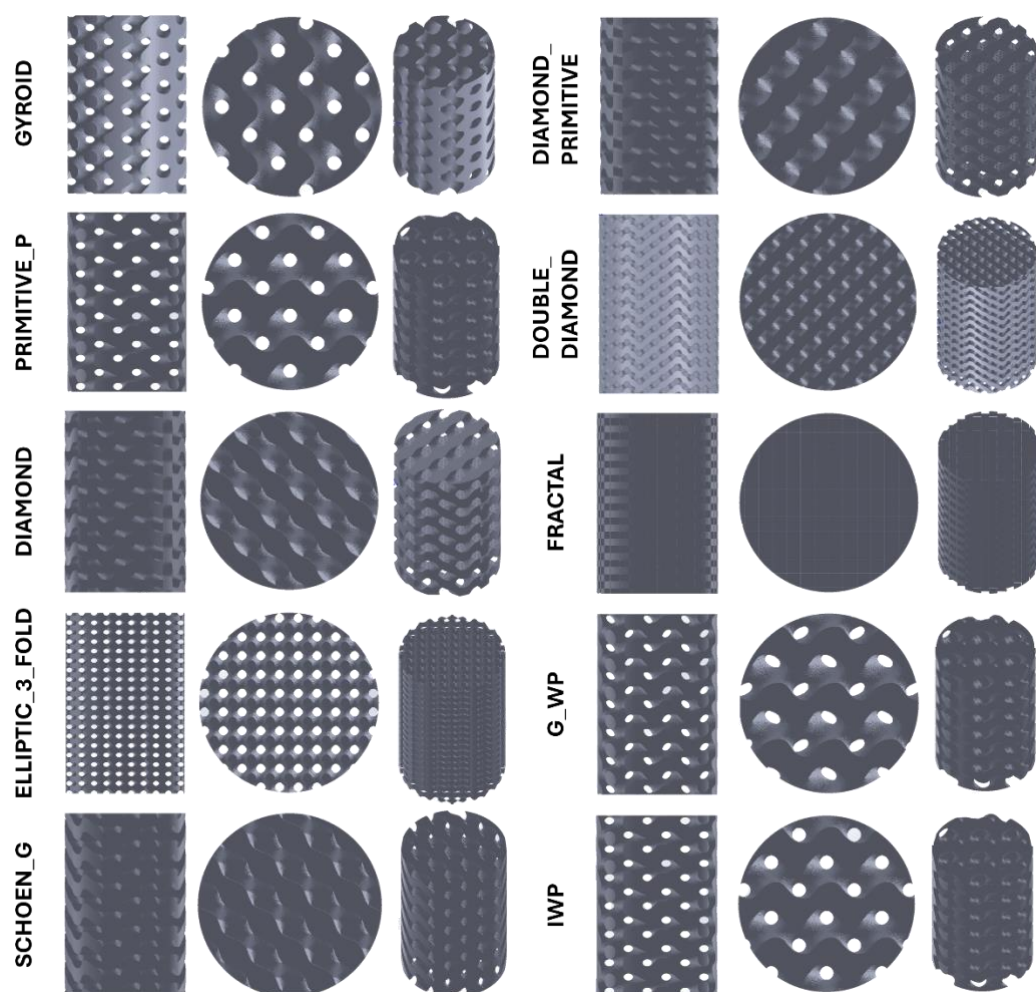


Figure S9. The first set of 10 reactor geometries generated by Reac-Gen, shown with multiple views (front, top, and isometric). Reactor size: 1 cm diameter, 1 cm height.

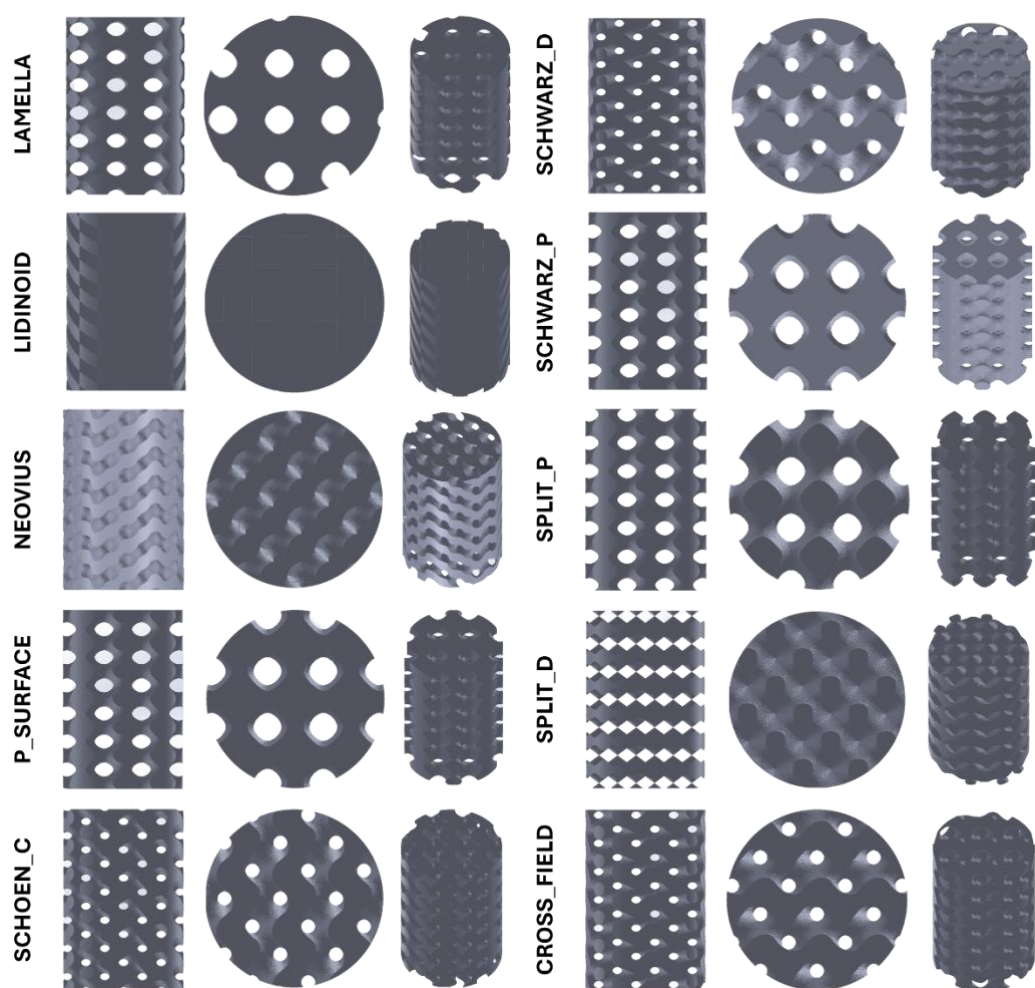


Figure S10. The second set of 10 reactor geometries generated by Reac-Gen, displayed with front, top, and isometric views. Reactor size: 1 cm diameter, 1 cm height.

H. Quantification of Geometric Metrics in Reac-Gen

In the Reac-Gen module, reactor descriptors are quantified using computational routines that evaluate both macroscopic and spatially resolved geometric properties of the periodic open cellular (POC) structures. These metrics are essential for correlating reactor topology with mass transfer behavior and catalytic performance. The workflow is illustrated in Figure S11 and includes the following analyses:

Free Volume: The free volume is determined by subtracting the solid volume of the structure from the total volume of the cylindrical bounding box. Using the voxel representation of the scalar field, the solid regions are identified, and their volume is calculated. In Figure S11 (top row, right), the visualization highlights the void spaces within the structure, showing the regions contributing to the free volume calculation.

Tortuosity: Tortuosity is evaluated by simulating vertical pathways through the structure, representing potential fluid flow paths. Rays are cast along the z-axis, and their lengths through the void regions are calculated. These values are normalized to the reactor height to achieve tortuosity. In Figure S11 (bottom row, left), vertical pathways are shown, illustrating how the flow paths are distributed and analyzed within the structure.

Surface Area: The surface area of the structure is calculated directly from the triangular mesh representation. Using the trimesh library, the sum of the areas of all triangles in the mesh is computed. In Figure S11 (top row, middle), the color-mapped visualization highlights the distribution of surface area across the geometry, providing insight into regions with higher or lower surface contributions.

Packing Percentage: The packing percentage is defined as the ratio of the solid volume to the total volume of the bounding box. This metric is calculated by dividing the solid volume (from the voxel representation) by the total cylindrical volume. The structure is analyzed to assess the distribution and ratio of solid regions to void spaces, providing a clear representation of the packing percentage.

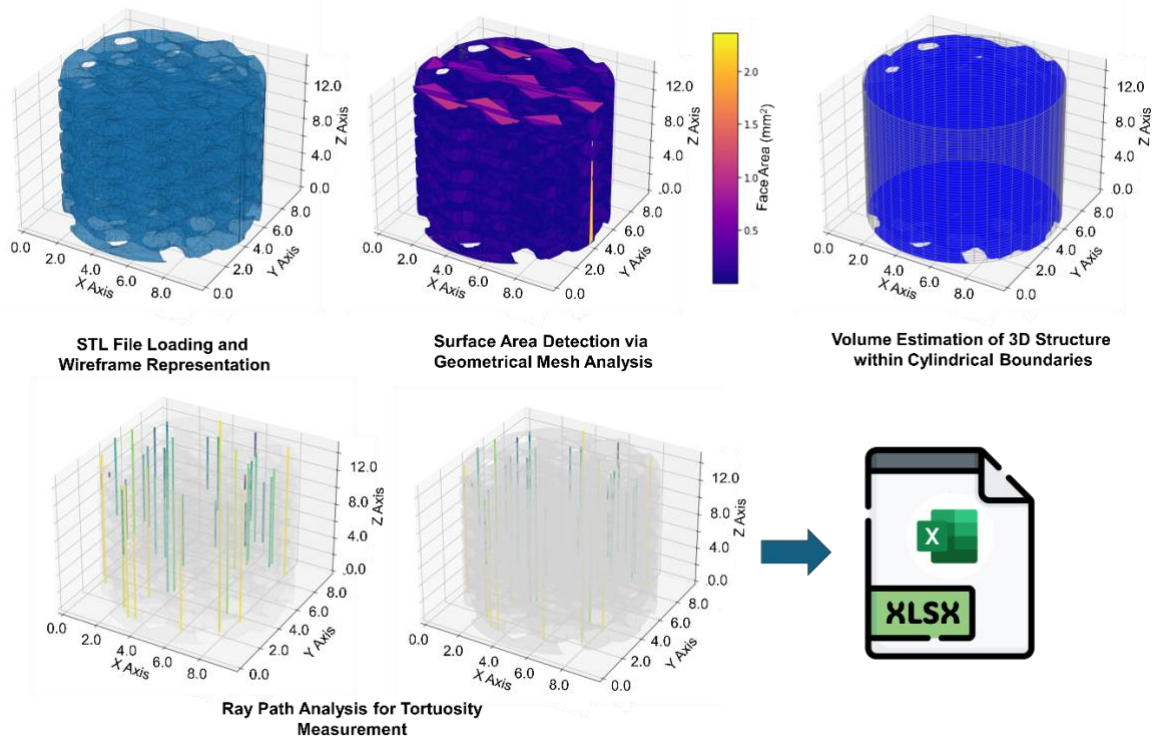


Figure S11. Quantification of geometric metrics in Reac-Gen: (top row) visualization of the complete structure, surface area distribution, and free volume; (bottom row) evaluation of relative tortuosity and packing percentage, followed by the export of metrics to an Excel file.

Wetted Perimeter (P): Evaluated slice-by-slice from binarized 2D cross-sections of the structure. The internal perimeter of the solid-fluid interface is computed using contour analysis methods and combined with the circular boundary interaction to determine the effective contact length.

Void Area (A_e): For each axial slice, the open cross-sectional area is calculated by thresholding the scalar field and integrating the resulting void mask. This metric characterizes the local flow capacity at each position along the reactor.

Hydraulic Diameter (d_h): Defined as $4 \cdot A_e(z)/P(z)$ for each slice, representing the local characteristic dimension of flow channels.

Local Porosity ϵ_G : The ratio of the void area to the total cross-sectional area of the reactor, evaluated for each slice to capture axial variations in packing density.

Specific Surface Area (SSA): The wetted perimeter normalized by total cross-sectional area ($P(z)/A_t$), capturing the intensity of fluid–solids contact.

Interstitial Velocity (u): Estimated by dividing the volumetric flow rate by the local void area ($Q/A_\epsilon(z)$), providing a slice-wise profile of flow velocity.

Reynolds Number (Re): Calculated for each slice using local velocity, hydraulic diameter, and fluid properties to characterize the flow regime.

Finally, all calculated metrics are systematically exported into an Excel file for further analysis and traceability.

The script developed for Reac-Gen is available in the following GitHub repository:

<https://github.com/catm542-ai/Reac-Discovery/blob/main/src/Reac-Gen.py>

1.2. Reac-Fab platform

1.2.1. Materials

All reagents and solvents used in this work were commercially available and were used without further purification. In general, the following materials were employed: Pentaerythritol Tetraacrylate (>99 %, Aldrich), **PETA**, Glycidyl methacrylate (97 %, Aldrich), **GMA**; Phenylbis(2,4,6-trimethylbenzoyl) phosphine oxide (97 %, Aldrich), **BAPO**; Methyl Red (ACS reagent, crystalline, Aldrich), **MR**; Pentaerythritol tetrakis (3,5-di-tert-butyl-4-hydroxyhydrocinnamate) (98 %, Aldrich); hydrochloric acid (37 %, Scharlab); 2-Propanol (for analysis, Supelco); Ethanol absolute (for analysis, Supelco).

Specific reagents used in each case study are described individually below:

Case Study 1

1-methylimidazole (99 %, Aldrich); hydrochloric acid (37 %, Scharlab); acetophenone (99 %, Aldrich); Sodium borohydride (98 %, Aldrich); Palladium(II) chloride (99.9 %, Aldrich), PdCl₂; Milli-Q water; Hydrogen gas (99.999 % purity) was supplied by Nippon Gases (Madrid, Spain).

Case Study 2

1-butylimidazole (98 %, Aldrich); Epichlorohydrin (98 %, Aldrich); Carbon dioxide (99.998 % purity) was supplied by Nippon Gases (Madrid, Spain).

1.2.2. 3D Printing Procedure

The formulation and 3D printing procedure were conducted based on our previous methodology: The structures generated by Reac-Gen were printed in Reac-Fab

using an Elegoo Mars 3 LCD UV-curing 3D printer. The STL files created in ReacGen were loaded into the slicing software Chitubox, allowing for fine-tuning of printing conditions. The following previously optimized parameters were used during 3D printing:

- Layer Thickness: 0.05 mm.
- Burn-in Layers: 10 layers with an exposure time of 22 seconds per layer.
- Normal Exposure Time: 18 seconds per layer.
- Waiting Time (after exposure): 2.5 seconds.

After printing, each structure was carefully removed from the build platform and washed in isopropanol (IPA) in three consecutive 25 mL washes to remove any uncured resin.

1.2.3. Printability Validation Algorithm

A printability validation algorithm was implemented using Python to classify the structures generated by Reac-Gen as printable or non-printable based on a neural network (NN) model. The features for this classification included design parameters (size and level threshold) and critical geometric attributes such as free volume, surface area, tortuosity, minimum hydraulic diameter, neck diameter, and Euler characteristic, with printability as the target variable.

To construct the model, 1 cm-sized sample structures with a variety of design parameters were printed and weighed. Given the known resin density, each sample's weight was compared to the expected theoretical weight. Samples with weights within a 0-5% error margin were labeled "Yes" (printable), while those outside this range were labeled "No" (non-printable). This dataset served as the training data for the NN classifier.

The model was developed using TensorFlow in Python, with data preprocessing handled in scikit-learn. Model architecture consisted of an input layer representing each feature, two hidden layers, and a binary output layer with a sigmoid activation function. Binary cross-entropy served as the loss function, with the Adam optimizer used for training. Hyperparameter tuning was performed to optimize layer count, neuron count per layer, and activation functions.

After training, the model was saved as an importable file to enable integration into the Reac-Fab workflow. This importable model allowed for real-time validation of Reac-Gen structures before printing, facilitating automated printability assessments based on design parameters without requiring physical testing.

Printability Validation Algorithm Calibration

The printability algorithm is a key feature of the Reac-Fab module, enabling the validation and optimization of SLA-printed reactors. Figure S12 provides a comprehensive overview of the process, divided into two components:

Part A illustrates the workflow for training the machine learning (ML) model responsible for printability validation. The training process began with the generation of 236 STL files of reactors using the Reac-Gen script, encompassing diverse geometries and geometric descriptors. These STL files were subsequently printed in batches of 20 reactors per print (1 cm in length and 1 cm in diameter), as shown in Part B of the figure. The printed reactors were cleaned with absolute ethanol and isopropanol to remove any residual resin trapped within the structured geometries. Following this cleaning process, the reactors were dried to ensure that no remaining solvents could influence the experimental weight. This step was critical for ensuring that the structural integrity of the printed reactors was preserved before weighing.

Geometric descriptors of each reactor, including free volume, surface area, tortuosity, structure size, solid fraction, minimum hydraulic diameter, neck diameter, and Euler characteristic, were calculated using Reac-Gen. The theoretical weight of each reactor was then determined based on the known density of the resin, and the experimental weight was subsequently measured. Reactors with a weight discrepancy of no more than 5% between the theoretical and experimental values were deemed printable, confirming that their structural integrity matched the intended design. Reactors exceeding this threshold were labeled non-printable, ensuring that only accurate and reproducible geometries were used in the process.

The data obtained from these evaluations formed the foundation for training the Reac-Fab Printability Validation Model, a supervised ML model designed to predict the printability of future reactor designs based on critical geometric attributes. The resulting model achieved a prediction accuracy of 91% on unseen data, confirming its reliability for pre-screening reactor designs based on their geometric properties. This model, as well as the training script, has been made available as part of the Reac-Discovery workflow through a GitHub repository (https://github.com/catm542-ai/Reac-Discovery/blob/main/src/Printability_Algorithm.py).

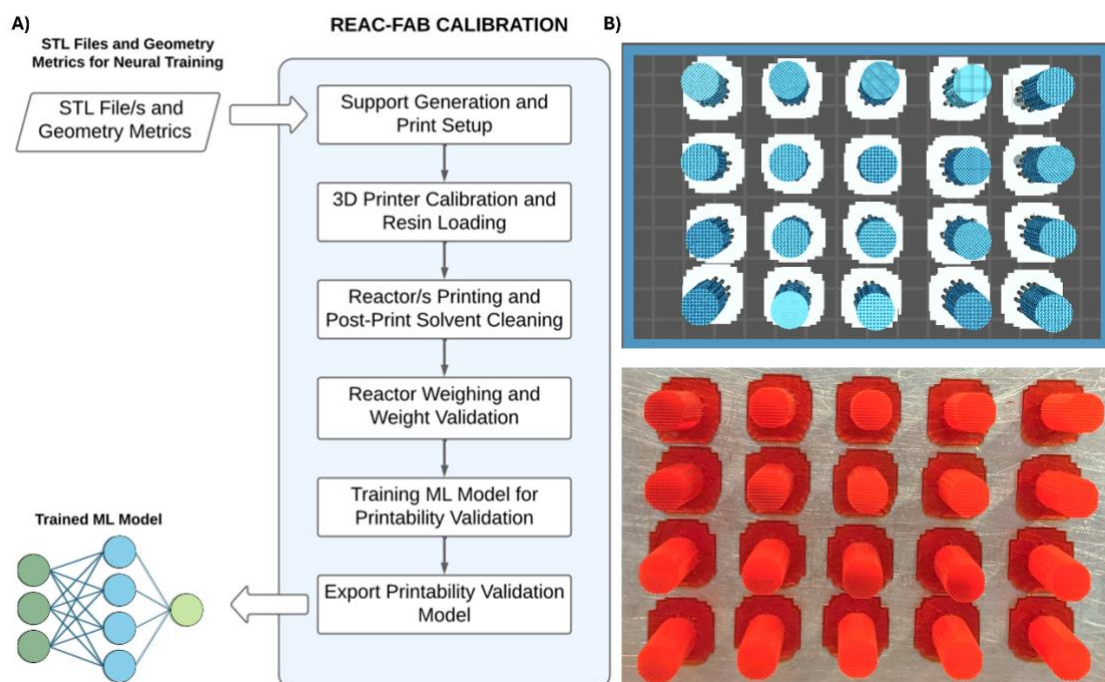


Figure S12. Printability validation workflow and reactor designs. A) Workflow for training the machine learning (ML)-based printability validation model using STL files (Standard Tessellation Language, a standard 3D geometry file format for additive manufacturing) generated in Reac-Gen. B) Visualization of STL reactor designs (top) and a printed batch of 20 reactors (bottom) used in the printability assessment.

This integration of experimental validation with ML algorithms ensures that reactor designs retain their intended geometric properties and meet high-resolution fabrication standards. This calibration technique, like the rest of the Reac-Discovery methodology, demonstrates the potential to be adapted for other printing techniques. The feasibility of this adaptation is illustrated by the successful fabrication of POC structures using Fused Deposition Modeling (FDM) technology (Figure S13), achieving free-standing, support-free structures. Although each printing technology is ultimately constrained by its intrinsic resolution limits, the structural strategies encoded by Reac-Gen enable robust manufacturing of intricate architectures across diverse materials and processes, paving the way for broader implementation across different 3D printing platforms.

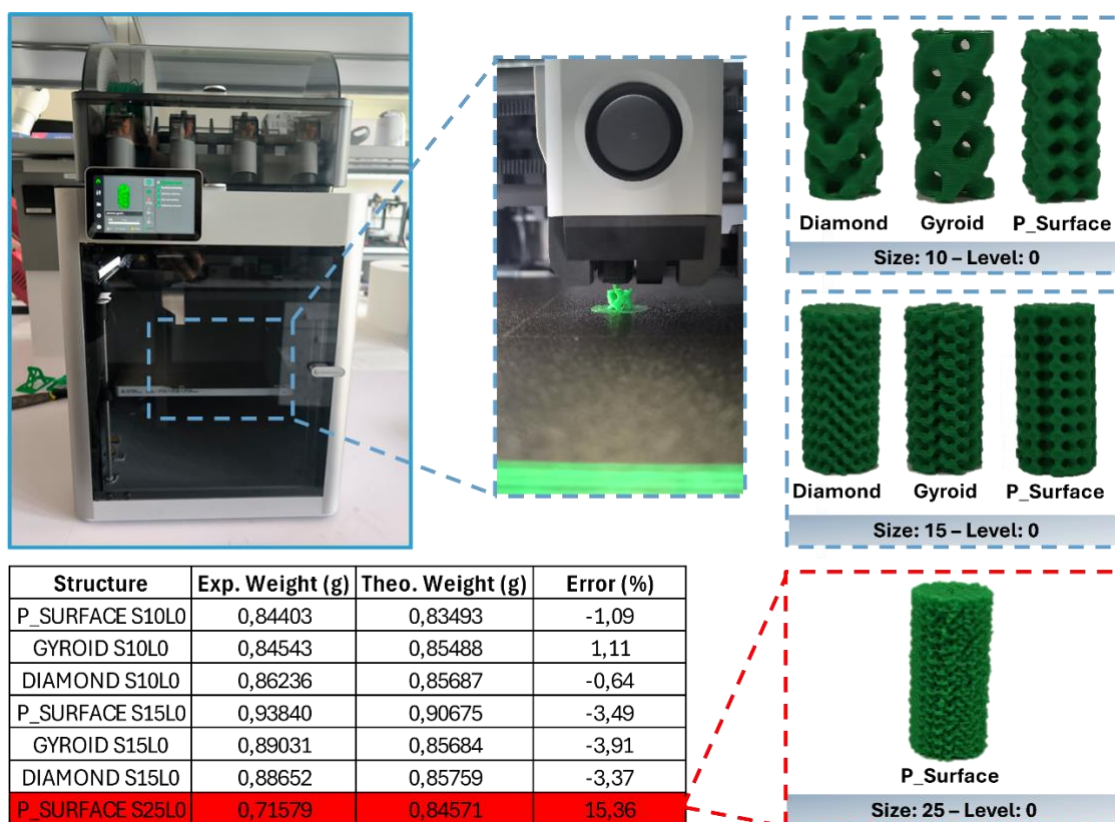


Figure S13. Printability validation of POC structures using FDM. Fabrication of periodic open-cell (POC) structures with a Bambu Lab X1-Carbon 3D printer using fused deposition modeling (FDM) technology. (Left) Printer setup and close-up of the printing process. (Right, top) Examples of successfully printed POC structures of different sizes and topologies. (Right, bottom) Validation of printability through comparison of predicted and experimental weights. The table shows the relative error for structure P_SURFACE S25L0, indicating that when the deviation exceeds a defined threshold, the design can be classified as non-printable.

1.2.4. Reac-Fab experimental procedure

A. Functionalization of 3D-Printed Structures in Reac-Fab

In the first case study, focused on the hydrogenation of acetophenone, palladium nanoparticle (PdNPs) immobilization was carried out in two complementary phases. The same functionalization procedure, previously optimized in earlier work, was employed across all 3D-printed reactor geometries.¹ For a reactor with a functionalization volume of 16 mL, 4.184 mL of 37 wt% HCl (≈ 47.4 mmol), 7.792 mL of absolute ethanol (≈ 133.9 mmol), and 4.024 mL of 1-methylimidazole (≈ 50.7 mmol) were added under ice-bath conditions (0–4 °C). The tube was then transferred to a 40 °C water bath and stirred at 250 rpm for 6 hours, during which the epoxide rings on the reactor surface opened and reacted to form a covalently anchored methylimidazolium layer (Figure S14). Upon completion, the reactors were rinsed thoroughly with absolute ethanol and left to dry under ambient conditions.

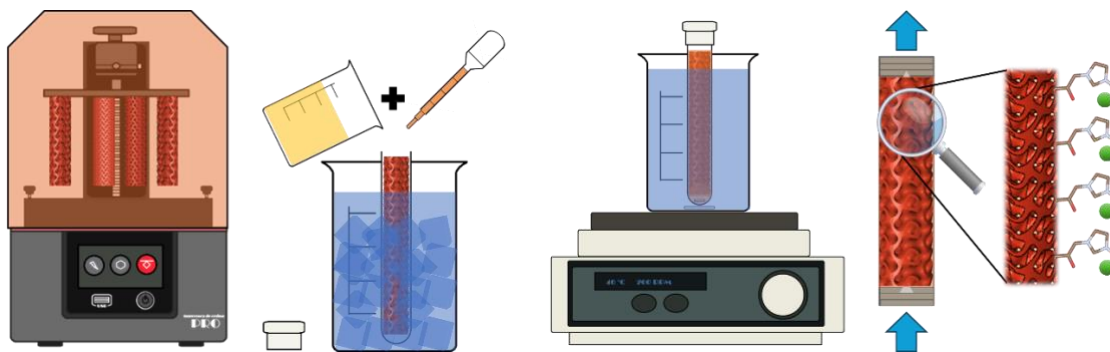


Figure S14. Workflow for functionalizing 3D-printed structures in Reac-Fab: 1) SLA 3D printing of the structures; 2) addition of reagents in a test tube with an ice bath; 3) functionalization in a water bath at 40°C with magnetic stirring; 4) the final functionalized reactor, ready for continuous flow applications.

In the second phase, under continuous-flow conditions, a 0.12 M PdCl₂ solution in Milli-Q water (prepared by adding five drops of concentrated HCl to 20 mL of solution) was pumped at 150 $\mu\text{L} \cdot \text{min}^{-1}$ for two hours through the reactor housed in an Omnifit column. Pd(II) adsorption was evidenced by the support color change from orange to dark brown. The reactor was then washed with Milli-Q water at 500 $\mu\text{L} \cdot \text{min}^{-1}$ for one hour to remove unbound palladium. In an ice bath, a 0.12 M NaBH₄ solution was prepared and immediately passed through the reactor at the same flow rate for one hour, reducing Pd(II) in situ to 2–5 nm Pd(0) nanoparticles. The reduction to Pd(0) was confirmed by the support color changing from dark brown to shiny black (Figure S15). A final wash with water and absolute ethanol completed the process, leaving the reactor ready for continuous hydrogenation of acetophenone.

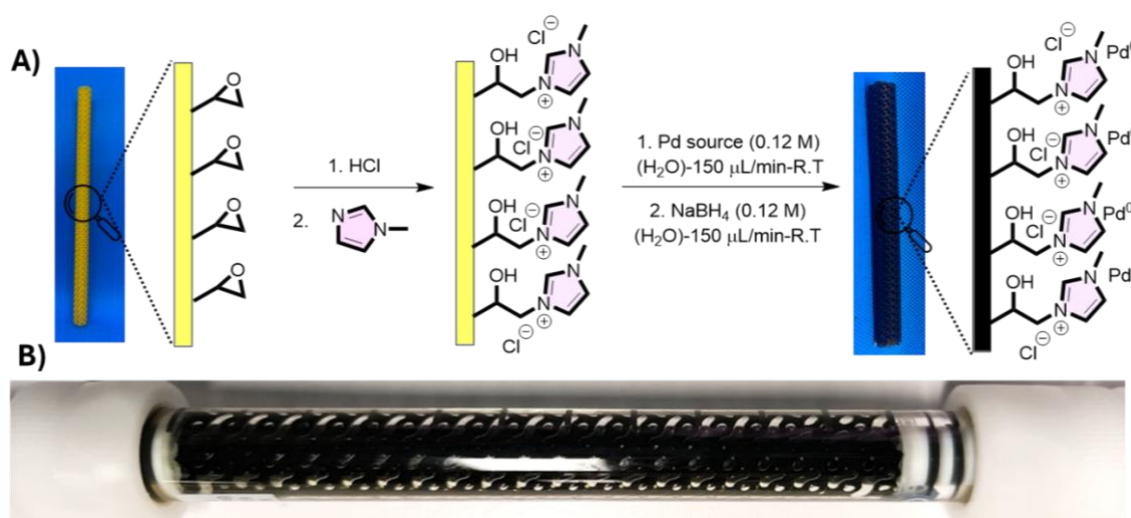


Figure S15. A) Schematic of the imidazole functionalization and Pd(II) adsorption process. B) Photograph of the 3D-printed reactor insert after in situ reduction, showing its shiny black appearance due to the deposition of Pd(0) nanoparticles.

The second case study, focused on CO₂ cycloaddition, involved a single-step functionalization using 1-butyylimidazole. The functionalization process, as described during the initial immobilization of palladium nanoparticles, was carried out in the same manner. For a functionalization volume of 16 mL, the mixture consisted of 3.580 mL of 37 wt % HCl (≈ 40.6 mmol), 6.649 mL of absolute ethanol (≈ 114.2 mmol), and 5.768 mL of 1-butyylimidazole (≈ 56.7 mmol). After functionalization, the reactors were rinsed thoroughly with absolute ethanol until the effluent ran clear and then dried under a gentle air stream. Finally, they were packed into Omnifit columns and integrated into the Reac-Eval platform.

B. Validation of Initial Reactor Geometries

In the Reac-Fab module, the basic geometries designed in Reac-Gen were fabricated using stereolithography (SLA) 3D printing to validate the feasibility of printing each reactor family. The structures generated for this section used standardized parameters: Size = 10, Level = 0, and Resolution = 600.

Figures S16 and S17 showcase the families of geometries generated by Reac-Gen (left) alongside their corresponding SLA-printed structures (right). The printed geometries were fabricated using the resin formulation and printing parameters described previously in the methodology section, achieving high fidelity and structural integrity.

These results confirm that the 20 initial reactor geometries generated by Reac-Gen are printable and will serve as foundational structures for subsequent stages within the Reac-Fab module.

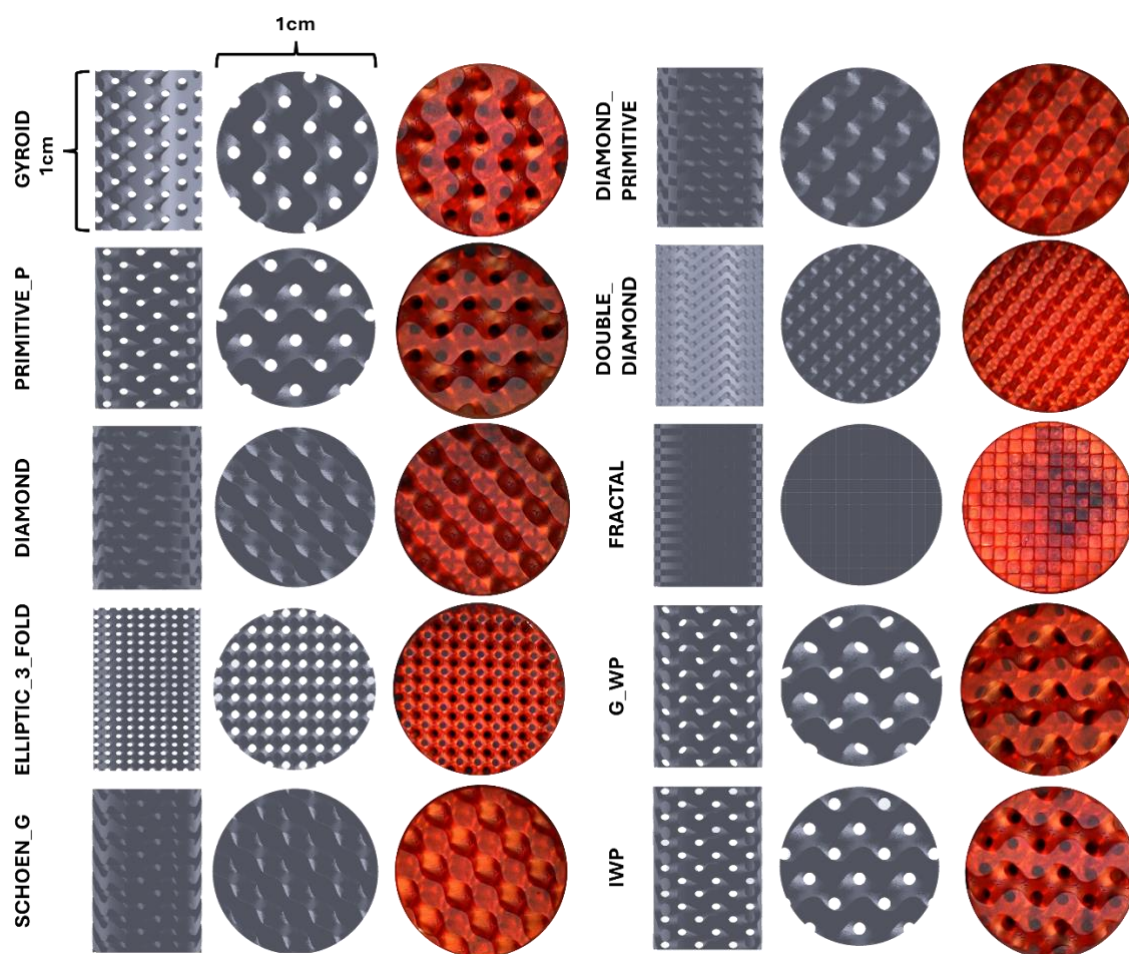


Figure S16. First set of 10 geometries designed in Reac-Gen and their corresponding SLA-printed structures. Reactor size: 1 cm diameter, 1 cm height.

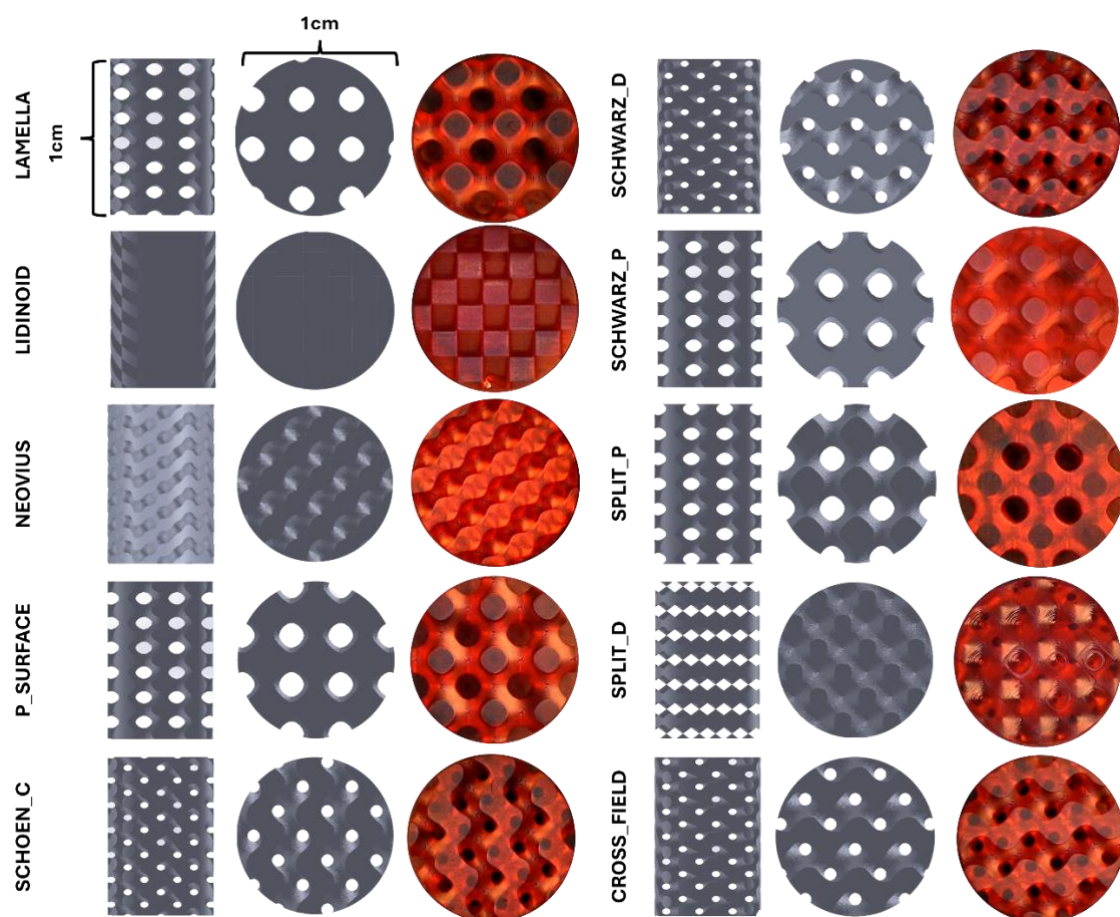


Figure S17. Second set of 10 geometries designed in Reac-Gen and their corresponding SLA-printed structures. Reactor size: 1 cm diameter, 1 cm height.

C. High-Resolution Fabrication of Catalytic Reactor Geometries

In the Reac-Fab module, high-resolution structures designed in Reac-Gen were fabricated using stereolithography (SLA) 3D printing. This section focuses on geometries generated with parameters Size = 35, Level = 0, and Resolution = 600, demonstrating the integration of design and fabrication processes to create catalytic reactors with intricate features. These structures exhibit key geometric metrics tailored for catalytic applications, such as high surface area and tortuosity. The cylindrical reactor geometries, with dimensions of 11 cm in length and 1 cm in diameter, were characterized using Reac-Gen, yielding the following metrics:

- Surface area: 23,632 to 51,700 mm².
- Relative tortuosity: 6 to 16.
- Packing percentage: 20% to 70%.
- Free volume: 1.76 to 3.78 mL.

The free volume and packing percentage values were experimentally validated. This validation involved placing the printed structures inside a glass Omnifit column of known volume, filling the column with water, and measuring the weight of the displaced water. These results confirm the accuracy of the computational predictions provided by Reac-Gen, demonstrating the reliability of the module for designing reactors with defined structural characteristics. These reactor descriptors confirm the feasibility of creating

truly tailored reactors, as demonstrated in this work through their integration with an ML-driven optimization framework.

Figures S18 and S19 present the families of geometries designed in Reac-Gen and their corresponding SLA-printed structures visualized under an optical microscope. These images highlight the exceptional resolution and structural integrity achieved through the integrated design and fabrication workflow. To better illustrate the scale of the printed structures, Figure S20 provides magnified optical microscope images of three geometries: Diamond, Gyroid, and Elliptic_3_fold. These images include scale bars (400 μm) to help contextualize the intricate features of the structures shown in Figures S18 and S19.

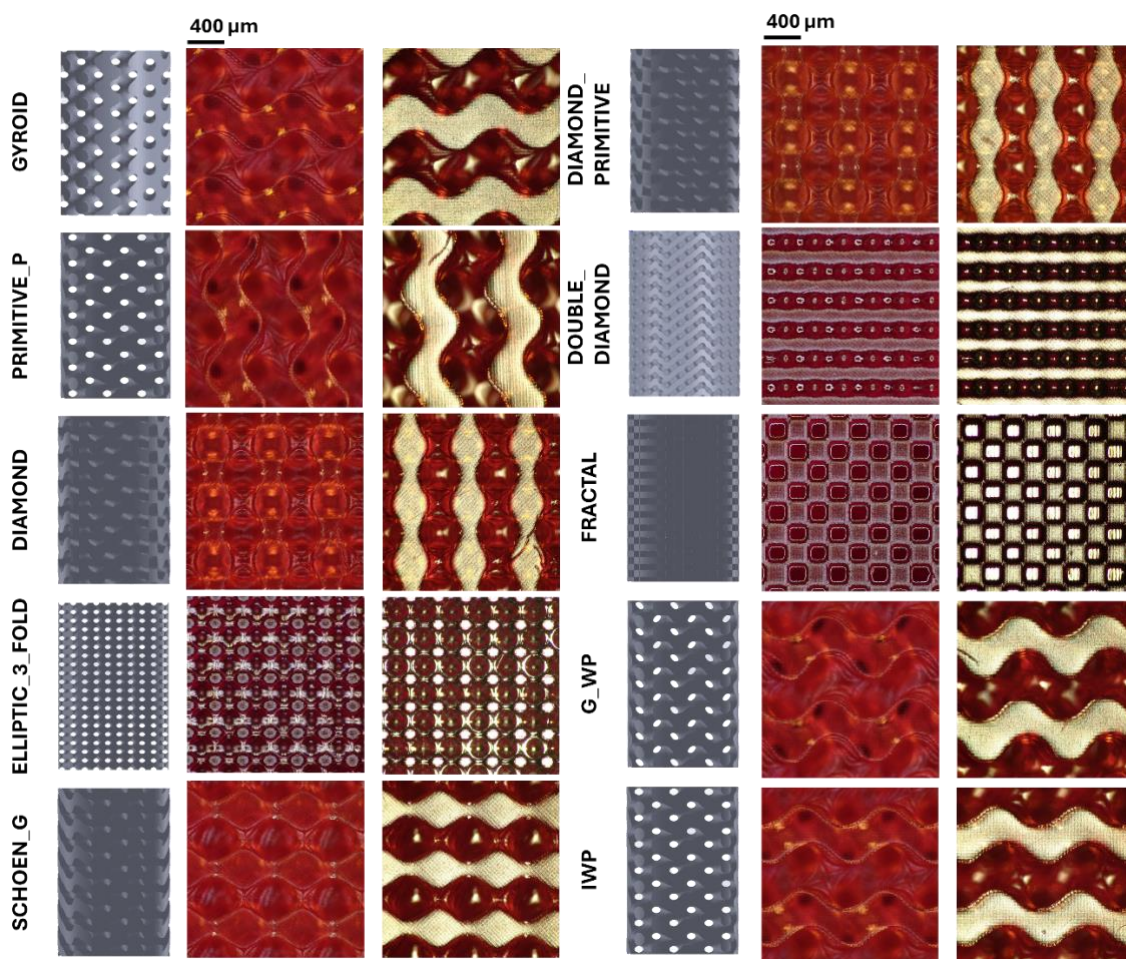


Figure S18. First set of 10 high-resolution reactor geometries designed in Reac-Gen and their corresponding SLA-printed structures under optical microscopy.

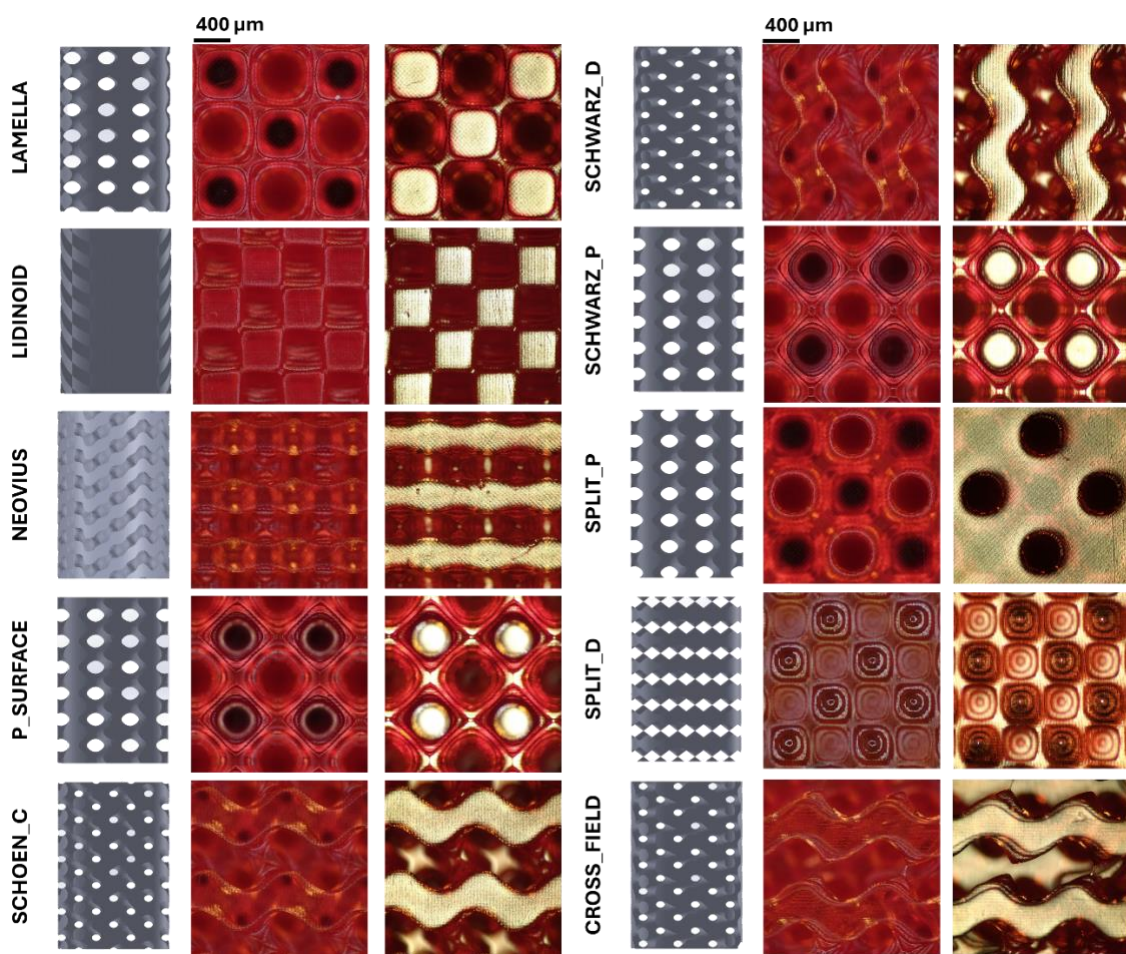


Figure S19. Second set of 10 high-resolution reactor geometries designed in Reac-Gen and their corresponding SLA-printed structures under optical microscopy.

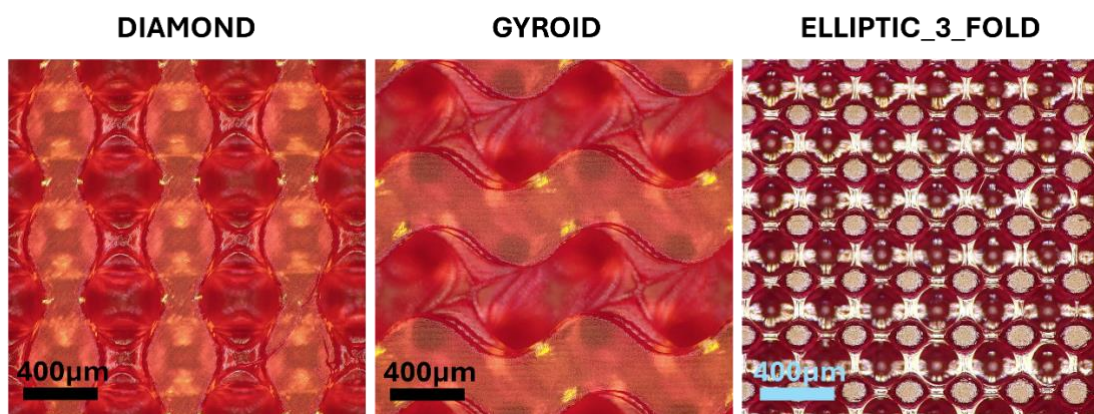


Figure S20. Magnified optical microscope images of three geometries.

Once designed, fabricated, and functionalized, the 3D-printed reactors are integrated into a flow system by assembling them into an Omnifit glass column. This setup embeds the structured catalytic reactor within a robust device, enabling its implementation in continuous flow chemistry applications. Figure S21 illustrates the assembly process, including the individual components and the fully assembled system.

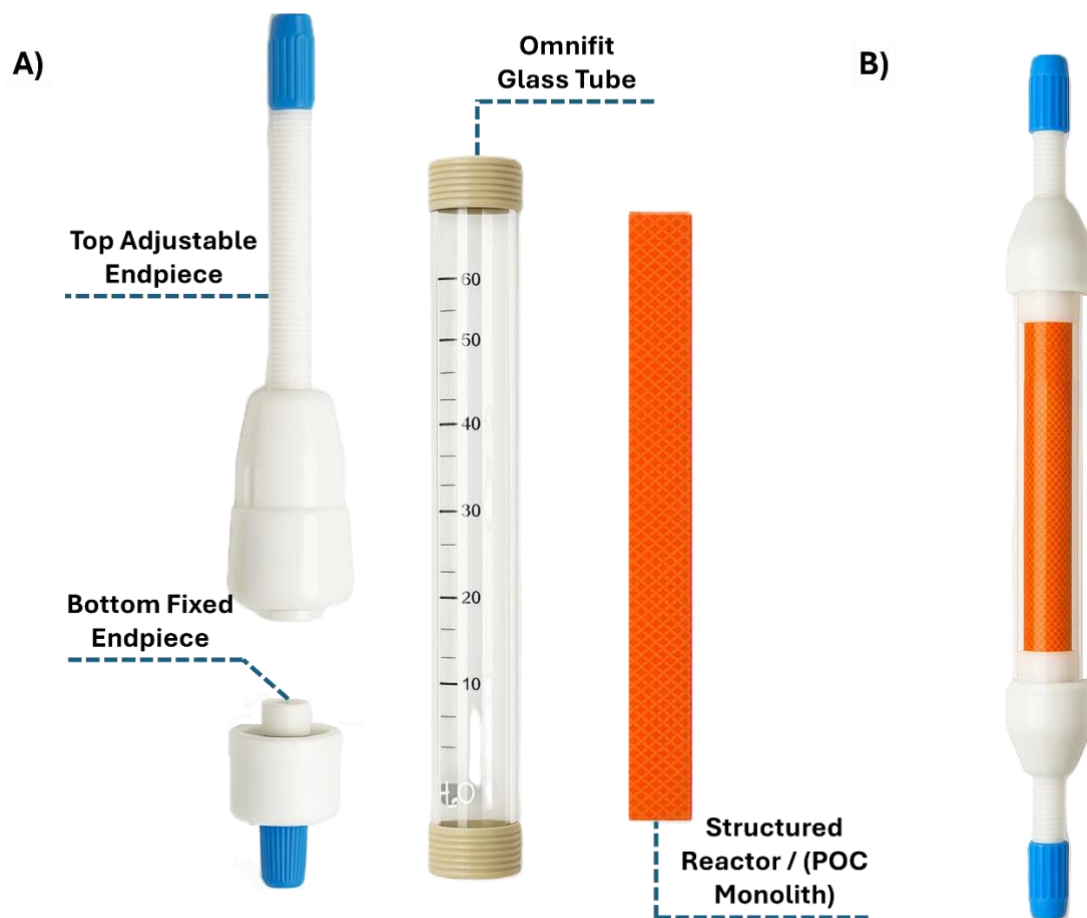


Figure S21. Packing of POC (Periodic Open Cellular) structures into flow reactors. A) Main components of the flow system. B) Fully assembled reactor configuration, ready for integration into a continuous flow setup.

1.3. Reac-Eval

1.3.1. Generation of the Random Reaction Set

To systematically explore the experimental design space while ensuring both diversity and efficiency, a structured randomization protocol was implemented using Python (version 3.13.0). The algorithm was built with the support of key scientific computing libraries such as NumPy (version 2.1.0) for numerical operations, Pandas for data structuring and manipulation, and random for stochastic sampling.

Upper and lower boundaries were explicitly defined for each experimental parameter, including gas and liquid flow rates, temperature, concentration, and reactor geometry descriptors such as size and level. Within these boundaries, a discrete grid of values was generated using equidistant sampling, resulting in a high-dimensional factorial design. From the complete design space (1975 possible

combinations), a representative subset of 3 % (i.e., 60 experiments) was selected using stratified random sampling, ensuring coverage across multiple levels of geometric and process parameters.

The choice of using 3 % of the total design space was based on balancing diversity and experimental efficiency. This subset size allowed a manageable number of experiments to be executed in parallel within the capacity of the automated Reac-Eval platform, while maintaining sufficient coverage of the multidimensional parameter space. Importantly, the number of required data points is directly correlated with the number of variables under optimization: systems with fewer variables can be modeled effectively with fewer experiments, whereas more complex systems demand broader exploration. In our case, the system involved six key parameters, both geometric and operational, making 60 points a practical yet diverse training dataset.

Although Reac-Discovery is designed to operate iteratively through sequential G1 and G2 optimization campaigns, in the cases presented, the initial training already enabled high-accuracy predictions without requiring retraining or feedback loops. This is evidenced by the high predictive accuracy and low MAPE values obtained in both case studies, and by the strong agreement between predicted and experimentally validated optimal conditions.

The effectiveness of this strategy was confirmed by the two case studies reported in this work. For both the hydrogenation of acetophenone and the CO₂ cycloaddition to epoxides, the models trained on this randomly selected dataset were able to accurately predict the optimal operating and geometric parameters. These predictions were experimentally validated with high precision, demonstrating that efficient optimization is achievable with a relatively small, well-structured dataset, even without iterative model refinement.

The Python script for this algorithm is available on the following GitHub repository:

https://github.com/catm542-ai/Reac-Discovery/blob/main/src/Random_Reaction_Set_Algorithm.py

Defined Parameter

Case Study 1

Gas and liquid flow rates were set in units of $\mu\text{L}/\text{min}$, within the following ranges: 2000-6000 $\mu\text{L}/\text{min}$ for gas flow and 100-400 $\mu\text{L}/\text{min}$ for liquid flow. The reactor structure was adjusted according to the following parameters: Size (2 to 8) and Level (0.25 to 0.75), optimizing tortuosity and contact area. Temperature limits were established between 30 and 70°C, and the acetonitrile concentration ranged from 0.5 to 3 M, allowing evaluation across a wide scope of reactive conditions.

Case Study 2

Gas and liquid flow rates were set in units of $\mu\text{L}/\text{min}$, within the following ranges: 100-500 $\mu\text{L}/\text{min}$ for gas flow and 50-300 $\mu\text{L}/\text{min}$ for liquid flow. The reactor structure was adjusted according to the following parameters: Size (2 to 8) and Level (0.25 to 0.75), optimizing tortuosity and contact area. Temperature limits were established between 30 and 120°C, and the epoxide (substrate) concentration ranged from 1 to 4 M, allowing evaluation across a wide scope of reactive conditions.

The parameter limits were defined based on the operational capabilities of the Vapourtec R-Series flow system and the physical constraints of the 3D-printed catalytic reactors. These limits ensure compatibility between experimental setups and computational predictions.

1.3.2. Execution and Analysis of Reactions

The self-driven Reac-Eval lab incorporated an 80 MHz SpinSolve benchtop NMR spectrometer (Magritek) for continuous flow, in situ monitoring of reaction progress. The system included the Vapourtec R-4 Flow Reactor Heater, R2S and R2C peristaltic and HPLC pumps, and an integrated autosampler. UA-OPC communication facilitated control over both the Vapourtec R-Series software and Magritek's SpinSolve software, ensuring coordinated management of reaction parameters.

The MASP_LIBRARY, a Python-based library developed by our research group, serves as the core automation tool for executing and analyzing reactions within the Reac-Eval module. This library integrates seamlessly with the 80 MHz SpinSolve benchtop NMR spectrometer (Magritek) and the Vapourtec R-Series flow system, enabling precise control over experimental parameters such as flow rates, temperature, and pressure. It also manages hardware components, including peristaltic and HPLC pumps, heaters, autosamplers, and valves, ensuring coordinated and automated execution of reactions.

MASP_LIBRARY was designed to implement experimental protocols based on input parameters generated by the Random Reaction Set algorithm. The library automates critical operations such as heating, reaction time adjustments, and flow control while continuously monitoring pressure and other parameters. By interfacing with the NMR spectrometer, MASP_LIBRARY facilitates real-time yield and selectivity monitoring, which is critical for the subsequent training of machine learning models.

In addition to reaction control, the library includes functions for NMR data analysis. Utilizing Python modules such as os, csv, Matplotlib, and Pandas, the library automates the detection, integration, and visualization of NMR spectral peaks. This ensures efficient and accurate processing of data to quantify reactant and product concentrations, enabling robust and reproducible analysis.

All resources related to the library, including its codebase, NMR data analysis script, and the example implementation, are publicly accessible in the following GitHub repositories:

MASP_LIBRARY GitHub Repository: https://github.com/catm542-ai/Reac-Discovery/blob/main/src/MASP_Library.py.

NMR Data Analysis Script Repository: https://github.com/catm542-ai/Reac-Discovery/blob/main/src/NMR_Spectrum_Analysis.py.

Example Script Repository: https://github.com/catm542-ai/Reac-Discovery/blob/main/src/Reaction_Protocol.py.

Data Analysis and NMR Result Integration

The NMR data analysis was conducted in Python, utilizing the *os* and *csv* modules (Python 3.13.0 standard libraries), along with *Matplotlib* (version 3.7.1) and *Pandas* (version 2.2.3) for automated data processing, peak identification, and quantitative integration. Initially, the script identified the latest folder containing NMR data files based on the current date. Within this directory, it accessed the spectrum data from the designated CSV file and processed the spectral values through custom algorithms for peak detection and area calculation.

The *os* library facilitated directory management, dynamically locating the latest folder of spectral data, while *csv* managed data extraction. The spectral values were processed by a peak detection algorithm designed to capture significant peaks based on a defined threshold, ensuring accurate identification of reactant and product signals. Each peak area was computed using trapezoidal integration methods to optimize accuracy across variable peak shapes.

For peak visualization, *Matplotlib* generated annotated plots of the spectrum, clearly marking the start and end points of each detected peak, providing a visual reference for verification of peak integrity and potential irregularities. Subsequently, *Pandas* stored the identified peak parameters—start position, end position, and calculated area—in a DataFrame format. The peak integration was performed using 1-metilimidazol signal as internal standard.

1.3.3. Optimization of Process Descriptors (G1)

The neural network model (M1) was developed in Python, using *TensorFlow* (version 2.12.0) and *Keras* (version 2.12.0) for architecture, training, and optimization. The model inputs included critical parameters such as gas and liquid flow rates, temperature, concentration, and reactor geometry (Size and Level), mapped to corresponding input nodes.

The network was structured as a multilayer perceptron (MLP) with hidden layers adjusted to balance both model complexity with training efficiency. ReLU activation functions were applied in the hidden layers to introduce non-linearity, while a linear activation function was used in the output layer, suitable for regression tasks such as predicting performance and conversion. The Mean Squared Error (MSE) loss function was employed to quantify prediction accuracy, and the Adam optimizer (configured with a learning rate of 0.001) managed the optimization process, adapting learning rates as needed to minimize the loss.

To prevent overfitting with limited data, early stopping was implemented using the Keras EarlyStopping callback. The model was monitored for improvements in validation loss, and training was halted when no improvement was observed for a set number of epochs (patience=10). Model validation employed a tolerance threshold of 5% error in performance and conversion predictions. In cases where the validation error exceeded this threshold, the model was retrained with an expanded dataset which incorporated the new experimental results.

This initial training focuses on optimizing process descriptors for a specific chemical reaction, forming the foundation of the Reac-Eval workflow. The script includes tools for data preparation, model training using a MLP architecture with early stopping to prevent overfitting, and prediction algorithms to generate optimal reaction conditions for subsequent evaluations.

GitHub Repository:

https://github.com/catm542-ai/Reac-Discovery/blob/main/src/ML_model_M1.py.

1.3.4. Optimization of Geometry Descriptors (G2)

The neural network training (M2) and optimization process was carried out in Python (version 3.13.0), utilizing *TensorFlow* (version 2.12.0) for the construction and training of the neural network, *Pandas* (version 2.2.3) for data manipulation, and *NumPy* (version 2.1.0) for mathematical operations.

After the reaction conditions were optimized, the initial dataset was modified by incorporating the metrics of the initial reactors provided by Reac-Gen. These metrics include tortuosity, surface area, structure volume, packing percentage, as well as the reactor construction parameters: size and level. This expanded dataset formed the basis for the subsequent optimization of reactor geometry.

The previously trained neural network model, along with a file generated by Reac-Gen containing multiple combinations of reactor descriptors, topological descriptors, geometry types, and previously optimized process parameters, was used to predict which reactor geometries would achieve the highest Space-Time Yield (STY). The neural network processed this input to predict the necessary descriptors that maximize STY, enabling the identification of the optimal geometry and its corresponding topological descriptors. STY was prioritized as the primary metric due to its direct correlation with reactor productivity, a critical parameter in industrial applications. Maximizing STY ensures that the reactor operates at its highest efficiency under optimized conditions, surpassing the limitations of traditional metrics like conversion alone. In order to achieve this, a set of potential reactor characteristics, generated by Reac-Gen, was passed to the model, which then selected the geometries with the highest STY.

The neural network used in this process was a MLP with two hidden layers and a ReLU activation function. The topology of the neural network consisted of 50 neurons in the first hidden layer and 30 neurons in the second hidden layer,

providing a balance between modeling capacity and computational complexity. The model was trained using the Adam optimizer with a learning rate of 0.001, and the mean squared error (MSE) was used as the loss function.

To avoid overfitting, the same methodology employed in the previous algorithm was applied. Once the model predicted the geometries with the highest STY, these were passed through Reac-Fab's printability algorithm to verify that the selected geometries were printable. This validation ensured that only geometries suitable for successfully 3D printed were considered. Ultimately, the top geometries-based on both the model's predictions and their printability validation, were selected for experimental validation in Reac-Eval.

This model focuses on optimizing geometric descriptors of the reactor, such as tortuosity, surface area, structure volume, and packing percentage, to achieve the highest Space-Time Yield (STY) under previously optimized process conditions. The script integrates advanced preprocessing methods, a MLP architecture for training, and algorithms for generating and ranking reactor geometries. Additionally, it incorporates the interaction with Reac-Fab's printability validation model to ensure the feasibility of 3D printing the predicted geometries.

GitHub Repository:

https://github.com/catm542-ai/Reac-Discovery/blob/main/src/ML_model_M2.py.

1.4. Case Studies

Both the hydrogenation of acetophenone and the cycloaddition of epichlorohydrin with CO₂ were carried out using the Reac-Discovery methodology, which integrates three modules: Reac-Gen, Reac-Fab, and Reac-Eval. Reaction conditions were optimized through two optimization campaigns: G1 and G2. The G1 campaign established initial correlations between reactor parameters, process conditions, and catalytic activity, while G2 refined these correlations to optimize both reactor geometry and operating conditions.

In Case Study 1, the optimized geometry selected for validation during the G2 campaign was a Lidinoid structure with a size of 15 and a level of 0. The operational conditions for the optimized reactor included a liquid flow rate of 200 $\mu\text{L}/\text{min}$, a gas flow rate of 6.8 mL/min, a concentration of 1.7 M acetophenone in acetonitrile, and a pressure of 8 bar. In Case Study 2, the optimized geometry selected for validation during the G2 campaign was a Schoen_G structure with a size of 35 and a level of 0. The operational conditions for this optimized reactor included a liquid flow rate of 300 $\mu\text{L}/\text{min}$, a gas flow rate of 490 $\mu\text{L}/\text{min}$, a concentration of 4 M epichlorohydrin in isopropanol, and a pressure of 5 bar. For both cases, each reactor had a specific residence time depending on its configuration, ensuring controlled and consistent reaction conditions.

The reactions were monitored in real-time, capturing and analyzing Yield and space-time yield (STY) data using the Reac-Eval module. The data obtained was

used to train the machine learning models M1 and M2 for both cases. Model M1 was employed to optimize process descriptors, while M2 refined the reactor's topological and geometric descriptors. This approach enabled continuous improvement of the catalytic reactor design and reaction conditions.

The space-time yield (STY) was calculated as a measure of the reactor's productivity, based on the following equation:

$$STY = \frac{\text{product weight}}{\text{reactor volume} \times \text{residence time}} = \frac{g}{L.h} \quad (1)$$

1.4.1. Characterization of functionalization of 3D-Printed Structures

Immobilization of Pd NPs.

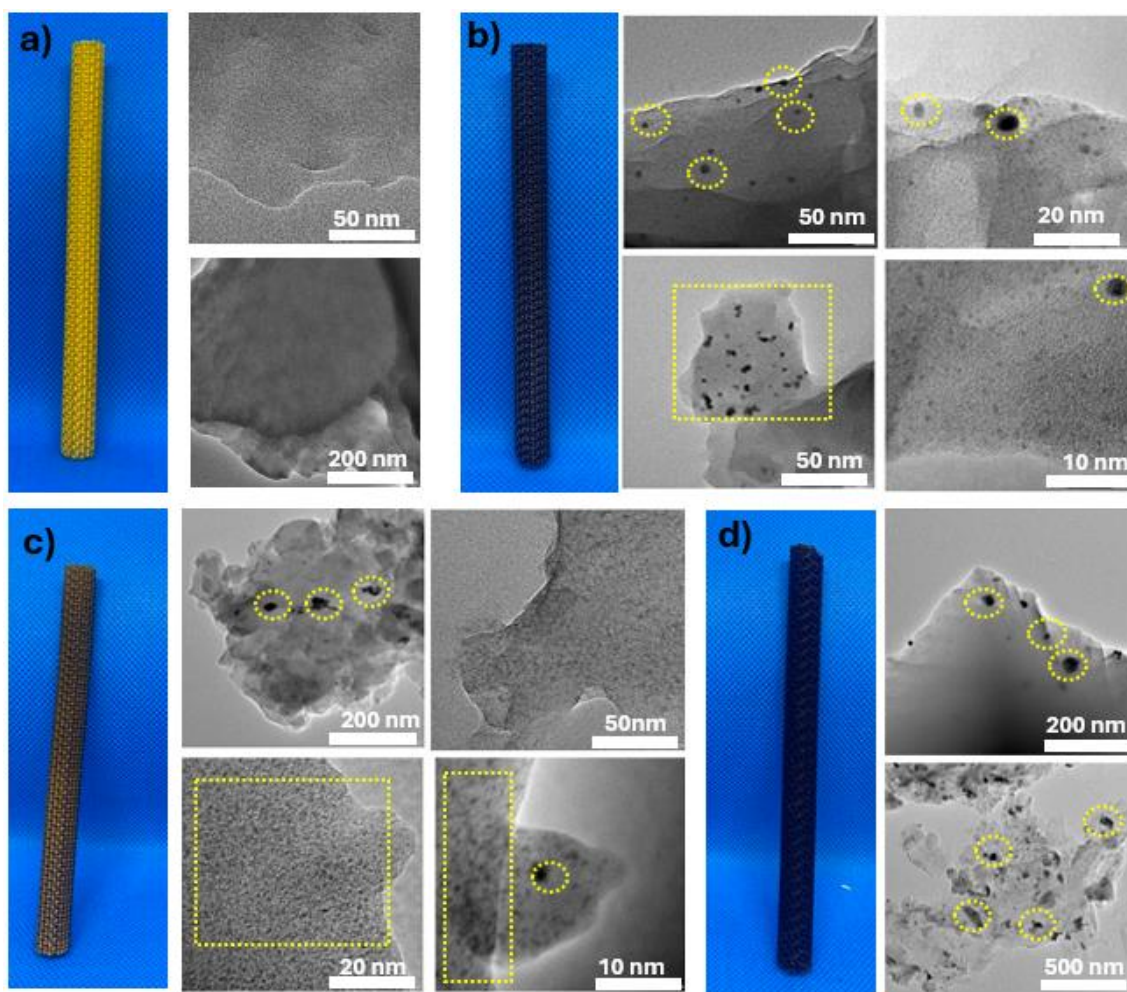


Figure S22. TEM images for the Pd modified 3D reactors. A) Unmodified 3D-reactor containing imidazole moiety B) Pd- modified using PdCl_2 (0.12 M) C) Pd-modified using PdCl_2 (0.06 M) and D) Pd-modified using $\text{Pd}(\text{AcO})_2$ (0.12 M).

The 3D-printed reactors were prepared using the previously described epoxy-rich formulation and subsequently functionalized with imidazole groups via HCl treatment and nucleophilic substitution. Pd immobilization was performed by impregnating with PdCl_2 or $\text{Pd}(\text{OAc})_2$ solutions, followed by in situ reduction with NaBH_4 to form $\text{Pd}(0)$ nanoparticles. TEM analysis confirmed well-dispersed Pd

nanoparticles (2–5 nm) across the reactor surface, with smaller particle sizes observed for the methyl imidazole functionalization compared to butyl and decyl analogues. Additionally, visual inspection revealed a color change from orange to shiny black upon reduction, indicating successful Pd nanoparticle formation. The ICP analyses showed a Pd loading of 3.89 ± 0.04 %wt for 3D printed structures prepared with 0.12 M, while the one prepared with 0.06 M yielded a Pd loading of 0.70 ± 0.02 %wt.

1.4.2. Integration of Reac-Discovery Modules

This section aims to clarify the integration of the Reac-Discovery modules: Reac-Gen, Reac-Fab, and Reac-Eval, and how they work together to achieve the iterative digital design of custom catalytic reactors. Figure S23 illustrates the complete workflow and the interactions between these modules, detailing each stage of the process.

The process begins with Reac-Gen, which generates initial digital structures (e.g., gyroid geometries) using mathematical equations. These structures are parameterized through geometric descriptors such as size, level, and resolution, while reactor metrics such as surface area, tortuosity, packing percentage, and free volume are calculated. As outputs, Reac-Gen produces STL files for 3D printing and an XLSX file containing the reactor descriptors.

These STL files and associated data are transferred to the Reac-Fab module, where a machine learning model evaluates the printability of the geometries. Structures that meet the printability criteria are 3D printed, functionalized, and prepared as catalytic reactors. The functionalized structures are then tested in Reac-Eval, where boundary conditions are defined, and a random reaction set is generated. These reaction conditions are executed experimentally, utilizing a benchtop NMR spectrometer to measure key metrics such as Yield and space-time yield (STY) in real time.

The data obtained in Reac-Eval is used in two optimization campaigns: G1 and G2. During the G1 campaign, initial correlations between geometric descriptors and process conditions are established. In the G2 campaign, these correlations are refined to improve both reactor geometry and operational conditions.

Two neural network models, M1 and M2, are trained during this process. Model M1 focuses on optimizing process descriptors, such as flow rates, temperature, and concentration, while model M2 optimizes the geometric descriptors generated by Reac-Gen, refining the structural geometry of the reactor. Both models generate predictions that are validated by the Reac-Fab printability model, ensuring that the optimized configurations are feasible for printing and operation in continuous flow. Validated configurations are sent back to Reac-Gen for the generation of optimized STL structures, which re-enter the iterative workflow until the optimal configuration is achieved.

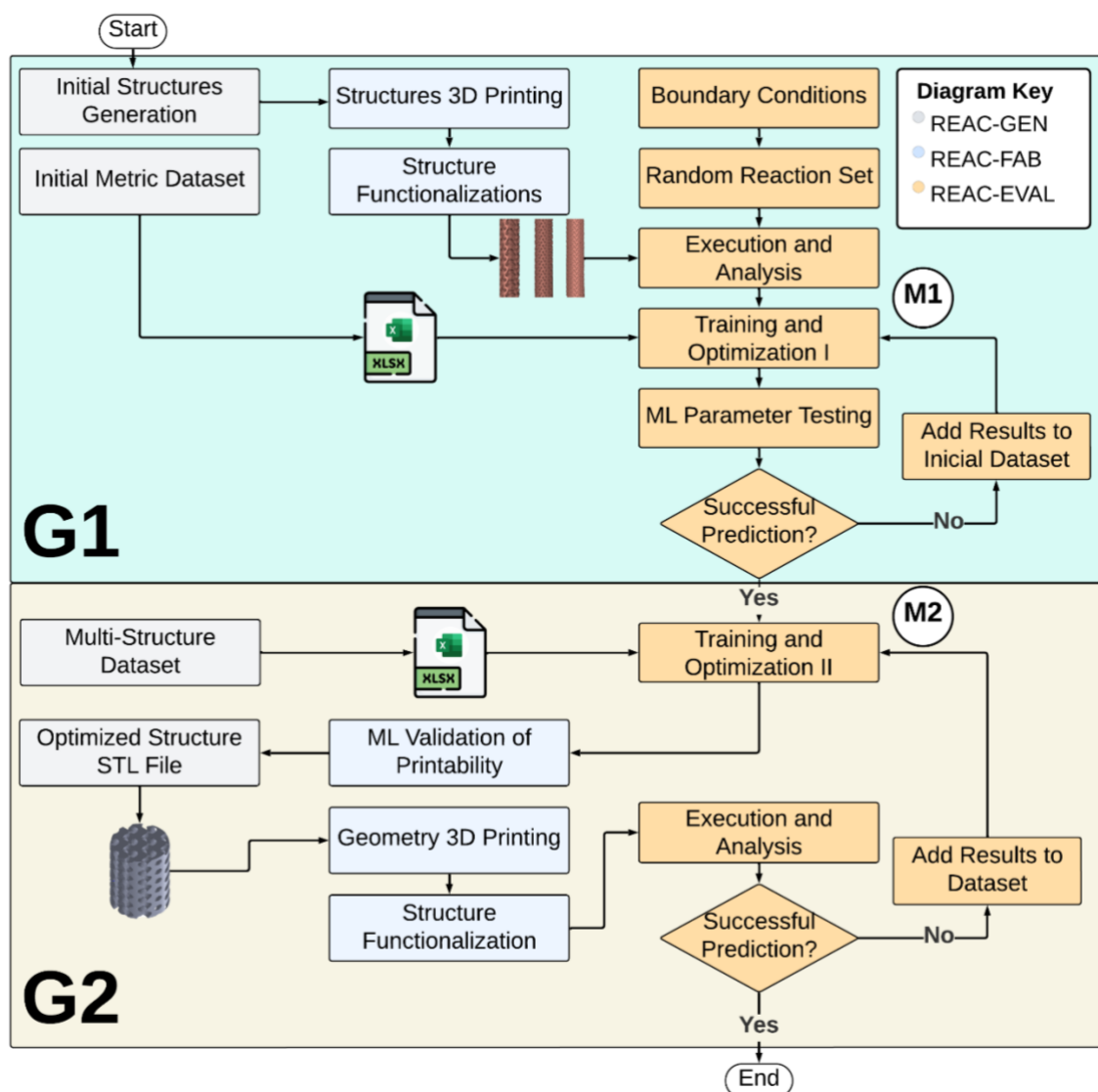


Figure S23. Schematic representation of the Reac-Discovery workflow. Together, Reac-Discovery enables the simultaneous optimization of both process and geometric descriptors, facilitating the digital design of custom catalytic reactors tailored for specific applications. Abbreviations: ML, Machine Learning; STL, Standard Tessellation Language; G1/G2, Reac-Discovery optimization campaigns; M1/M2, predictive models used within the workflow.

1.4.3. Case Study 1: Hydrogenation of Acetophenone

A. Initial Reactor Characterization through Reac-Gen

The application of Reac-Discovery begins with the Reac-Gen module generating nine gyroid-type reactor geometries. These geometries are characterized by variations in geometric descriptors such as size and level, which directly influence reactor descriptors like surface area, relative tortuosity, free volume, and packing percentage. This variability ensures a diverse dataset for evaluating reactor performance under specific reaction conditions. Although the present application uses gyroid structures, the platform is flexible and allows starting from different families of architectures; the key objective is

to maximize geometric diversity across the initial reactor population. To support this claim, Table S1 provides a summary of the calculated reactor descriptors for the nine initial gyroid geometries generated by Reac-Gen.

Table S1. Reactor descriptors for nine initial gyroid geometries generated by Reac-Gen. Source data are provided as a Source Data file.

Size	Level (Thickness μm)	Free Volume (mL)	Packing Percentage	Surface Area (mm^2)	Tortuosity
10	250	7.37	15	10532.64	3.32
	424	6.61	25	10665.95	3.30
	600	5.65	35	10713.61	3.23
16	250	6.63	23	16662.72	4.97
	424	5.29	39	16498.05	4.48
	600	4.01	54	15877.83	4.77
22	250	5.98	31	21616.39	5.61
	424	4.20	51	20470.32	5.50
	600	2.65	69	17476.27	5.07

B. Reaction Dataset Boundary Conditions

The reaction dataset generated by Reac-Eval comprised 60 reaction conditions, delimited by predefined boundary conditions to ensure diverse and representative experimental coverage. For process descriptors, the liquid flow rate was defined within a range of 100 to 400 $\mu\text{L}/\text{min}$, and the gas flow rate spanned from 2 to 6 mL/min . Exact concentrations of 0.5 M, 1.0 M, and 1.5 M were specified to enhance the visibility of reactants and products in the benchtop NMR spectrometer used for real-time analysis. For geometric descriptors, the dataset included the nine gyroid geometries with parameters detailed in Table S1.

C. Execution and Analysis of the 60 Reaction Experiments

To evaluate the performance of the Acetophenone hydrogenation reaction, a total of 60 experiments were conducted using the Reac-Eval platform as part of the G1 and G2 optimization campaigns. The experimental conditions, defined within the boundary conditions of the reaction dataset, covered a wide range of process descriptors (liquid flow rate, gas flow rate, and concentration) and geometric descriptors (nine gyroid geometries with variations in size, level, and other reactor metrics). Each experiment was

executed sequentially under continuous flow conditions, with real-time monitoring facilitated by the integrated benchtop NMR spectrometer.

The characterization and quantification of the products were performed using ^1H -NMR spectroscopy. The NMR data provided direct insight into the conversion, yield, and space-time yield (STY) of the reaction. The quantification was based on a direct comparison between the signals of acetophenone and the hydrogenated product, 1-phenylethanol. Specifically, the integration of the characteristic aromatic protons of acetophenone (signal "a", corresponding to two equivalent protons in ortho to carbonyl) was compared to the integration of the CH proton of 1-phenylethanol (signal "b"), which appears as a multiplet around 4.4–4.5 ppm due to coupling with the adjacent CH_3 group and aromatic protons (Figure S24). Given the high selectivity of the reaction (>99%), this direct ratio between reactant and product signals was used to determine the reaction yield accurately.

Since no other by-products were observed, the following formula was applied to determine the yield:

$$\text{Yield}(\%) = 100 \times \frac{I_b}{\frac{I_a}{2} + I_b} \quad (2)$$

The space-time yield (STY) was calculated to evaluate the reactor's productivity under each experimental condition. The formula used was:

$$\text{STY} = \frac{\text{product weight}}{\text{volume reactor} \times \text{residence time}} = \frac{g}{L \cdot h} \quad (3)$$

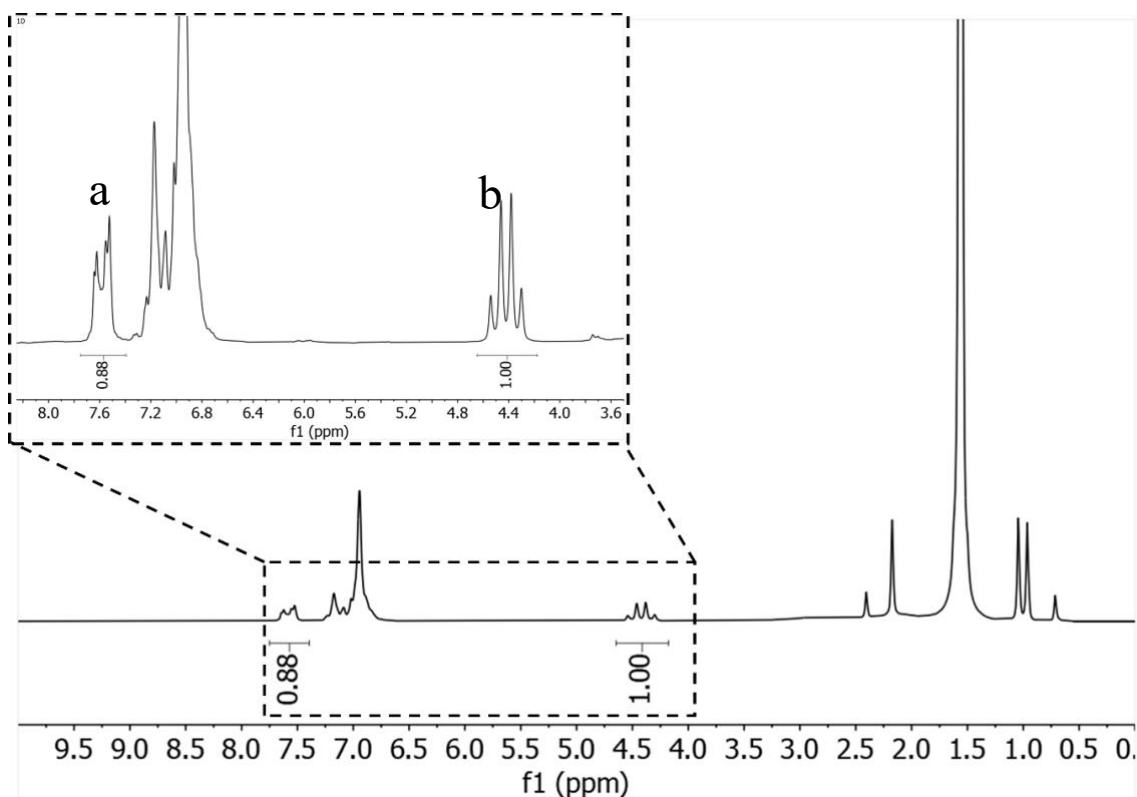


Figure S24. Representative ^1H -NMR (80 MHz) spectrum for the Hydrogenation of Acetophenone. **a** corresponds to the aromatic protons of acetophenone (2 equivalent protons) and **b** corresponds to the CH proton of 1-phenylethanol.

Results from the experimental phase showed maximum experimental values of 69% yield and STY of 192 g L⁻¹ h⁻¹. Higher flow rates correlated to lower residence times, which STY values, while higher temperatures increased kinetics (max. 70°C due to Pd nanoparticle PdNP instability at higher temperatures) and therefore improved both yield and STY. These results served as the basis for defining the input features and targets used during M1 training, as shown in. Figure S25, emphasizes the influence of process and geometric descriptors on reaction performance.

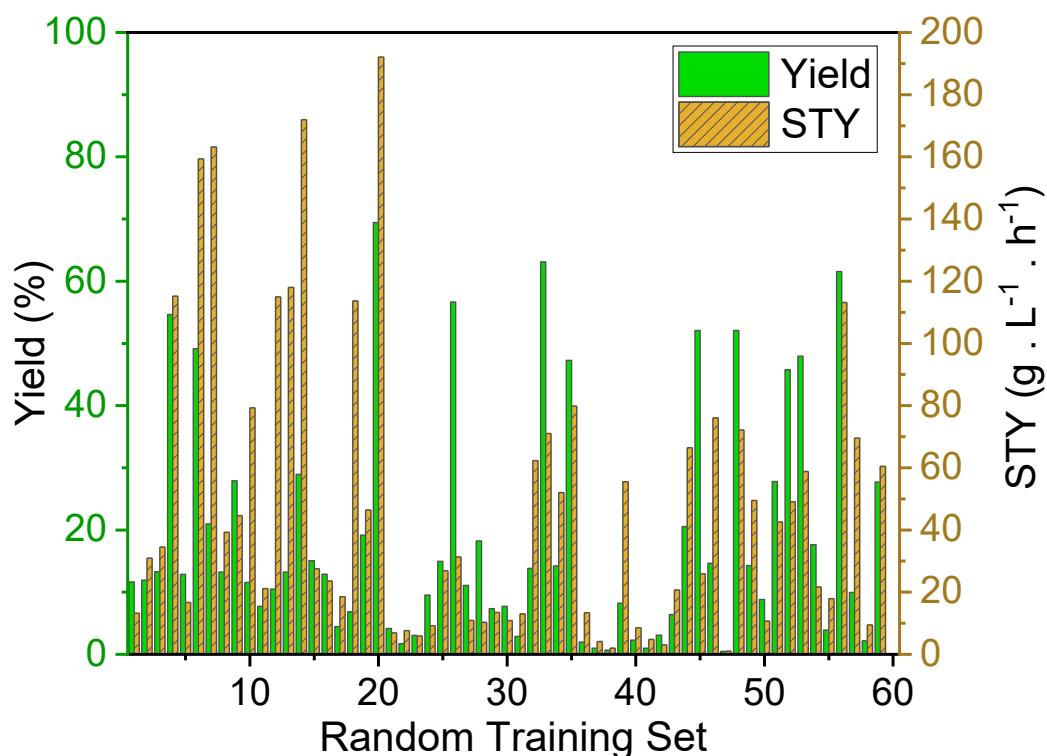


Figure S25. Yield (%) and space-time yield (STY, g L⁻¹ h⁻¹) results for the 60 experiments conducted under varying process and geometric descriptors in Case Study 1 using the Reac-Eval platform. Source data are provided as a Source Data file.

D. Optimization of Process Descriptors

The maximum yield predicted through the optimization of process descriptors by model M1 was 100%, experimentally validated with a value of 98% under the selected optimal conditions (Figure S26A). Similarly, the maximum space-time yield (STY) predicted by model M1 through the same optimization was 264 g L⁻¹ h⁻¹, with an experimental value of 279 g L⁻¹ h⁻¹, confirming the accuracy of the Reac-Discovery predictive model (Figure S26B).

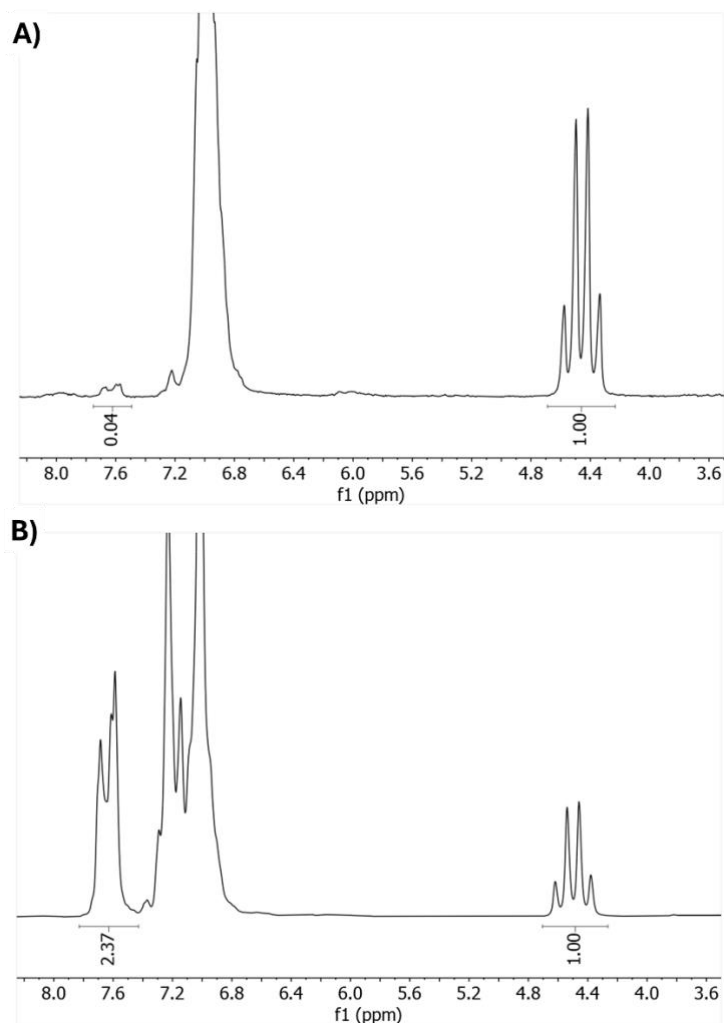


Figure S26. Results of the G1 optimization campaign. A) ^1H NMR (80 MHz) Spectrum for Yield (98%) and STY ($43 \text{ g L}^{-1} \text{ h}^{-1}$) with $200 \text{ }\mu\text{L/min}$ liquid flow, 7.3 mL/min gas flow, 70°C , 0.5 M , 4.20 mL free volume, and 8 bar ; B) Yield (46%) and STY ($279 \text{ g L}^{-1} \text{ h}^{-1}$) with $200 \text{ }\mu\text{L/min}$ liquid flow, 6.8 mL/min gas flow, 70°C , 1.7M , 4.01 mL free volume, and 5 bar .

E. Optimization of Geometry Descriptors

Reac-Discovery predicted the STY value for the optimized Lidinoid reactor geometry. The experimental results confirmed this prediction, yielding an STY value of $337 \text{ g L}^{-1} \text{ h}^{-1}$ for the Lidinoid geometry (Figure S27).

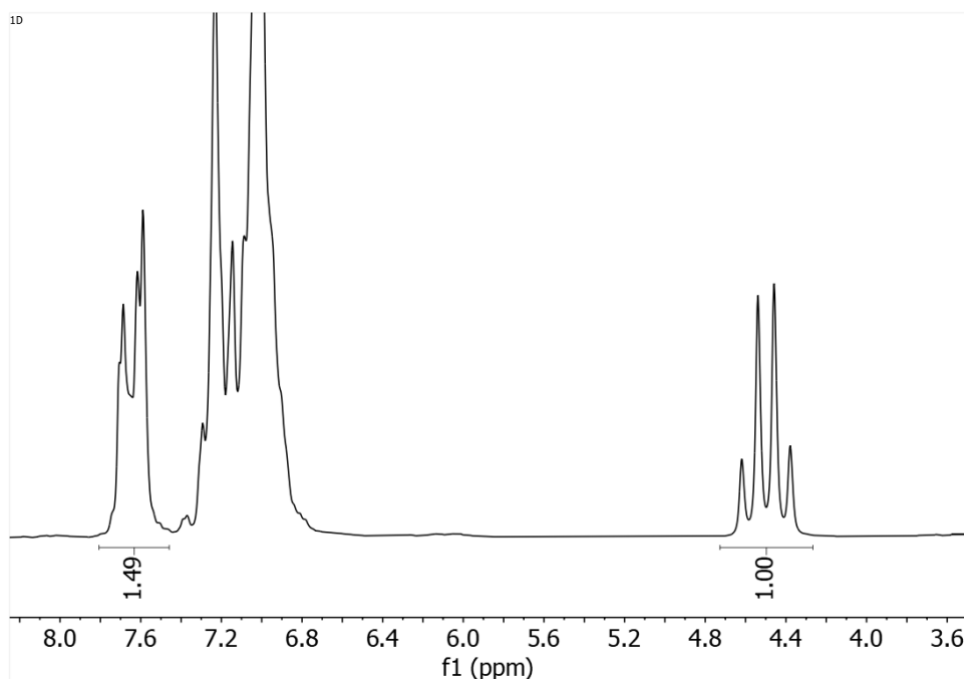


Figure S27. ¹H NMR (80 MHz) Spectrum for Yield (58%) and STY (337 g L⁻¹ h⁻¹) with 50 μL/min liquid flow, 6.8 mL/min gas flow, 70°C, 1.7 M, 4.28 mL free volume, and 8 bar.

1.4.4. Functionalization of reactors with covalently immobilized ionic liquids

The functionalization of the 3DP structures were characterized by FTIR spectra (Figure S28), following the disappearance of epoxy groups at 905 cm⁻¹ (C-O stretching, highlighted in red) of the GMA and the appearance of specific bands related to the imidazole ring in butyl imidazole at 1560 cm⁻¹ (C=N ring stretching) and around 625 cm⁻¹ (out-of-plane ring vibrations), highlighted in blue. Moreover, no significant changes were observed in the thermal analysis or DSC measurements after functionalization.

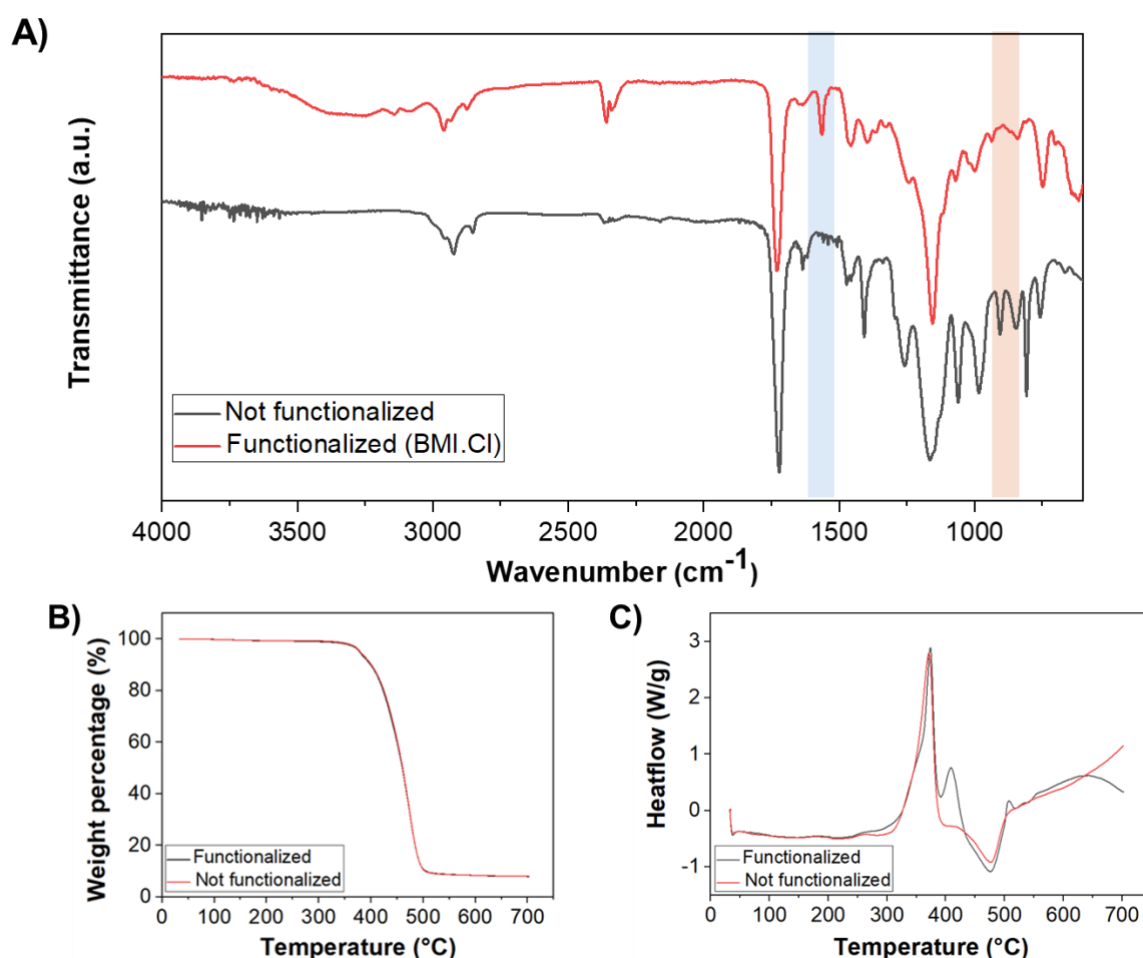


Figure S28. Characterization of 3DP formulation functionalization. A) FTIR-ATR (Fourier Transform Infrared Spectroscopy with Attenuated Total Reflection) spectra of the polymeric material before modification (in black) and after imidazolium functionalization. B) TGA (Thermogravimetric Analysis) of the functionalized 3DP (Three-Dimensional Printed) formulation. C) DSC (Differential Scanning Calorimetry) analysis.

1.4.5. Case Study 2: CO₂ Cycloaddition

A. Initial Reactor Characterization through Reac-Gen

As in Case Study 1, Case Study 2 began with the generation of initial reactor geometries using the Reac-Gen module. This ensured variation in key descriptors such as size, level, surface area, free volume, packing percentage, and tortuosity to explore geometric diversity. Table S1 summarizes the calculated reactor descriptors for the initial geometries generated.

B. Reaction Dataset Boundary Conditions

The reaction dataset generated by Reac-Eval comprised 60 reaction conditions, delimited by predefined boundary conditions to ensure diverse and representative experimental

coverage. For process descriptors, the liquid flow rate was defined within a range of 50 to 200 $\mu\text{L}/\text{min}$, and the gas flow rate spanned from 50 to 500 $\mu\text{L}/\text{min}$. Exact concentrations of 2 M, 3 M, and 4 M were specified to enhance the visibility of reactants and products in the benchtop NMR spectrometer used for real-time analysis. For geometric descriptors, the dataset included the nine gyroid geometries with parameters detailed in Table S1.

C. Execution and Analysis of the 60 Reaction Experiments

To evaluate the performance of the CO_2 cycloaddition reaction, a total of 60 experiments were conducted using the Reac-Eval platform as part of the G1 and G2 optimization campaigns. The experimental conditions, defined within the boundary conditions of the reaction dataset, covered a wide range of process descriptors (liquid flow rate, gas flow rate, and concentration) and geometric descriptors (nine gyroid geometries with variations in size, level, and other reactor metrics). Each experiment was executed sequentially under continuous flow conditions, with real-time monitoring facilitated by the integrated benchtop NMR spectrometer.

The characterization and quantification of the products were performed using ^1H -NMR spectroscopy. The NMR data provided direct insight into the conversion and yield of the reaction, as well as the space-time yield (STY). For this purpose, 1-methylimidazole was used as an external standard due to its well-defined peaks in the aromatic region (6.75–7 ppm). The integral of 1-methylimidazole added in each experiment was adjusted to establish a direct correlation with the converted product. The quantification of the remaining epichlorohydrin was based on the integration of its characteristic signals corresponding to the two protons on the CH_2 group of the epoxide ring (near the oxygen atom). These protons (denoted as signal "a") were directly compared to the signals of the internal standard (denoted as "b"). The signal corresponding to the cyclic carbonate produced (signal "c") was also evaluated and isolated, and a mass balance was performed (Figure S29).

Since no other by-products was observed, the following formula was applied to determine the yield:

$$\text{Yield}(\%) = 100 - \frac{\text{Moles of remaining epichlorohydrine}}{\text{Moles of initial epichlorohydrine}} \times 100 \quad (4)$$

The space-time yield (STY) was calculated to evaluate the reactor's productivity under each experimental condition. The formula used was:

$$\text{STY} = \frac{\text{product weight}}{\text{volume reactor} \times \text{residence time}} = \frac{g}{L.h} \quad (5)$$

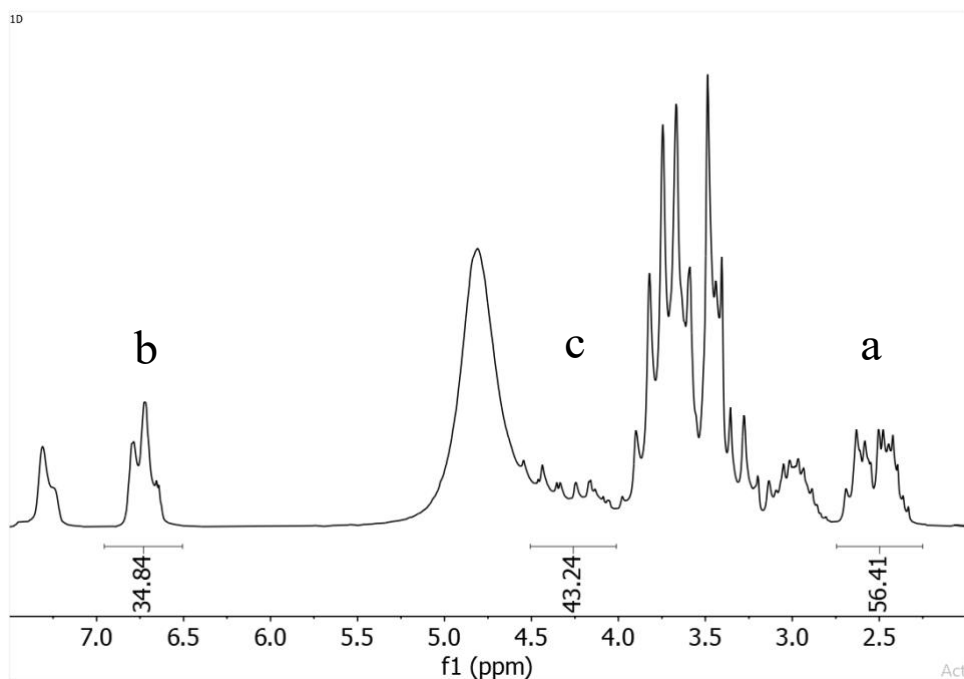


Figure S29. Representative ^1H -NMR (80 MHz) spectrum for the CO_2 cycloaddition reaction. In the spectrum, **a** corresponds to the protons on the CH_2 group of the epoxide ring (near the oxygen atom) of the epichlorohydrin. **b** corresponds to the CH_3 group of the methylimidazole employed as internal standard. **c** corresponds to 2 protons of the ring $\text{O}-\text{CH}_2-\text{CH}(\text{CH}_2\text{Cl})-\text{O}$ protons of the 1,3-dioxolan-2-one.

Results from 60 experiments highlight the yield and STY values achieved under diverse experimental conditions, as illustrated in Figure S21. Maximum values of 70% yield and $412 \text{ g L}^{-1} \text{ h}^{-1}$ STY, shown in Figure S31.

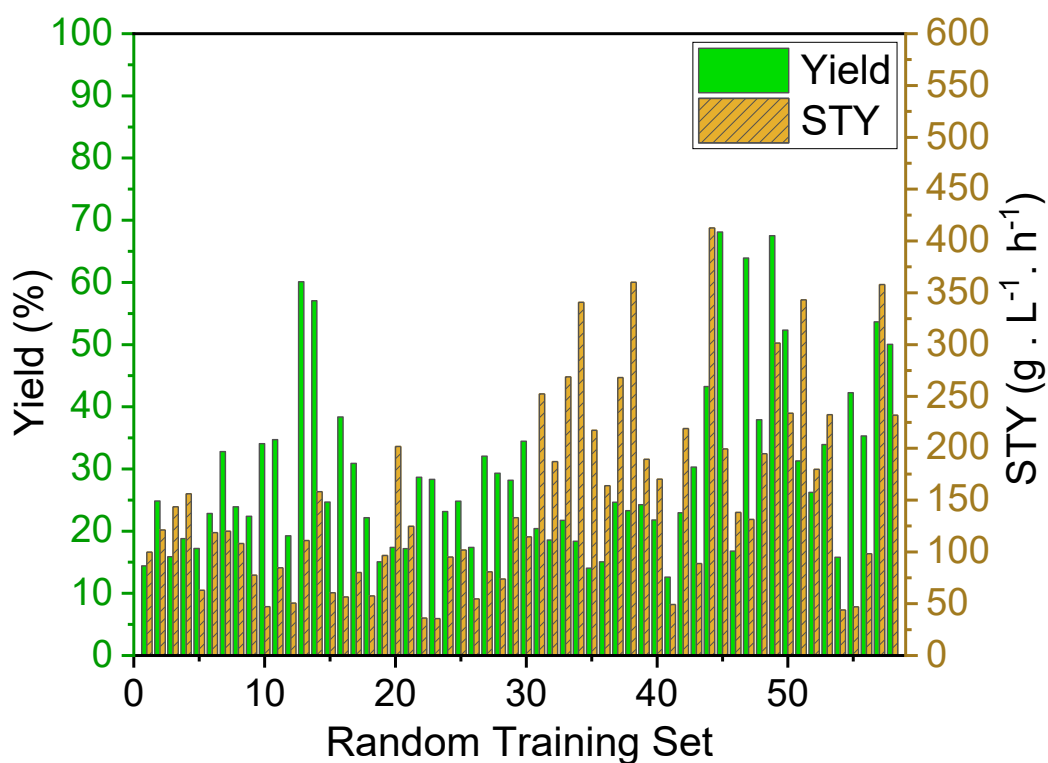


Figure S30. Yield (%) and space-time yield (STY, $\text{g L}^{-1} \text{h}^{-1}$) results for the 60 experiments conducted under varying process and geometric descriptors using the Reac-Eval platform. Source data are provided as a Source Data file.

D. Optimization of Process Descriptors

The predicted yield was achieved using a 1 M solution of epichlorohydrin in isopropanol at 120°C , with a liquid flow rate of $50 \mu\text{L min}^{-1}$ (residence time: 120 min) and a gas flow rate of $490 \mu\text{L min}^{-1}$, under a fixed pressure of 5 bar; using the gyroid reactor design with size 22 and level 0.75. Similarly, the maximum STY was achieved under conditions of 4 M concentration, 120°C , a liquid flow rate of $300 \mu\text{L min}^{-1}$, a gas flow rate of $490 \mu\text{L min}^{-1}$, a free volume of 4.20 mL, and 5 bar, with the same gyroid geometry. The experimental results confirmed the model predictions, achieving a yield of 90% (predicted: 90%) and an STY of $563 \text{ g L}^{-1} \text{h}^{-1}$ (predicted: $565 \text{ g L}^{-1} \text{h}^{-1}$), further demonstrating the high accuracy of the M1 model (Figure S31).

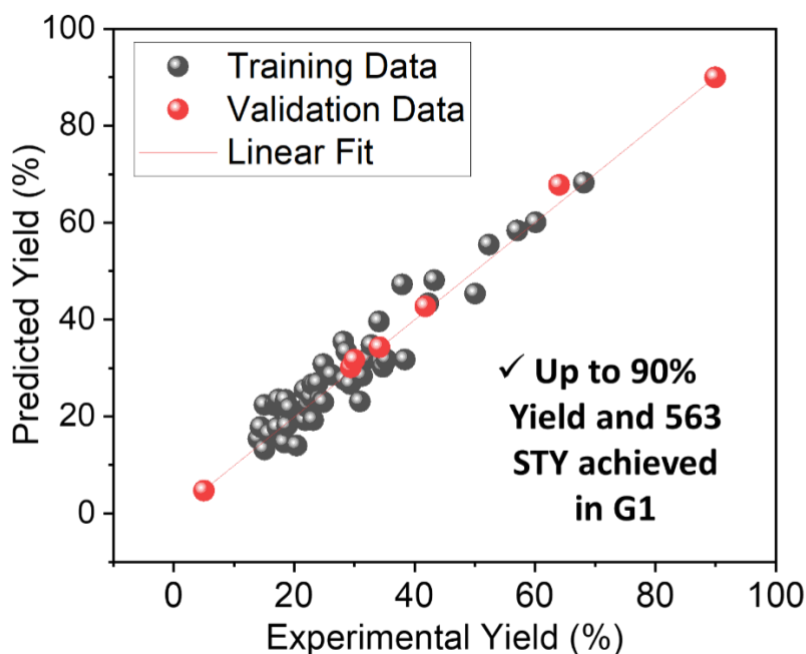


Figure S31. M1 model correlation with training data and Experimental results. Source data are provided as a Source Data file.

E. Optimization of Geometry Descriptors

Reac-Discovery predicted STY values for four optimized reactor geometries: N1, N2, N3, and N4. The experimental results confirmed these predictions, yielding STY values of $803 \text{ g L}^{-1} \text{h}^{-1}$, $780 \text{ g L}^{-1} \text{h}^{-1}$, $757 \text{ g L}^{-1} \text{h}^{-1}$, and $735 \text{ g L}^{-1} \text{h}^{-1}$ for the Schoen_G, Diamond_Primitive, Diamond, and Neovius geometries, respectively (Figure 32).

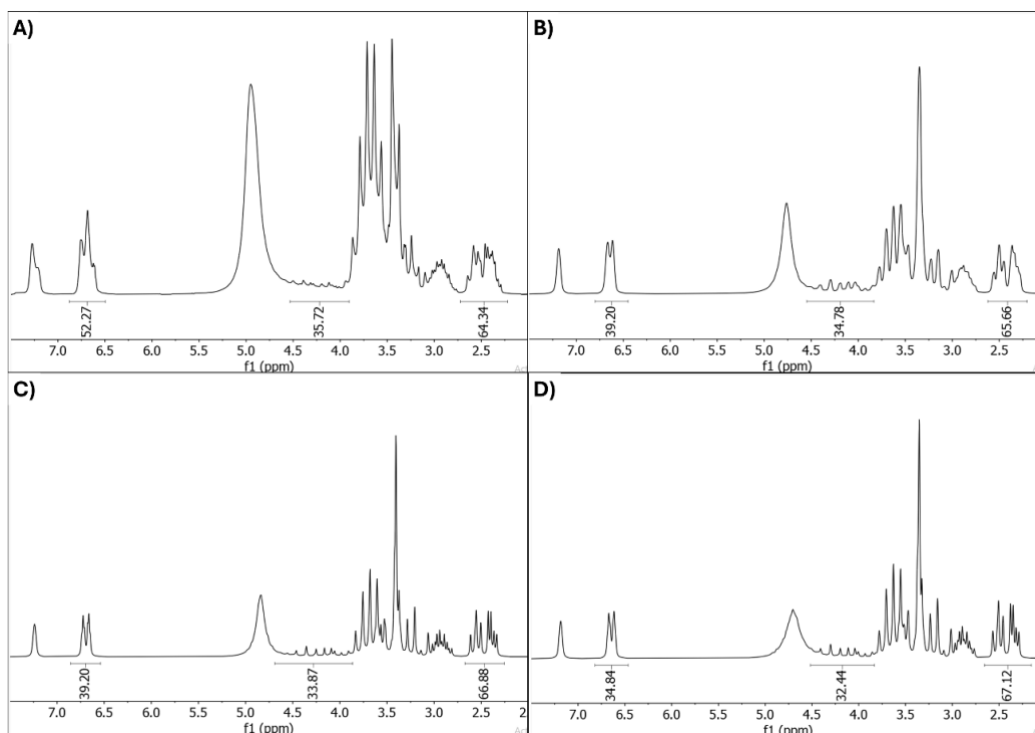


Figure S32. Comparison of the Four Best Performing Reactors in G2 Optimization. ^1H NMR (80 MHz) spectra for the four optimized reactor geometries designed by Reac-Discovery, showing the experimental yield values used to calculate the corresponding STY: (A) Schoen_G, (B) Diamond_Primitive, (C) Diamond, and (D) Neovius. 300 $\mu\text{L}/\text{min}$ liquid flow, 490 $\mu\text{L}/\text{min}$ gas flow, 120°C, 4M, 4.28 mL free volume, and 5 bar

Once the optimized structures were validated, the scope of the reaction was further explored under the conditions established after the two optimization campaigns, G1 and G2, by testing different reagents. The results are illustrated in Figure S33.

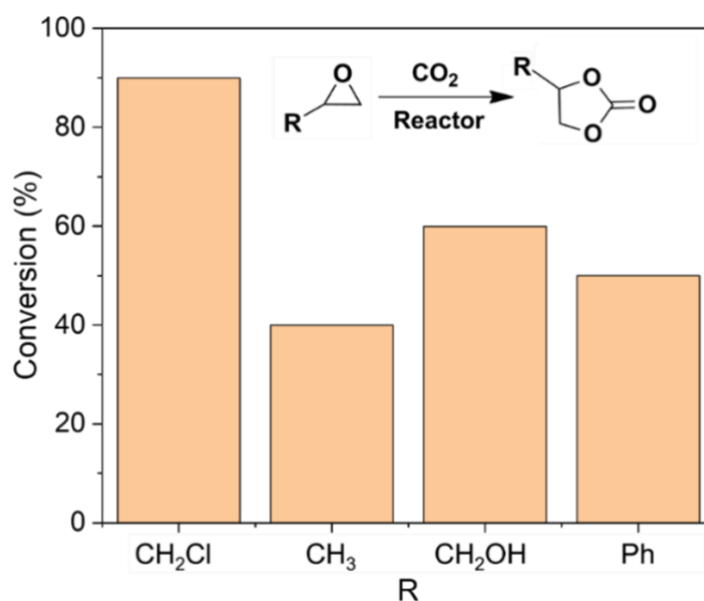


Figure S33. Conversion comparison of cyclic carbonate synthesis using various epoxide derivatives under Y1 optimized conditions (G1). Source data are provided as a Source Data file.

Additionally, we tested the cycloaddition reaction of CO₂ with epichlorohydrin using the previously optimized conditions but employing flue gas with a 15% CO₂ concentration. This setup simulates the typical conditions of CO₂ emissions from chimneys. Under these conditions, a yield of 20% was obtained.

An additional experiment was conducted using a classical honeycomb reactor geometry. This honeycomb structure was fabricated via 3D printing at the highest possible resolution. It is important to note that printing this geometry presented significant challenges due to its poor internal interconnection compared to the highly structured and interconnected nature of POC geometries. This lack of interconnectivity contributed to its low mechanical stability after the reaction, as observed in Figure S34.

The comparison was performed using reactors occupying the same volume, ensuring a fair evaluation under identical conditions. The results showed that the optimized Schoen_G S35L0 reactor achieved a yield of 90% and an STY of 804 g·L⁻¹·h⁻¹, whereas the honeycomb reactor achieved a lower yield of 73% and an STY of 168 g·L⁻¹·h⁻¹. This clearly demonstrates the advantages of POC structures over conventional honeycomb geometries, as their superior geometric complexity, higher surface area, and enhanced internal connectivity significantly improve mass transfer, mechanical stability, and overall reaction performance under optimized conditions.

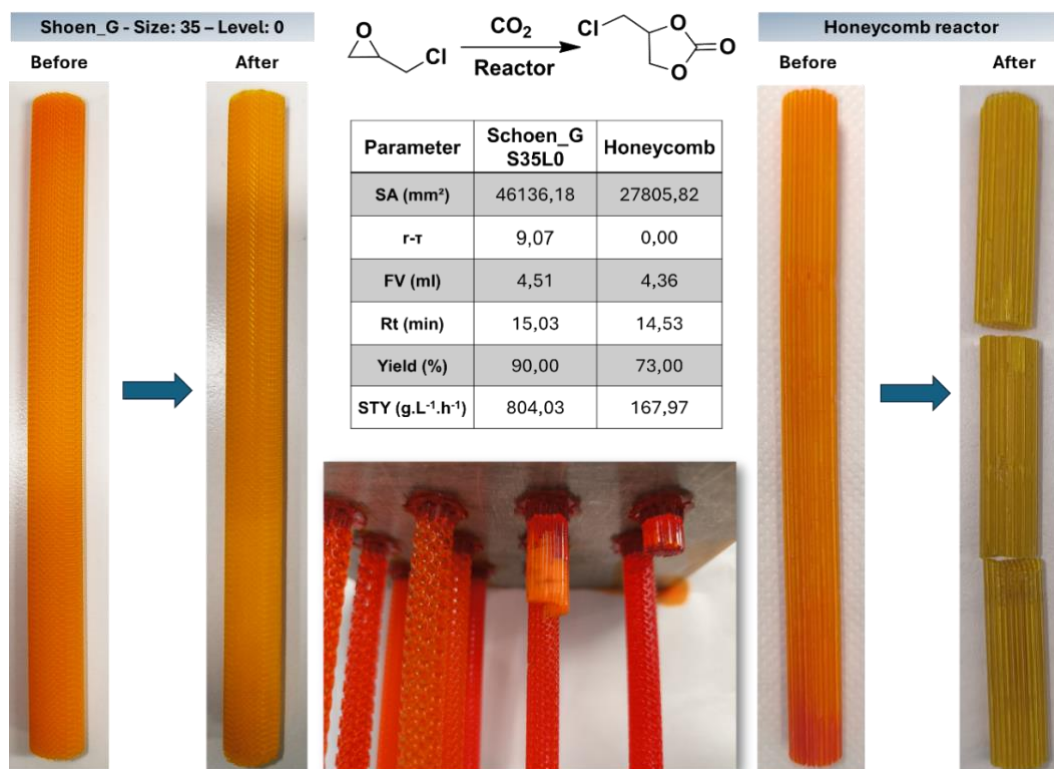


Figure S34. Comparison between the optimized Schoen_G (Size 35, Level 0) reactor and a conventional honeycomb reactor (wall thickness of 0.3 mm). Left: images of the Schoen_G reactor before and after a CO₂ cycloaddition reaction. Right: images of the honeycomb reactor before and after the same reaction, showing evidence of its reduced mechanical resistance. The upper center panel presents a comparative table summarizing the geometric features and catalytic performance of each reactor. The lower center image

illustrates the experimental difficulties encountered during the printing of honeycomb structures, in contrast to the smooth fabrication of periodic open cellular structures.

1.4.6. Comparison of Space-Time Yield (STY)

The optimized conditions in our study resulted in a space-time yield (STY) of $803 \text{ g L}^{-1} \text{ h}^{-1}$, which represents the highest value reported for this reaction using immobilized catalytic reactors. The following table summarizes some of the results reported in the literature, highlighting the significant improvement achieved in our work.

Table S2. Comparison of Space-Time Yield (STY) Case Study 2.

Substrate/epoxide	Epoxide flow rate (mL/min)	CO ₂ flow rate (mL/min)	Volumen Libre (mL)	Reaction conditions (T, P)	Catalyst req.	Residence Time (min)	Yield	STY (g L ⁻¹ h ⁻¹)
Epichlorohydrin ²	0.015	50.00	3.94	130°C ; 20 bar	PSIL(IMD)	0.08	43	170.12
Styrene oxide (SO) ³	0.005	0,05	2.75	150°C ; 140 bar	SILLP	50.00	53	83.23
Epichlorohydrin ⁴	0.01	15.00	4.4	120°C ; 13 bar	MMFR	0.30	100	237.38
Glicidol Oxide ⁵	0.155	NA	4.1	70°C ; 13 bar	TBD@Merrifield	26.42	99	87.62
Epichlorohydrin ¹	0.05	0.20	5.75	120°C ; 6 bar	SILLP	23.00	67	95.45
Epichlorohydrin ⁶	0.025	5.00	5.50	140°C ; 11 bar	PPSI	1.10	89	6.63

Note: PSIL(IMD) refers to a polymer-supported ionic liquid based on an imidazolium moiety. SILLP stands for Supported Ionic Liquid-Like Phase, meaning a solid material functionalized with ionic liquid fragments that mimics the behavior of a liquid ionic phase. MMFR denotes a Merrifield resin functionalized with catalytically active species, TBD@Merrifield indicates Merrifield resin modified with the organic base TBD (1,5,7-triazabicyclo[4.4.0]dec-5-ene), while PPSI indicates Porous Polystyrene-supported Imidazolium.

Finally, the repository and associated files related to Reac-Discovery are available at the following link: <https://github.com/catm542-ai/Reac-Discovery/tree/main>.

References

1. Marchetti, S. *et al.* High-resolution 3D printable inks based on functional polymeric ionic liquids for applications in carbon dioxide valorization. *Addit. Manuf.* **89**, 104304 (2024).
2. Wang, T. *et al.* Highly recyclable polymer supported ionic liquids as efficient heterogeneous catalysts for batch and flow conversion of CO₂ to cyclic carbonates. *RSC Adv.* **7**, 2836–2841 (2017).
3. Valverde, D., Porcar, R., Lozano, P., García-Verdugo, E. & Luis, S. V. Multifunctional Polymers Based on Ionic Liquid and Rose Bengal Fragments for the Conversion of CO₂ to Carbonates. *ACS Sustain. Chem. Eng.* **9**, 2309–2318 (2021).
4. Bui, T. Q., Konwar, L. J., Samikannu, A., Nikjoo, D. & Mikkola, J.-P. Mesoporous Melamine-Formaldehyde Resins as Efficient Heterogeneous Catalysts for Continuous Synthesis of Cyclic Carbonates from Epoxides and Gaseous CO₂. *ACS Sustain. Chem. Eng.* **8**, 12852–12869 (2020).
5. Zanda, N., Sobolewska, A., Alza, E., Kleij, A. W. & Pericàs, M. A. Organocatalytic and Halide-Free Synthesis of Glycerol Carbonate under Continuous Flow. *ACS Sustain. Chem. Eng.* **9**, 4391–4397 (2021).
6. Yu, Z., Ishitani, H. & Kobayashi, S. Continuous-flow synthesis of cyclic carbonates with polymer-supported imidazolium-based ionic liquid (Im-PSIL) catalysts. *GREEN Chem.* **26**, 11548–11555 (2024).