Is machine learning applicable in retrosynthesis of chemicals?

CHEM0027: Chemical Literature

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Contents

Reflective Commentary

My interest in computer-assisted synthesis planning (CASP) began during my studies in organic chemistry. I was fascinated by the complexity of synthesizing natural products, but I also found it to be an incredibly challenging task. Retrosynthesis analysis requires breaking down complex molecules into simpler precursors, and when done manually, it can be highly inefficient. This process often relies heavily on the chemist's experience and intuition, making it time-consuming and limited in scope.

Recognizing these challenges, I became interested in exploring how machine learning could enhance retrosynthesis. My initial study involved a literature review by Zhong et al.[1], which provided a comprehensive overview of advancements in machine learning-based retrosynthesis. This paper introduced me to various algorithms and evaluation metrics, offering a clear framework for understanding the field.

Building on this foundational knowledge, I explored the history and evolution of CASP to gain a well-rounded understanding of its development. To analyze the role of machine learning in retrosynthesis, I selected three representative algorithms: proof number search (PNS)[2,3], Monte Carlo tree search (MCTS)[4,5], and A* search[6,7]. Each of these algorithms embodies a distinct computational strategy, illustrating different machine learning approaches to retrosynthesis planning. Before delving into their applications, I will first provide an overview of retrosynthesis[8,9], highlighting its fundamental principles and the limitations of traditional rule-based methods.

To assess the impact and progression of machine learning in retrosynthesis, I have carefully selected two key papers for each algorithm. The first paper represents an early application of the algorithm to retrosynthesis, offering insight into its initial effectiveness and challenges. The second paper showcases a more recent, refined implementation, reflecting advancements in algorithmic efficiency, predictive accuracy, or scalability. By comparing these works, I aim to track the evolution of machine learning methodologies in this field, evaluating improvements in both computational performance and chemical relevance.

Finally, I will compare the performance of different algorithms. To ensure an objective evaluation, I will draw on performance data from Zhong et al.'s study[1], which provides a benchmark for assessing the effectiveness of various machine learning approaches in retrosynthesis. Through this structured approach, I aim to provide a comprehensive evaluation of how machine learning-driven retrosynthesis has evolved and its potential to transform modern synthetic chemistry.

Literature Review

Introduction

The ability to design and synthesize complex molecules is fundamental to organic chemistry, enabling the development of pharmaceuticals, materials, and agrochemicals that are not readily available in nature. Retrosynthesis, a problem-solving technique introduced by E.J. Corey[9], aims to identify feasible pathways for synthesizing novel molecules and plays a crucial role in chemistry and drug discovery. Given a target molecule and a set of available precursor molecules, the objective is to construct a synthesis pathway where each step corresponds to a viable chemical reaction, until reaching commercially available starting materials (Figure 1). Efficient retrosynthetic planning is essential for accelerating drug development, optimizing material synthesis, and reducing the cost of chemical production. Traditionally, this process has relied heavily on human expertise and intuition. However, as the number of possible synthetic routes increases exponentially with molecular complexity, manual retrosynthetic planning becomes time-consuming and challenging.

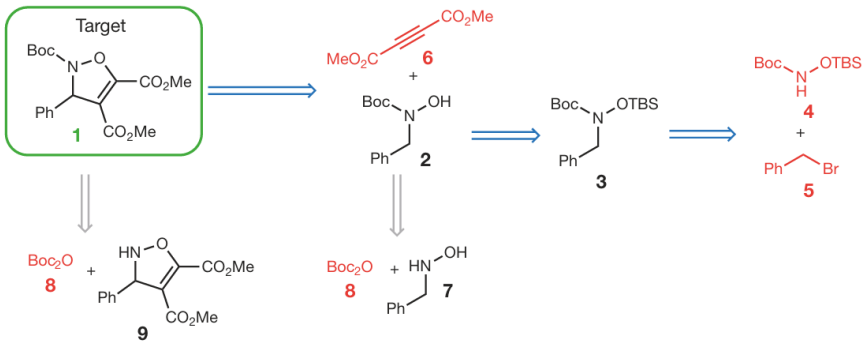

Figure 1: The diagram shows the process of retrosynthesis and the red molecules are commercially available. (adapted from Segler et al, 2018)[4]

Corey et al. made one of the first attempts at computer-aided synthesis planning (CASP) in the 1960s[8]. In recent years, CASP has seen significant advancements, with algorithms evolving to address the limitations of early models. While initial approaches, such as Proof Number Search (PNS), Monte Carlo Tree Search (MCTS), and A* search, demonstrated the feasibility of automated synthesis planning, their effectiveness was often hindered by inefficiencies like high computational cost, limited scalability, and an inability to account for real-world synthetic constraints. To overcome these challenges, improved versions of these algorithms have been developed, incorporating techniques such as heuristic edge weighting, graph-based search optimization, and neural network-guided decision-making. These advancements have led to more practical and reliable retrosynthetic planning tools,

capable of generating optimized synthetic routes with higher accuracy and efficiency. This review explores the evolution of these search algorithms, analyzing how their newer iterations improve upon previous methods and assessing their impact on modern chemical synthesis.

Algorithms

Proof Number Search

Traditional retrosynthetic planning methods, such as rule-based heuristics and machine learning models, often struggle with the complexity of chemical reaction networks. One promising approach to address these challenges is heuristic search, a strategy that guides the search process toward promising solutions by using rules of thumb rather than exhaustive evaluation. For example, Proof Number Search (PNS) is a heuristic search method that prioritizes reaction pathways based on their likelihood of success, systematically exploring possible routes while avoiding unnecessary computations.

Proof Number Search (PNS) structures decision-making problems as AND/OR trees (Figure 2), assigning each node a proof number (pn), which represents the minimum steps needed to confirm a valid solution, and a disproof number (dn), which represents the steps required to prove that no solution exists. To understand this intuitively, imagine searching for an escape route in a maze. Each intersection represents a choice point: some paths may lead to the exit, while others lead to dead ends. Proof and disproof numbers act as guides, indicating how difficult it is to confirm whether a path will ultimately succeed or fail. In retrosynthetic analysis, molecules function as nodes and reactions as edges, guiding the decomposition of a target molecule into simpler precursors.

While Heifets et al.[2] first introduced PNS for retrosynthesis, proposing the Depth-First Proof-Number Search (DFPN) algorithm, their approach suffered from inefficient exploration in complex chemical spaces. DFPN aimed to improve efficiency by structuring the search in a depth-first manner, meaning it explores one potential retrosynthetic pathway as deeply as possible before backtracking to examine alternative routes. By focusing on a single pathway at a time, DFPN reduces memory usage and minimizes redundant node expansions. However, DFPN proved ineffective in retrosynthesis due to the uneven distribution of branching factors: OR nodes (molecules) often had an overwhelming number of possible disconnections, while AND nodes (reactions) had relatively few possible pathways. This imbalance led to nearly uniform proof numbers across different choices, preventing the algorithm from effectively prioritizing the most promising synthetic routes.

DFPN-E, proposed by Kishimoto et al.[3], introduces key enhancements to over-

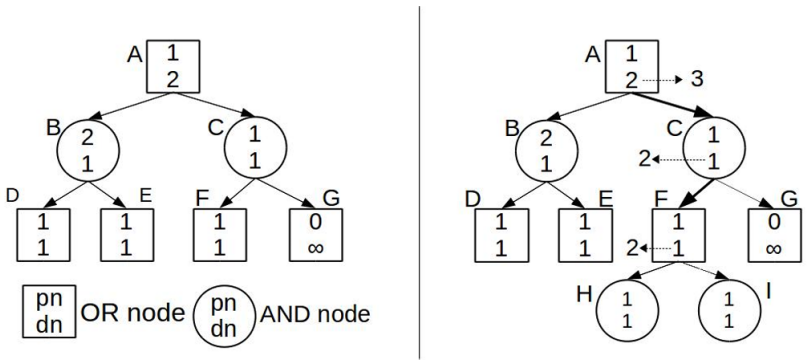

Figure 2: Example of Proof Number Search, an AND/OR tree with proof and disproof numbers (adapted from Heifets et al.)[3]

come these challenges. By assigning heuristic edge costs based on reaction difficulty, DFPN-E directs search efforts toward more promising pathways. Heuristic edge initialization prioritizes reaction steps that are easier or more likely to succeed, helping the algorithm focus on efficient routes while avoiding time-consuming dead ends. These costs are estimated using a neural network trained on retrosynthetic reaction data, which evaluates reaction complexity at the edge level rather than treating all reactions as equally difficult. Unlike previous methods that relied solely on node-level heuristics, DFPN-E refines the search process by distinguishing between straightforward and complex reaction steps, improving overall efficiency. Additionally, threshold control dynamically adjusts proof and disproof number limits, reducing unnecessary node expansions and maintaining computational efficiency. This results in a balanced search process that prevents excessively deep, impractical pathways while ensuring comprehensive solution coverage.

Empirical evaluations demonstrate that DFPN-E significantly outperforms Monte Carlo Tree Search (MCTS) and standard DFPN[3]. Across a dataset of 897 retrosynthetic problems, DFPN-E achieved a threefold reduction in search time compared to MCTS and a 3.6-fold improvement over DFPN. Its efficiency stems from the ability to prioritize promising pathways while mitigating redundant explorations. The algorithm successfully completed all tasks in 5,654 seconds, while MCTS required 18,552 seconds and DFPN 20,133 seconds. Additionally, DFPN-E processed an average of 68,719 nodes per problem, a significant reduction compared to MCTS (184,347 nodes) and DFPN (730,241 nodes). Not only does this minimize computational overhead, but it also enhances real-time applicability in complex synthesis planning. Importantly, DFPN-E maintains practical pathway lengths, generating solutions averaging 5.72 steps, compared to MCTS (5.58 steps) and the excessively deep pathways of DFPN, which occasionally exceeded 2,000 steps. These results illustrate that DFPN-E successfully balances pathway length and solution coverage, making it a more practical tool for retrosynthetic planning.

Beyond efficiency, DFPN-E demonstrates robustness in addressing lopsided search spaces, a persistent challenge in retrosynthetic analysis. Excessive branching at OR nodes can lead to inefficient solution generation in conventional PNS variants, producing either impractically deep pathways or computational bottlenecks. DFPN-E effectively mitigates these issues through heuristic edge initialization, ensuring that search efforts concentrate on viable pathways while avoiding unnecessary expansions. Its success highlights its potential for broader applications in computational chemistry and heuristic search optimization.

Future research could improve DFPN-E by incorporating reinforcement learning (RL) to make the search process more flexible and efficient. RL is a method where a system learns from experience, adjusting its decisions based on what works best over time. This would allow the algorithm to adapt better to different types of molecules and reaction networks. Another promising direction involves leveraging graph neural networks (GNNs) to model retrosynthetic pathways more effectively. Encoding molecular structures as graph representations could enable DFPN-E to generalize across unseen chemical domains, bridging the gap between heuristic-based search and data-driven algorithm methodologies. Additionally, incorporating experimental constraints such as reaction conditions, yield predictions, and reagent availability would enhance the algorithm's real-world applicability.

Monte Carlo Tree Search

Monte Carlo Tree Search (MCTS) has emerged as a powerful tool for retrosynthetic route planning, addressing the challenges faced by traditional rule-based approaches. Conventional retrosynthesis methods rely on manually encoded heuristics and predefined reaction rules to navigate chemical space, but as the number of synthetic steps increases, these approaches struggle with the exponential growth of possibilities. MCTS, originally developed for decision-making in games such as chess and Go, offers an alternative by efficiently exploring vast search spaces through a balance of exploration (discovering new pathways) and exploitation (refining promising routes) (Figure 3). This makes MCTS particularly well-suited for retrosynthesis, where the goal is to systematically break down a target molecule into simpler, synthesizable precursors.

A key application of MCTS in retrosynthesis is the 3N-MCTS model developed by Segler et al.[4], which demonstrated that a purely data-driven algorithm could effectively propose synthesis routes without relying on manually curated reaction rules. In double-blind AB tests, chemists found no significant preference for literature routes over the algorithm-generated ones, confirming its viability for synthetic planning. However, despite its strengths, 3N-MCTS has limitations. The

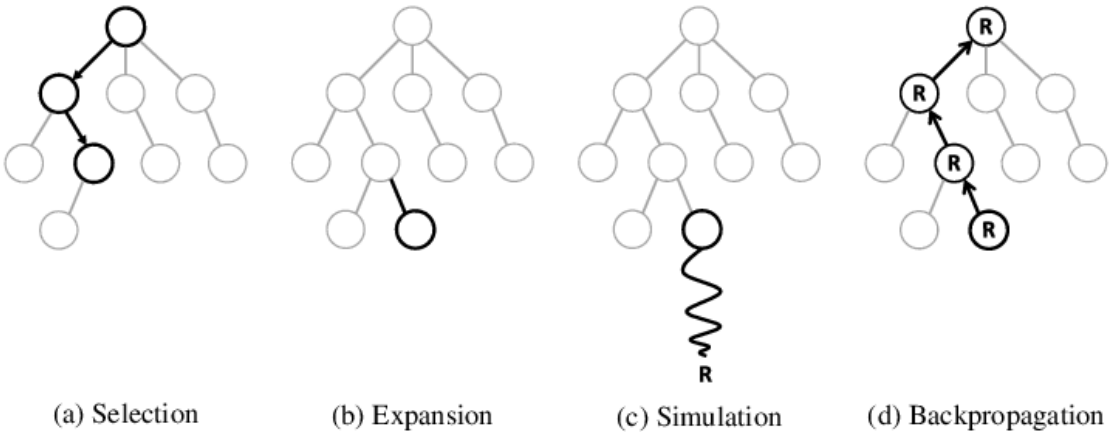

Figure 3: Phases of the Monte Carlo tree search algorithm. The search tree is grown by repeating four stages above (adapted from S. Documentation) [10]

model prioritizes novelty by exploring less common reaction pathways, sometimes leading to impractical synthetic routes. Additionally, it does not account for reaction mechanisms, stereochemistry, or three-dimensional molecular structures, all of which are crucial for complex molecule synthesis.

To address these issues, Ishida et al. [5] introduced ReTReK, an enhanced version of MCTS that incorporates domain-specific chemical knowledge to refine retrosynthetic predictions. While 3N-MCTS relies purely on statistical probabilities to evaluate synthetic pathways, ReTReK improves upon this by integrating four key retrosynthetic knowledge scores. The Convergent Disconnection Score (CDScore) favors pathways that efficiently merge precursors, reducing the total number of steps required. The Selective Transformation Score (STScore) prioritizes high-yielding reactions with minimal side products, increasing practical feasibility. The Ring Disconnection Score (RDScore) improves the deconstruction of cyclic molecules, which are often challenging in synthesis. Finally, the Available Substances Score (ASScore) ensures that proposed pathways favor commercially available starting materials, making the algorithm-generated routes more applicable in real-world scenarios. By embedding these chemically relevant heuristics into MCTS, ReTReK strikes a balance between data-driven discovery and the practical constraints of synthetic chemistry.

Beyond its heuristic-guided search, ReTReK incorporates a Graph Convolutional Network (GCN) to enhance its structural understanding of molecules. In simple terms, GCNs allow machine learning models to "see" molecules as interconnected networks of atoms and bonds, rather than just lists of chemical rules. This enables ReTReK to generalize reaction feasibility based on atomic connectivity and functional group interactions, overcoming some limitations of traditional rule-based retrosynthesis. This added layer of understanding makes it particularly effective for handling regioselectivity challenges and protecting group strategies, which of-

ten confound conventional synthesis planning methods. Experimental validation confirmed that ReTReK-generated routes were preferred over purely data-driven alternatives, reinforcing the importance of incorporating chemically meaningful scoring functions into retrosynthesis machine learning models.

ReTReK's performance was evaluated using 161 molecules from the ChEMBL dataset[5], where it demonstrated significant improvements over unguided MCTS. When guided by retrosynthetic knowledge, ReTReK successfully solved 90 molecules with a default expansion size of 50, compared to only 59 molecules without such guidance. Expansion size, in this context, refers to the number of possible synthetic pathways the algorithm considers at each decision point. Increasing the expansion size to 200 further improved performance, solving 101 molecules, though the gains plateaued due to computational cost constraints. Among the retrosynthetic knowledge scores, CDScore had the greatest impact, increasing the number of successfully solved molecules by 53

One of ReTReK's most significant strengths is its ability to dynamically adjust its search direction based on retrosynthetic knowledge, mitigating common pitfalls of unguided machine learning models. Traditional MCTS can waste computational resources exploring impractical pathways, but ReTReK's knowledge scores steer the search toward feasible solutions. For example, ASScore ensures that routes are biased toward widely available chemical building blocks, increasing their real-world applicability. This demonstrates ReTReK's efficiency in handling complex molecules with large search spaces.

Despite its advantages, ReTReK still faces challenges. Its reliance on reaction databases such as Reaxys means that incomplete or biased data can influence its predictions. Additionally, while its heuristics improve search efficiency, they remain approximations of real-world chemistry and may not fully capture all reaction complexities, particularly for unconventional transformations. Another key limitation is that ReTReK does not explicitly predict reaction conditions, which remain crucial for practical implementation. Future improvements could involve integrating algorithms that predict optimal reaction conditions alongside retrosynthetic pathways, bridging the gap between in silico planning and experimental feasibility.

A promising direction for future research is the development of self-improving retrosynthesis models that integrate real-time experimental feedback. This could be achieved by coupling machine learning-driven retrosynthesis planning with automated synthesis platforms, allowing experimental results to continuously refine and optimize algorithm predictions. Another exciting possibility involves incorporating mechanistic modeling into retrosynthesis algorithms to improve reaction sequence predictions by considering competing side reactions, kinetic barriers, and solvent effects. By combining quantum chemistry-based reaction profiling

with deep learning, future models could achieve even greater predictive accuracy, further transforming computer-aided synthesis planning.

A* Search

Retro* is an algorithm proposed by Chen et al.[6]. It is inspired by the A* search algorithm, which is widely used in pathfinding and graph traversal problems. In this framework, retrosynthesis is modeled as an AND-OR tree (Figure 4), where OR nodes correspond to molecules that can be synthesized via multiple reactions, and AND nodes represent reactions that require all precursor molecules before proceeding. Retro* uses a best-first search strategy, selecting promising nodes based on a cost function that combines the known cost of reaching a molecule with an estimated cost to complete the synthesis. Instead of relying on manually crafted heuristics, Retro* employs a neural network trained on historical retrosynthesis data, allowing it to make informed decisions and adapt to complex chemical spaces.

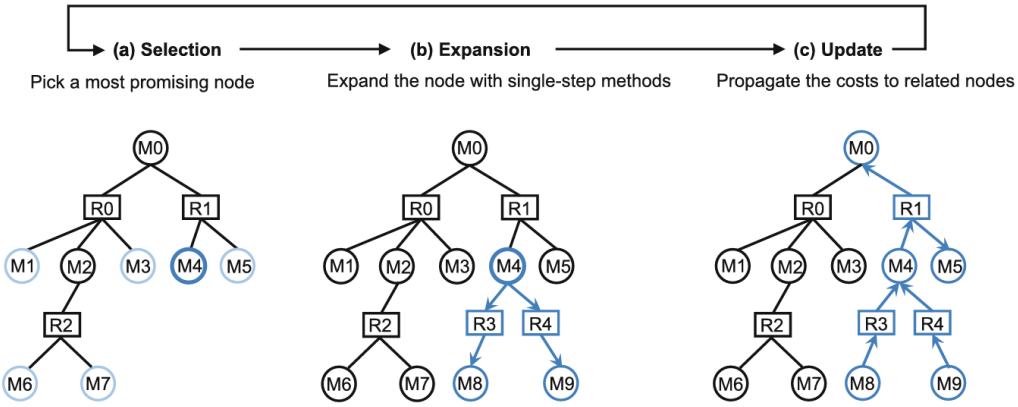

Figure 4: The work flow of A*Search. The "M" nodes are OR nodes and represent molecules. The "R" nodes are AND nodes and represent potential reactions.(There is no distinction between AND and OR nodes in MCTS)(Adapted from Zhong et al)[1]

Despite these innovations, Retro* suffers from redundancy, leading to inefficiencies. Intra-target redundancy occurs when the same intermediate molecule appears multiple times within the retrosynthetic tree of a single target, resulting in redundant computations. Inter-target redundancy arises when solving for multiple molecules, as common intermediates are treated independently instead of being shared. These issues increase computational costs and limit the scalability of Retro* for large-scale retrosynthetic planning.

RetroGraph, proposed by Xie et al.[7], improves upon Retro* by addressing redundancy issues through a more efficient representation. Instead of treating retrosynthetic planning as a tree, where the same intermediate molecules might appear multiple times, RetroGraph organizes the process as a directed graph (Figure:

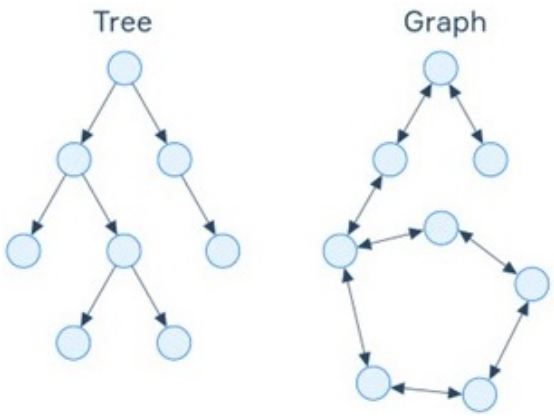

Figure 5: A tree is a hierarchical structure with a single starting point (called the root). Each element (node) is connected by only one unique path—there. A graph is a more flexible structure where nodes can be connected in multiple ways, including loops and shared connections.(adapted from Hyperskill) [11]

5). This ensures that each molecule appears only once, avoiding redundant calculations. Imagine mapping retrosynthesis like a network of roads rather than separate branching paths—common intermediates can be recognized and shared across different routes. This approach not only streamlines the search but also significantly reduces computational costs, making retrosynthetic planning faster and more scalable.

A key innovation of RetroGraph is its use of a Graph Neural Network (GNN) to guide node selection. Unlike traditional approaches that rely on predefined heuristics, a GNN allows RetroGraph to learn retrosynthetic patterns directly from data. A GNN is a type of artificial neural network designed to process graph-structured information by considering the relationships between nodes and their neighbors. In the context of retrosynthesis, the GNN evaluates the entire retrosynthetic graph holistically, capturing complex dependencies between molecules and reactions. This enables RetroGraph to prioritize the most promising molecules for expansion, leading to more efficient searches and higher success rates. By leveraging shared molecular substructures and reaction patterns, RetroGraph improves both the accuracy and interpretability of retrosynthetic planning.

RetroGraph's effectiveness is evident in benchmark evaluations using the USPTO dataset [7]. The USPTO dataset, created by Chen et al. [6], contains 299,902 training routes, 65,274 validation routes, and 189 test routes. Compared to alternatives like DFPN-E and Monte Carlo Tree Search (MCTS), RetroGraph achieves a success rate of 99.47

The advantages of RetroGraph become even more pronounced on larger datasets, such as USPTO-EXT [7], where it continues to outperform Retro* and other methods. By leveraging shared intermediates across multiple retrosynthetic targets

and reducing redundancy, RetroGraph is well-suited for large-scale applications, including automated retrosynthetic planning in industrial and pharmaceutical settings. Beyond retrosynthesis, this approach could extend to reaction condition optimization, catalyst design, and green chemistry initiatives, where minimizing waste and maximizing synthetic efficiency are critical goals.

Despite its successes, RetroGraph's performance is influenced by the accuracy of its underlying models. In particular, the single-step retrosynthetic model, which predicts possible precursor molecules for a given target, plays a critical role in determining the quality of the generated synthetic routes. Errors in this model could lead to suboptimal retrosynthetic plans, highlighting the need for continued refinement. Additionally, the computational cost of training and deploying GNNs can be substantial, requiring optimization strategies to improve scalability.

Future research could enhance RetroGraph by integrating reinforcement learning (RL), a machine learning approach that allows algorithms to improve through trial and error. In retrosynthetic planning, RL could help RetroGraph adaptively refine its search strategies based on feedback from past successes and failures, similar to how a chemist refines synthetic routes based on experimental results. Additionally, hybrid approaches that combine symbolic AI with GNNs could offer greater interpretability, allowing chemists to better understand and trust the decisions made by the algorithm. Moreover, refining the single-step retrosynthetic model and expanding RetroGraph's applications beyond retrosynthesis—such as in reaction prediction—could further extend its impact in computational chemistry.

Comparison between different algorithms

Segler et al.[4] conducted a double-blind AB test to choose the better route from those found in the literature and those generated by their algorithm. Despite being highly practical and straightforward, this method is too costly and time-consuming to be applied for evaluation on large datasets. Instead, these methods are typically assessed on widely accepted benchmarks, such as the USPTO dataset. Zhong et al. evaluated the performance of DFPN-E, MCTS (3N-MCTS), Retro*, and RetroGraph on the USPTO dataset[1].

When tested on these datasets, RetroGraph consistently outperforms DFPN-E and MCTS in both success rate and computational efficiency (Figure: 6). On the USPTO dataset, RetroGraph achieves an impressive 99.47

In contrast, DFPN-E, despite its heuristic edge-cost optimization, struggles with computational inefficiencies due to its reliance on proof-number search strategies. While this approach enables a focused search, it becomes a bottleneck in complex chemical spaces, leading to longer processing times and reduced overall success

	Success rate of iteration limit (%) ↑							
Algorithm	**100**	**200**	**300**	**400**	**500**	**Iteration ↓**	**Rec. Nodes ↓**	**Mol. Nodes ↓**
DFPN-E	50.53	58.42	64.21	68.42	75.26	208.12	3123.33	4635.08
MCTS	43.68	47.37	54.74	58.95	62.63	254.32	–	–
Retro*	52.11	66.32	76.84	81.05	86.84	166.72	2927.92	4174.52
RetroGraph	88.42	97.89	98.95	99.47	99.47	45.13	674.22	500.43

Figure 6: Performance comparison of the USPTO dataset's multi-step algorithms. Under the 500 limit, the average number of iterations, reaction (Rec.) nodes, and molecule (Mol.) nodes are displayed. (Adapted from Zhong et al.)[1]

rates. Similarly, MCTS suffers from its four-step update process, which significantly hampers runtime efficiency. This limitation is evident in its performance on the USPTO dataset, where it not only achieves the lowest success rate but also requires the highest number of iterations per solution. These fundamental constraints highlight why RetroGraph, with its more structured and globally informed approach, achieves superior results across different datasets and problem scales.

One of RetroGraph's major strengths is its use of a Graph Neural Network (GNN) to guide its search. Unlike traditional methods that evaluate nodes individually, RetroGraph's GNN provides a global perspective by analyzing molecular structures and predicting promising reaction pathways. This allows it to prioritize routes that are not only synthetically feasible but also computationally efficient. However, while this approach greatly enhances its performance, it also introduces a potential limitation: rare intermediates may be underrepresented in the training data, potentially leading to biased predictions. Addressing this issue by incorporating reinforcement learning or alternative graph representations could further improve RetroGraph's generalizability.

Despite its advantages, it is important to recognize that success rate alone does not fully determine the best retrosynthesis algorithm. One key aspect not captured in these benchmarks is route diversity, or the ability of an algorithm to discover alternative synthesis routes. While MCTS performs poorly in both success rate and computational efficiency, it might still excel in exploring diverse pathways, which could be valuable for applications requiring novel synthetic strategies. Additionally, the ReTReK model was not included in these comparisons. Future research should aim to evaluate retrosynthesis algorithms not only based on efficiency and accuracy but also in terms of their ability to generate innovative and practical synthetic routes.

Conclusion

The application of machine learning in retrosynthesis has seen significant advancements, as demonstrated by the performance of DFPN-E, Monte Carlo Tree Search (MCTS), and RetroGraph. These algorithms have shown the capability to generate viable synthetic routes, overcoming many of the inefficiencies associated with traditional retrosynthetic planning. In particular, RetroGraph's graph-based representation and GNN-guided search allow it to eliminate redundancies and enhance computational efficiency, positioning it as one of the most promising approaches in machine learning-driven retrosynthesis. Compared to earlier methods, these algorithms provide more optimized and scalable solutions, with success rates that often exceed those of human-designed synthetic routes.

However, several limitations remain. While these machine learning-based methods excel in efficiency and accuracy, they still heavily rely on pre-existing reaction databases and predefined heuristics. Unlike human chemists, these algorithms lack the ability to autonomously learn from emerging chemical literature or adapt dynamically to novel reactions without retraining. This limitation restricts their applicability to unexplored chemical spaces, particularly in the synthesis of highly complex or novel molecules. Additionally, computational demands remain high, with advanced models requiring substantial hardware resources, making large-scale retrosynthetic analysis computationally expensive.

Another critical challenge is the reliance on the quality and completeness of reaction data. The scarcity of reaction information for certain chemical classes, particularly in natural product synthesis, hinders the generalizability of current retrosynthetic models. For example, while algorithms like ReTReK integrate retrosynthetic knowledge scores to improve search efficiency, they still struggle when data coverage is limited, leading to suboptimal or impractical synthetic routes. Addressing these challenges will require the integration of adaptive learning frameworks, reinforcement learning techniques, and experimental feedback loops to further refine machine learning-driven retrosynthetic planning.

Despite these challenges, machine learning-driven retrosynthesis represents a transformative shift in chemical synthesis. With continued advancements in computational power, improved reaction data integration, and hybrid machine learning models that combine symbolic reasoning with deep learning, the applicability of these algorithms will expand beyond their current limitations. In the future, fully autonomous retrosynthetic planning systems may become a reality, bridging the gap between theoretical synthesis predictions and practical laboratory execution. As machine learning continues to evolve, retrosynthetic planning driven by machine learning has the potential to revolutionize drug discovery, materials science,

and industrial chemistry, making complex molecular synthesis faster, more cost-effective, and more accessible.

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GenAI Statement

I have used Generative AI in an assistive role for this coursework in accordance with UCL guidelines.
GenAI System Used: ChatGPT (Version: February 2025)
Publisher: OpenAI
URL: https://chat.openai.com
Context of Use: I used ChatGPT to check spelling and grammar and to proofread my work to ensure clarity and coherence. No content generated by the AI has been directly copied and pasted into my submission.

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