STM JOURNALS

International Journal of
Cheminformatics

Volume 1, Issue 2, 2023
July- December
DOI (Journal): 10.37591/IJCI

https://journals.stmjournals.com/ijci/

Review IJCI

Recent Applications and Influences of Artificial Intelligence (AI) in Chemical and Allied Sciences

Anindya S. Manna[1], Antara Roy[1], Rajjakfur Rahaman[2,*] , Dilip K. Maiti[3,*]

Abstract

Artificial Intelligence (AI), the future tool of mankind that can revolutionise scientific research by making it faster, add more efficiently and accurately. During the pandemic situation, the scientific community was parted into two distinct groups, the computation-dependent community could easily continue their research work from their resident, while the works of the other group of researchers with lab-oriented research stopped entirely. In this connection use of AI becomes important and applied in various areas of chemistry and biochemistry for helping and enhancement of research towards the drug molecule development, retrosynthetic path finding of the targeted valuable compounds with their property prediction. Also, the possibility of applications of AI went beyond and applied in the food science and nano-technology through its experimental data dependent predictions for a faster and cost-effective research towards real applications. In this short review we discussed covering the different areas of chemistry and biochemistry, how AI is assisting the scientists in advancing these impactful research fields.

Keywords: Machine learning; AI in chemistry; automated research tool; synthetic route design; drug molecule design

INTRODUCTION

In recent pandemic situation, researchers engaged in designing or finding the molecules for the real application in the field of science and synthetic chemistry. The industries such as healthcare for human and animal, agrochemical products, consumable products and others have observed a drastic change in their work environments due to lack of demand and supply chain coordination along with physical contacts for real practical [1]. This troublesome situation directs the search for an impactful alternate pathway through which the research work will not stop completely if this type of pandemic situation remains for several years [2]. Possibly we might see several purposes built "remotely accessed" laboratories that deliver this as a facility. In the synthetic field, several research laboratories have been already tested with part or completely self-directed synthetic methods, although in medicinal optimization it has been completely robotic for years with nominal human effort [3–6]. In spite of this various automation, the attendance of scientist for manually operated laboratory work is still required. Nevertheless, together if we set these, we can program the whole method and access it remotely such as the design-make-testing series (Figure 1) and is completely self-directed across the industrial laboratories [7].

***Author for Correspondence**
Rajjakfur Rahaman
E-mail: razzaqchem@gmail.com

[1]Senior Research Scholar, Department of Chemistry, University of Calcutta, 92 A.P.C. Road, Kolkata, India.
[2]Postdoctoral Research Scholar, Department of Chemistry, University of Calcutta, 92 A.P.C. Road, Kolkata, India.
[3]Professor, Department of Chemistry, University of Calcutta, 92 A.P.C. Road, Kolkata, India.

Received Date: April 11, 2023
Accepted Date: June 01, 2023
Published Date:

Citation: Anindya S. Manna, Antara Roy, Rajjakfur Rahaman, Dilip K. Mait. Recent Applications and Influences of Artificial Intelligence (AI) in Chemical and Allied Sciences. International Journal of Cheminformatics. 2023; 1(2): 22–48p.

Such type of implementation can reduce the effort of design and experimental execution through the laboratory automation. Possibly, in the similar pathway that we see various laboratories have installed liquid dispensing machine through repetitive automated operation [8, 9]. Despite the

huge attention and publicity on AI, with its great future, its applications in chemistry are yet to become more mature for the effective vast practicable use utilizing a massive collection of experimental information. This short review is about how computational workflows for autonomous molecular design for retrosynthesis, drug discovery, nano science, organic reaction prediction, etc. that could support in achieving laboratory automation as it relates to active learning strategies. In the end, we focused on recent utilization of AI tools for the design and synthesis of targeted products. In this connection the utilization of AI facility should contain its complete potent for fast and more accurate implication in the field of practical chemistry (Figure 2).

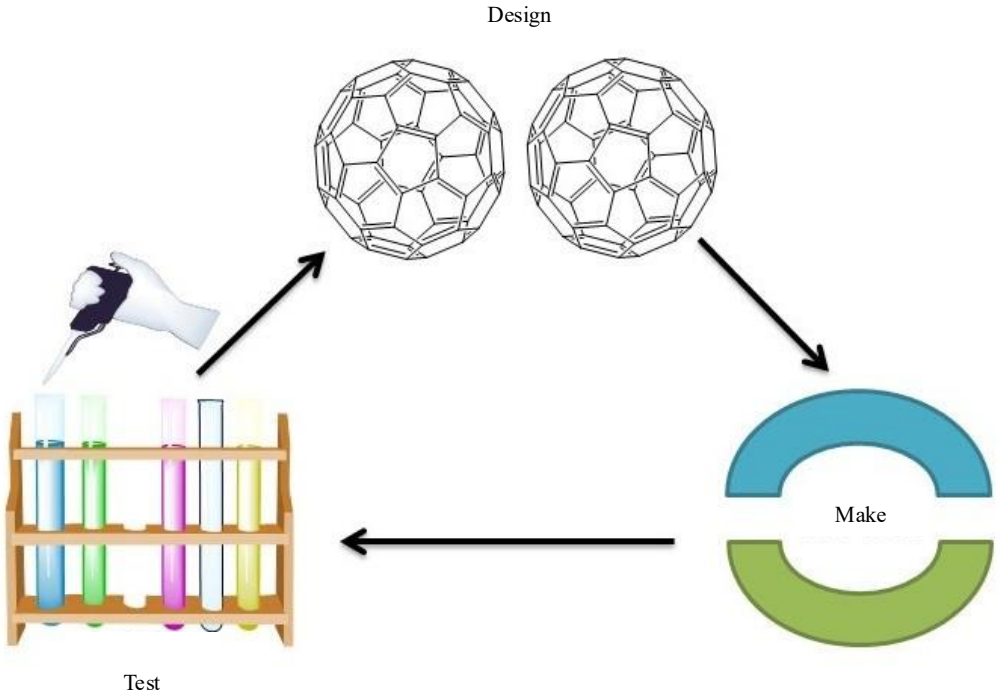

Figure 1. The design-make-testing cycle.

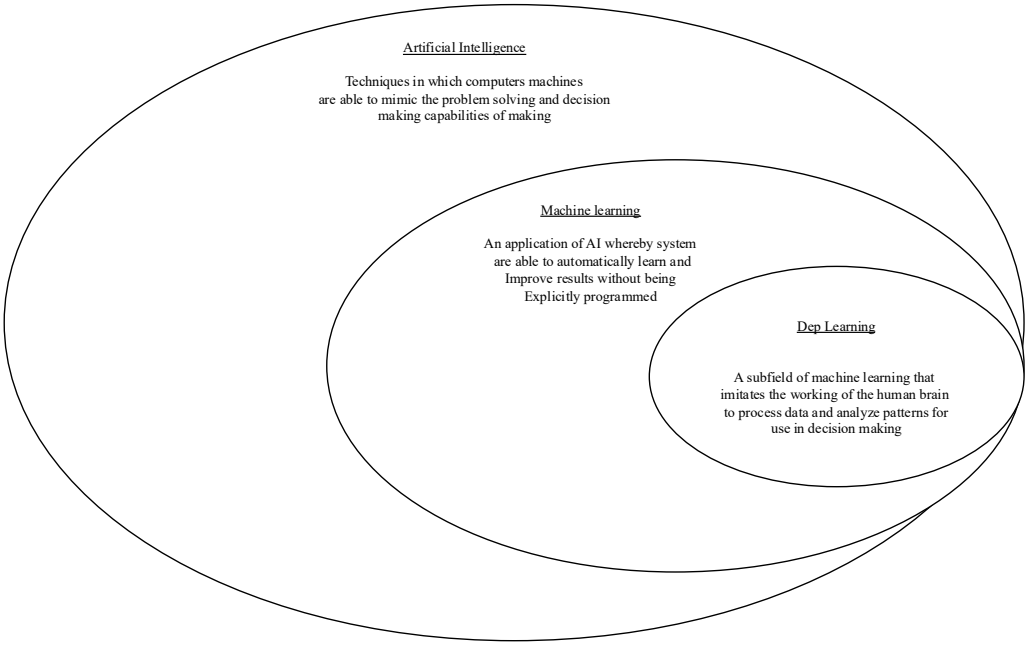

Figure 2. Complete utilization of AI in chemistry should be a target.

ADVANCEMENTS IN MOLECULAR DESIGN THROUGH AI

Molecular Design is the process of creation of new molecules with desired properties for a given problem in chemistry, nanotechnology or material science. Automated research such that the design, make, test and analysis cycle in chemistry is a fast-growing field that can be beneficial from their own fixed review [10]. Chemical research is based on processes where experiments are planned, carried out and then improved upon in order to achieve an objective. The researchers' expertise and own judgement plays a critical role in developing the first design and followed by optimization, something which was previously impossible through autonomous systems that perform chemistry research. But study in chemistry is adjusting itself with the digital era and using some of the easily available platforms such as PubChem, ChEMBL etc. along with the other sources like FigShare, GitHub etc., it is possible to design a molecule for a specific purpose [11, 12].

There is also a considerable amount of information that cannot be accessed in the firms for commercial purposes. This type of automation domain and data accessibility are attractive to address so that students and the scientific community can learn from this existing information. Recently developed REINVENT 4, a command line software which is a latest open-source generative AI tool for the design of organic small molecules [13]. Recurrent neural networks along with the transformer architectures are utilized in this software to design and drive the molecule generation. These generators are generally embedded in the machine learning algorithms, reinforcement learning, transfer learning and curriculum learning. REINVENT 4 facilitates and enables the de novo design, library design, R-group replacement, scaffold hopping, linker design and optimization of molecule. Several AI model architectures have been designed for generative molecular design e.g. variational autoencoders (VAE) [14, 15], generative adversarial networks(GAN) [16], recurrent neural networks (RNN) [17-20], transformers [21, 22], flow models [23, 24] and diffusion models [25] (either directly generating in 3D [26, 27] or from 1D SMILES strings [28]), reaction based models [29]. A neural network is a set of algorithms designed to recognize connections, within a dataset by mimicking the functions of the brain. While, machine learning is a discipline of artificial intelligence that focuses on creating and studying the algorithms of statistics, i.e. data analysis, so that it can find patterns and make prognostication, which doesn't require the algorithms to be instructed directly. The molecular representation used for these algorithms can be different and can generally be divided by their dimensionality [30]. All these methods have their pros and there are no uniform solutions to outperform one another. Different benchmarks have been developed towards the validation of molecular generation and optimization techniques [31, 32]. Along with these advancements another addition is Chemistry42 software platform that facilitates the small molecule design and optimization through the integration of AI techniques in addition to the computational and chemical methodologies [33].

Artificial Intelligence in Retrosynthesis

Retrosynthesis is a technique for transformation of a target molecule into initial precursor so that commercially available or easily synthesized frameworks can be obtained with various potential disconnections that might lead to effective and environmentally friendly solutions [34]. It follows inverse molecular design protocol, which is also employed in synthesis of highly complex target molecules with multiple functional groups whose starting materials are hard to find and synthesis is challenging. The fact that it was amongst the first research scientists who saw use of far ahead computing in natural sciences as early as 1960s is somewhat surprising and is in the organic synthesis field; however, its application was difficult because it could only do rather simple tasks done by a human [35]. The concept of retrosynthesis came from the practical barriers of its execution in the laboratory, and from there, a number of target pathways for the target reach went into research that generated the practical concept of retrosynthesis (Figure 3).

Early attempts on the retrosynthesis of the target molecular formula were positioned at the origin, with branches signifying alternate or convergent paths connecting to intermediate reagents [36]. Corey's LHASA [37], Johnson's SYNLMA [38] and Gelernter's SYNCHEM [39] were the outcome of such

early pioneering works in this field. The size and time for the reaction search space is therefore determined by the number of encoded reactions, a lot of literature survey are also available for the synthetic planning tools in more detail [40, 41]. Latendresse et al. has presented an updated and new computer aided software namely SynRoute related to the retrosynthetic planning very recently [42]. Wei and coworkers reported a new tool, RetroExplainer, works following a quantitatively interpretable molecular assembly method guided by chemical knowledge and DL for retrosynthesis prediction and used the standard datasets USPTO-50K, USPTO-MIT, and USPTO-FULL for all of reported experiments [43]. AI-driven one-step and manifold retrosynthesis approaches have made significant advances in recent years and are closely related to each other since multi-step process passes through single-steps [44]. The rarest bonds are suggested for disconnections by Cadeddu et al. [45] from the perspectives of chemical linguistics. To expedite molecular complexity reduction, some other techniques therefore try to do it as fast as possible [46]. However, just identifying reaction sites does not suffice to propose synthons [47], which are nonphysical fragments of precursors. Whether a proposed retrosynthetic step yields one or more synthons, synthetic equivalents must still be designed using certain functionalities-for example specifying leaving groups.

Without data, artificial intelligence (AI) cannot exist. Therefore, dataset quality, scale, and size are important considerations for contemporary machine learning applications. Data collection and compilation, encompassing regions from the element atomic spectrum to material macroscopical properties, has a long history in the area of chemistry, which created chemical informatics, a field that helps to flourish AI applications in chemistry [48]. A short list of popular chemical databases is provided below (Table 1).

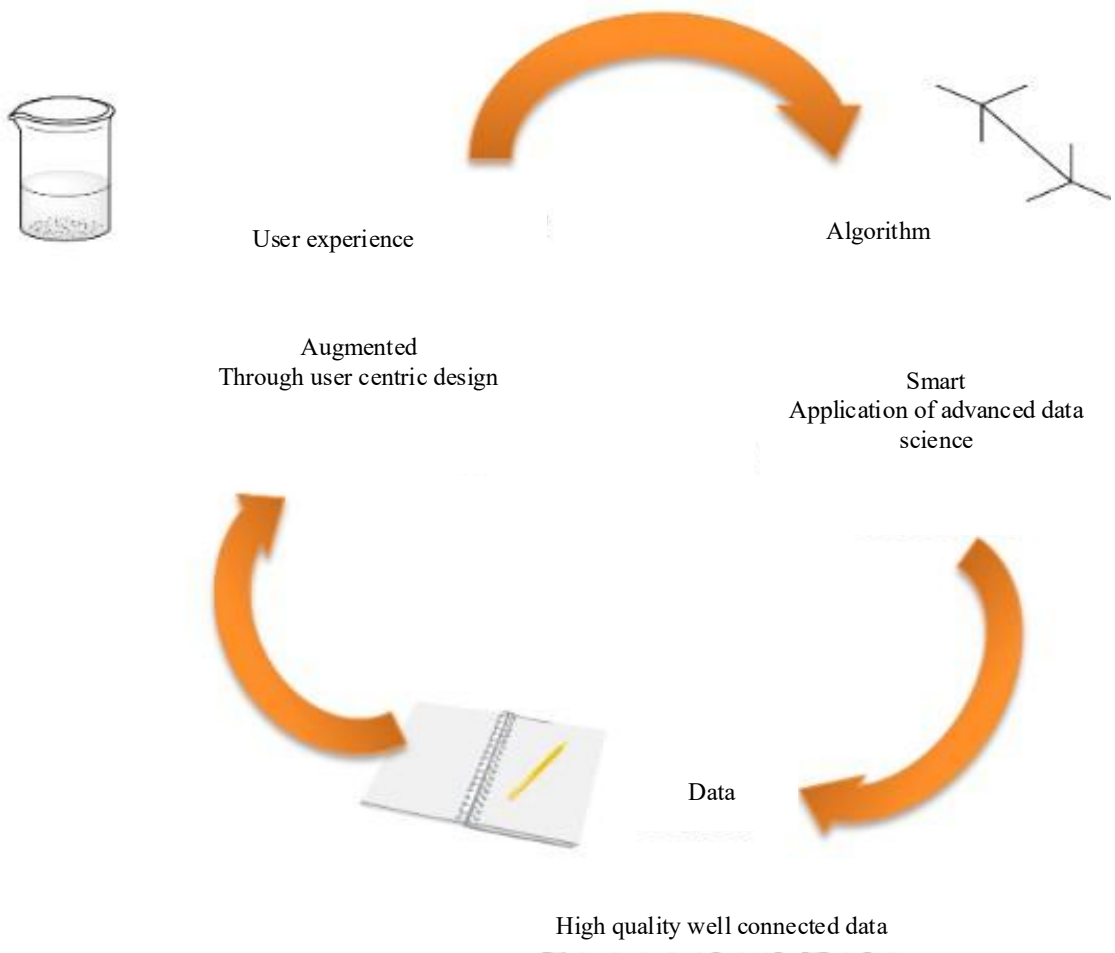

Figure 3. Origin of the practical concept of retrosynthesis

Table 1. Popular chemical databases

Type	Identity	Information
Chemical Reaction	SciFinder	Data on compounds, its properties, chemical reactions and bibliographic information
	Reaxys	Chemical reaction, bibliographic information
	ORD	Organic chemical reaction related information
	USPTO	Structure and reaction
Molecular Property	PubChem	Biological activities, chemical and physical properties and toxicity
	ChemSpider	Structure and property related information
	DrugBank	Data related to drug molecules
	Tox21	Toxicilty database
Material	ESOL	Water solubility related data
	Lipophilicity	Lipid solubility data of organic materials
	MatWeb	Thermoset and thermoplastic of polymers, material and metals
	HTEM	Investigated data of inorganic thin filmingredients
Computational database	GDB-17	Structural properties of organic molecules up to 17 atoms
	Materials Project	Properties related to DFT relaxed material and their properties
	Atom3D	3D structure of materials and biomolecules
	QM9	Quantum database of organic molecules

ORD: Open Reaction Database, USPTO: United States Patent and Trademark Office, HTEM: High-Throughput Experimental Materials, DFT: Density Functional Theory.

The limits of AI models are set by data and features. The input for the AI model consists of pre-processed source data, also known as representations or descriptors. Molecule descriptors are subdivided into two categories, such as 2D and 3D. 2D features neglect the spatial conformation but focus on the bonding arrangement in molecules. Example: SMILES presents a saturated molecule in a string that is readable by humans (like "CO" for methanol), and representation by the International Chemical Identifier (InChI) of the International Union of Pure and Applied Chemistry (IUPAC) uses a string that is strictly unique and is hard to read by humans. In addition to strings, a vector of float numbers is also utilized to abstract the topology of a molecule. Using the Morgan algorithm, the extended-connectivity fingerprint (ECFP) explores substructures and encrypts them into a complicated form. 3D characteristics are stored in atomic structures, with a skiving of permutation, translation, or rotation invariance that restricts them from the direct input of an AI model [48–50].

Two essential CASP modules are retrosynthesis and reaction prediction. Retrosynthesis is based on reaction prediction. Template-based and template-free methods are the two subcategories of reaction prediction [51]. One reactant can frequently give many potential products through the template-based approach, leading to excess candidate reactions. Wei et al. attempted to predict template applicability using machine learning in 2016 [52, 53]. Eventually, the method was used on more intricately investigated data from Reaxys by Segler and Waller [54]. The recent advent of the template-free method has the potential to overcome the shortcomings of the template-oriented method in terms of completeness and quality, and the seq2seq model is an important one to mention. For retrosynthesis in past decades, expert chemists used to make the ultimate decision once a few options were recommended by CASP programs (such as LHASA and SECS), and in this connection, the work by Coley et al. on synthetic complexity score (SCScore) as a measure for molecular ranking is important [55]. Through the use of an in-scope filter system to determine whether a reaction is truly viable, several studies have been conducted in connection with the construction of asymmetrically promising sub-synthetic trees.

Natural product synthesis is still difficult despite recent advancements. The measurable yield of enantiomers is typically absent in maximum models, apart from the sparsity of the exercise data for

complicated compounds, although it is crucial for accurately assessing a synthetic route [56, 57]. Despite of a lot of researches are ongoing in this field a lot more potential avenues are open for future research in the form of (a) Out-of-distribution simplification and finding (b) Route evaluation (c) Knowledge diagrams and reasoning with continuous updating of related databases [58, 59].

Artificial intelligence for organic reaction outcomes

Synthetic organic chemistry is the basis of several branches in chemistry including drug discovery, chemical biology, materials science and engineering. On its own though, complex chemical synthesis constitutes a formidable task that requires expert knowledge typically acquired through many years of learning and practical experience in the laboratory. There has been a fifty-year-old persistent dream of technology that could simplify and automate chemical synthesis yet it remains unfulfilled till date. Improved computer processing capacities, more information as well as algorithms have revived interest in artificial intelligence (AI) after limited success was attained in the past. In the last decade, we saw an unexpected spurt in the usage of artificial intelligence for computationally oriented reaction modelling and calculation [60]. Assuming the variety of these AI methods, we believe it will help to evaluate them using a broad theoretical outline within which the diverse approaches reside. The goal is to classify the various methods into sub-categories such as symbolic artificial intelligence, purely data-driven or numeric artificial intelligence, and hybrid artificial intelligence.

Symbolic Artificial Intelligence, the oldest form of all artificial intelligence, which was initiated in the early 1960s and 1970s, is considered an obvious illustration of domain knowledge as proper facts, guidelines, and logical constructions that decode human thoughts into computer-based forms that mimic human practiced intellectual [61]. In reaction modeling, these systems have been established by applying the validation of chemistry-oriented rules changes to reactions that plot the varies in atomic connections in the time of reaction, chemistry-informed heuristics for efficient searching through a combinatorial bulky planetary, and knowledge illustration systems for reactions by way of directed diagrams with well-preserved semantic statistics [62].

A pure data-driven process usually does not need to incorporate obvious chemical information, which can be fruitful when the related data is largely available. But if the information is partial, one might be overwhelmed, and it can be challenging because of the lack of accuracy, the chemical in acceptability, or the calculations not being plausible. These deliver a summary of those approaches, which are divided into deep neural networks, sequence-to-sequence modelling, diagram neural systems, and small-sample methods [63–66].

Hybrid modelling lies among the dual extremes of representative artificial intelligence and fully data-determined processes, and it influences the influential abilities of data-driven modelling while incorporating field information motivated by symbolic artificial intelligence (Figure 4). A variety of sub-sections of hybrid approaches are improved with rich chemistry illustrations, chemistry-knowledgeable examination, skilled humanoid chemists, and chemistry constraints [67–69].

Artificial Intelligence in Drug Discovery

Drug discovery, the method of finding and creating novel medicinally important molecules, is a difficult and drawn-out process that depends on labor-intensive methods such as high-throughput screening and trial-and-error research [72]. These methods examine a lot of latent drug compounds to find their potency, are expensive, time-consuming, and frequently produce inaccurate results [73]. In addition, it is very difficult to accurately predict their behaviour in the body system owing to the limited and laborious availability of suitable test compounds [74]. The pharmaceutical industry has seen a sharp rise in the digitalization of data in recent years, and with digitalization, the difficulty of learning, examining, and using that information to address intricate clinical issues is also a serious issue [75]. This motivates the utilization of AI for the analysis of a large volume of data set towards era of enhanced automation [76]. Significant advancements for the effective use of artificial intelligence have been made in a number of sectors, most notably bio-technologies, to lower the time, cost, and failure rate of drug

discovery and development processes [77]. Recently, we saw a high rise in interest in the effective application of AI in medicinal chemistry to accurately forecast the efficacy of pharmacological compounds and their toxicity also [78].

Modern methods such as natural language processing and machine learning (ML) can speed up and enhance this process through involvement of multiple approaches including a core machine learning paradigm, reasoning, knowledge representation, and solution search [79]. ML makes use of algorithms that can identify patterns in a collection of data that has undergone additional classification such as deep learning (DL), a way of teaching computers to process information in a way that mimics the way the human brain processes information through the use of artificial neural networks (ANNs). These consist of a network of interconnected complex computational components that imitate the way electrical impulses are sent in the human brain through "perceptions" akin to those of biological neurons [80]. Various AI-based algorithms, such as reinforcement, supervised and unsupervised learning techniques, and evolutionary or rule-based algorithms, may be able to help with these issues [81-83]. Additionally, by using current technology-based algorithms, novel targets for drug development, such as certain proteins or genetic pathways implicated in disorders, can also be found [84]. Artificial intelligence, sometimes known as machine intelligence, is the simulation of human intelligence, whereby a machine replicates the cognitive processes associated in learning and problem-solving in the human brain utilizing tools and software and large database that enable autonomous decision-making for certain objectives [85, 86] and this is extended to the complex drug discovery process too. Hence AI mimics the human brain function for the retrosynthesis also (Figure 5). In drug discovery, AI is commonly used for virtual screening [87], de-novo design for drug molecules [88], retrosynthesis and prediction of reaction [89] and protein molecule design [90]. These applications can be categorized into two, which include predictive tasks and generative tasks. The AI techniques that drive these applications are numerous and varied, with model architectures advancing from conventional machine learning models to deep neural networks like convolutional neural networks, recurrent neural networks, graph neural networks, transformers etc. Learning paradigms have also shifted from supervised learning to self-supervised learning and reinforcement learning. Using a bacterial biomarkers and global explanatory approach, Rynazal et al. Studies have shown a method that utilizes the machine learning tool to find the relation of colorectal cancer (CRC) with subgroups of different CRC probabilities and gut microbiome compositions [91].

Several prominent pharmaceutical corporations, including Roche, Bayer and Pfizer, have started the partnerships with information technology (IT) firms to create AI-driven approaches for drug development. In a recent development, Insilico Medicine Comapany utilized AI technology to identify a drug for idiopathic pulmonary fibrosis, yielding promising outcomes in Phase I clinical trials. This discovery underscores the transformative impact of AI techniques on the landscape of drug discovery and development [92]. DL has exhibited remarkable success in proposing potent pharmaceutical candidates and accurately predicting their properties, as well as identifying potential toxicity risks [93]. By leveraging AI methods [94], DL has effectively addressed previous challenges in drug development, such as the analysis of extensive datasets and the laborious screening of compounds, while minimizing standard error. This has resulted in significant reductions in both R&D costs and time, which previously exceeded US$2.5 billion and spanned over a decade [95]. Furthermore, AI technology enables the facilitation of new studies aimed at assisting the identification of novel drug targets, rational drug design, and drug repurposing [96, 97]. An optimal AI tool for aiding in clinical trials should possess the ability to accurately detect diseases in patients, identify the gene targets involved, and forecast the impact of the designed molecule, as well as its on- and off-target effects. In the context of a Phase II trial involving individuals afflicted with schizophrenia, a groundbreaking mobile application named AiCure was developed as an innovative AI platform to assess medication adherence. Notably, it was observed that AiCure significantly enhanced adherence by 25% when compared to the conventional "modified directly observed therapy" [98]. The process of patient selection for clinical trials holds immense importance. By investigating the correlation between human-relevant biomarkers and in vitro

phenotypes, a more reliable and quantifiable evaluation of the uncertainty surrounding therapeutic responses in a specific patient can be achieved. The advancement of AI methodologies in the identification and prediction of human-relevant biomarkers of diseases enables the recruitment of a targeted patient population for Phase II and III clinical trials. Employing AI predictive modelling in the selection of patient populations would consequently elevate the success rate of clinical trials [99, 100]. According to the literature reports, researchers have used the in silico methods to predict pharmacological properties of drugs and repurpose them for different biological systems and conditions. These methods rely on deep neural networks (DNNs), which are highly adaptive multilayer systems composed of interconnected artificial neurons. By utilizing high-level representations of data, DNNs are able to perform various data transformations [101]. Aliper et al. conducted a study demonstrating that DNNs can classify complex drug action mechanisms at the pathway level, enabling the categorization of drugs based on their functional class, efficacy, therapeutic use, and toxicity [102]. Furthermore, advancements in precision medicine have led to the development of next-generation artificial intelligence (AI) capable of designing drug molecules using generative adversarial networks (GANs) [103]. GANs utilize DL to generate photo-realistic images from text descriptions [104]. This platform not only analyses data but also has the ability to imagine or create new data based on real data. The GAN technique involves an adversarial game between two DNNs, where one DNN evaluates the output of the other iteratively. Through this adversarial process, the two networks learn to generate increasingly accurate molecules [105].

Recently, the prevailing paradigm in disease research is the 'one-disease–multiple-targets' approach, which has gained prominence due to a deeper understanding of the molecular-level pathological processes underlying various diseases. This approach, also known as polypharmacology, recognizes that diseases often involve multiple targets rather than a single target [106]. To facilitate research in this area, numerous databases such as ZINC, PubChem, Ligand Expo, KEGG, ChEMBL, DrugBank, STITCH, BindingDB, Supertarget, and PDB have been developed. These databases serve as valuable

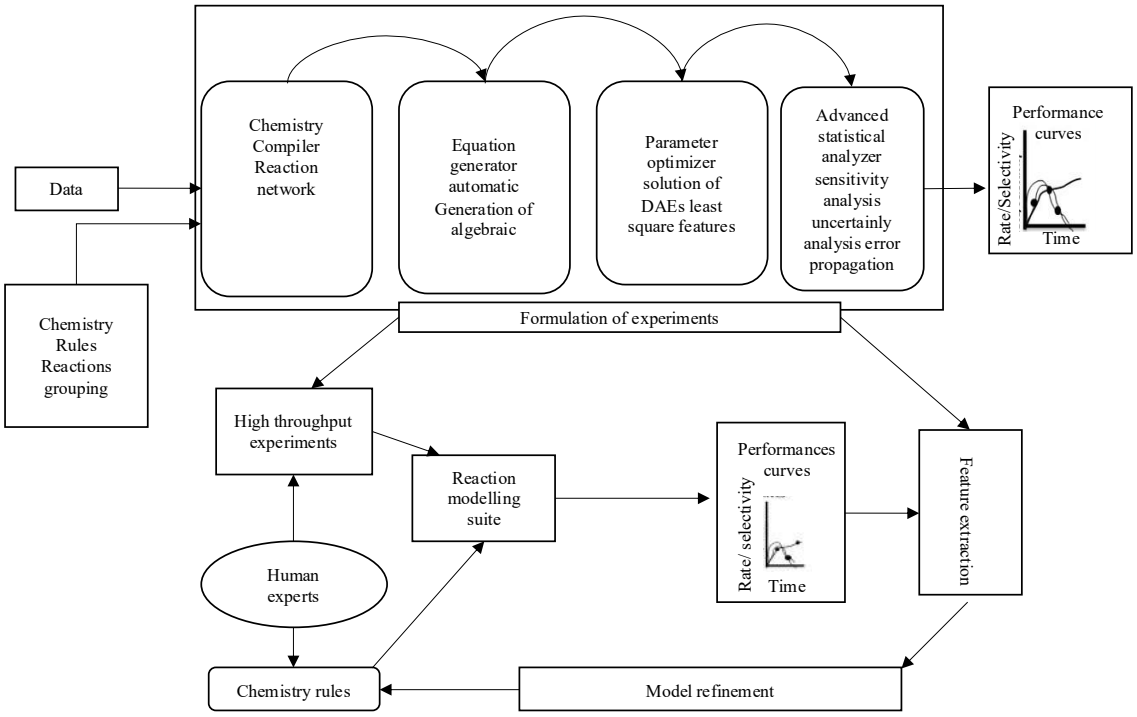

Figure 4. A hybrid approach integrating area knowledge, past data, and the physical values of the structure into the model is called statistics. These approaches exploit human skill and reasoning laterally with machine knowledge approaches to search for kinetic parameters of a catalytic method that increase aromatic yield. [70, 71].

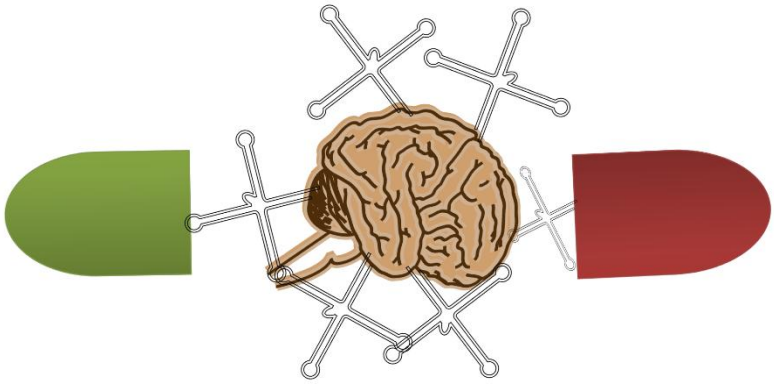

Figure 5. Human intelligence and drug discovery are interconnected by use of intelligence

resources for integrating diverse information on molecular pathways, crystal structures, binding affinities, drug targets, disease relevance, chemical properties, and biological activities. Leveraging thepower of artificial intelligence (AI), these databases can be probed to design polypharmacological agents. A recent success story in this field involves the development of a computational platform called DeepDDI, which utilizes AI to enhance our understanding of drug–drug interactions, associated mechanisms, and the prediction of alternative drugs for clinical use without adverse health effects [105].

Traditional medicines made from plants has been used extensively for a variety of situations for which chemical therapy has not yet been developed, is also less expensive, less time-consuming, and less hazardous than modern medication [107]. In this connection Radinsky and Harel introduced the prototype-driven diversity network, a generative chemistry framework that relies on VAE to empower chemists in producing a wide range of target molecules possessing specific properties starting from a molecular prototype [108]. Through the computation of radiographic RBL and interproximal alveolar bone level, Chin-Chang-Chen et al. built a model of AI-based detection utilizing Convolutional Neural Networks (CNN), which can be effective for dental professionals' diagnosis and treatment [109, 110]. Nevertheless, this contemporary method can also significantly aid in the subsequent integration of the developed medication in its appropriate dosage form and its optimization. It can also facilitate prompt decision-making, which can speed up the production of higher-quality products and ensure batch-to-batch consistency. Additionally, through thorough market research and forecasting, it may help prove the product's performance and safety in clinical trials and guarantee appropriate pricing and positioning in the marketplace. Despite the fact that no medications are presently commercially available, according to the expert researchers, in the near future AI-based methods for the drug discovery difficulties will be important powerful and more accurate resources for the pharmaceutical sector [92,111].

Artificial Intelligence for Molecular Property Prediction

Predicting molecular characteristics is an imperative task in the drug discovery industry. Within the realm of AI applications, molecular property prediction holds particular importance for the drug discovery process. This is primarily because a large number of algorithms and methods depend on predicted properties for the purpose of assessing, selecting, and producing molecules [110]. Instead of depending on predefined rules set by humans, deep learning approaches are trained to produce novel molecules by studying groups of established molecules [112]. Property prediction refers to the plenty of compounds that are inherently synthesized in a drug discovery program, which is thought to anticipate a molecule's physical characteristics and biological activity [113]. Subsequent experiments are then prioritized based on these projected qualities. Predicting molecular properties throughout the drug discovery process is a time- and money-consuming procedure with a high attrition rate. According to a recent study, the average cost of developing new drugs has been steadily rising to over $1 billion. There are numerous candidates to validate, and the validation procedure is significantly complex and long [114].

The arena of molecular property prediction targeting drug discovery has seen important changes over the past decade due to developments in artificial intelligence (AI, Figure 6). Molecular property prediction in the field of molecular representation learning continues to face significant challenges due to the limited exploration of key elements, despite the advancements in techniques. This lack of understanding hinders the progress of this field [113]. These techniques have the potential to greatly reduce the time of the process for discovery to a better drug molecule in a faster and cheaper way [115]. Three representations are commonly used to predict the represent molecules: linear notations, such as Simplified Molecular Input Line Entry System (SMILES) strings; molecular graphs; and fixed representations, such that structural keys and fingerprints, which indicate the existence of specific structural pattern of a molecule. Many neural networks, especially recurrent neural networks (RNNs), convolutional neural networks (CNNs), and graph neural networks (GNNs), have been postulated for molecular representation learning with the initiation of deep learning method [116]. It has been noted that deep representation learning which outperforms fixed molecular representations as an auspicious technique for predicting the property of a molecular [117].

The molecular fingerprint technique, widely recognized for its efficacy, employs a hash function to encode the molecular structure, thereby representing substructures [118]. In machine learning models, features are used with additional descriptors like hydrogen bond acceptors (HBA), hydrogen bond donors (HBD), partition coefficients (logP), polar surface area (PSA), etc. Those restrictions can solve a fingerprint based on neural networks. to learn molecular embedding by Seq2seq fingerprint recurrent neural networks (RNN) [119]. With the Simplified Molecular-Input Line-Entry System (SMILES), one line can represent several molecules in text. As it is a text-based and sequential technique, NLP-inspired techniques such as word implanting and RNN have been planned. To overcome the disadvantages of fingerprint word2vec and Mol2Vec10 representation techniques for predicting the molecule and RNN on SMILES tokens, Smiles2Vec9 learns a method for molecular representation [120].

The accuracy of predictive models is critically dependent on the availability of suitable data [121]. Neural models, with their vast number of parameters, necessitate a sufficient amount of training data to effectively learn an optimal molecular representation and subsequently perform the prediction task. While traditional molecular-fingerprint-based models can be trained on a small number of molecules, this quantity of data is inadequate for neural models. To commence their training, a minimum of a few thousand molecules is required. Regrettably, in numerous drug discovery scenarios, obtaining a large

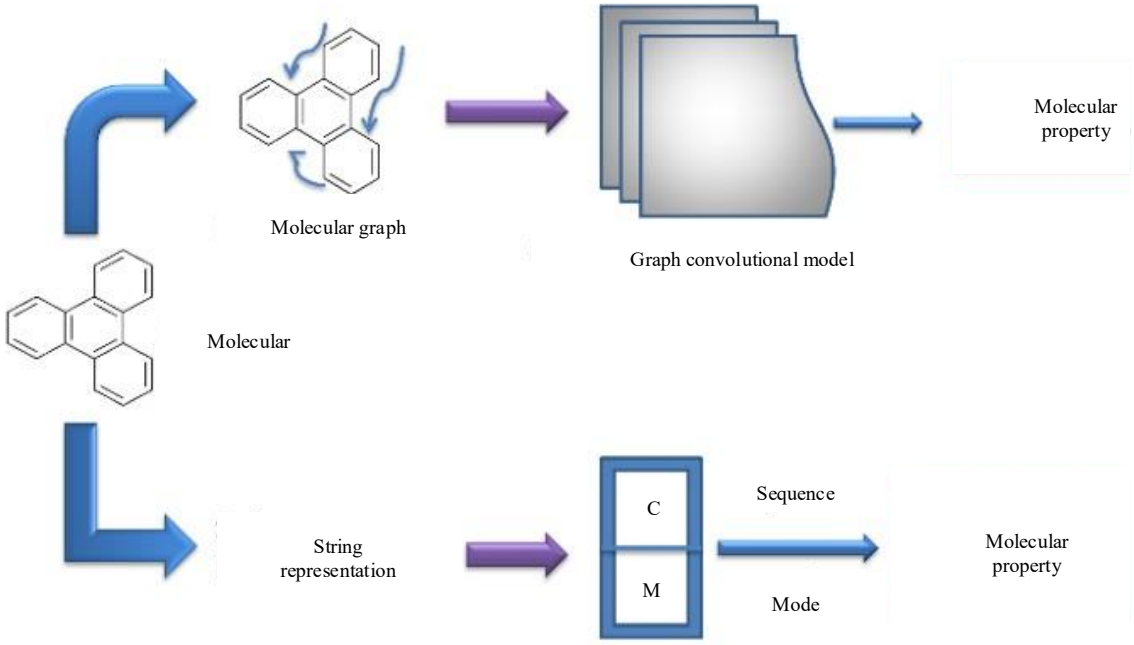

Figure 6. Process of molecular property prediction through AI

sample may not be feasible. Even a typical pharmaceutical lead optimization endeavour, which generates a few thousand molecules, may not provide enough data to adequately train a neural model [112].

For predicting chemical features, convolutional neural networks (CNN) are also useful [122]. One drawback is that molecule chemical structure and locations cannot be entirely covered by using SMILEs. Because of this, degradation occurs in training the model when a precise structure is not recognized. When a model like Transformer is pre-trained and self-supervised, it does not need any labeled data to perform better on most natural language processing (NLP) tasks [123]. By engaging in pre-training, those techniques generate a huge language model that can be useful for a diverse range of applications. It reveals how extensive data may be used to figure out a generalized model and how fine-tuning downstream tasks can help attain this [124]. SMILES-Transformer17, used for the encoder's production of abstract latent vectors, is used as a molecular fingerprint. In small-data settings, it executes better than other techniques. SMILES-BERT18 performs well in various prediction tests after employing BERT14's pre-training task for SMILES [125].

The training data is a crucial element in the development of any machine learning model. The quality of the model and the accuracy of its predictions heavily rely on the training data used [126]. The uncertainty in molecular property prediction arises from various sources, including dataset split, experimental data, and model training. Although databases like PubChem [127, 128] and ChEMBL [129] provide access to vast amounts of scientific data, the reliability of this data can sometimes be questionable. Additionally, variations can be introduced during model training, such as random weight initialization and random mini-batch shuffling [130]. To mitigate the uncertainty related to model training and improve prediction accuracy, ensembling techniques have been proposed [131]. Therefore, it is important to consider experimental uncertainty to enhance the reliability of molecular property prediction. Secondly, the study does not cover the explainability of the molecular property prediction models. Explainable AI, which aims to make predictions more understandable by domain experts, is crucial in building trust towards effective AI tools in drug discovery.

Artificial intelligence in Nutrition and Food science

Modern technology would be able to analyze the data, which would take years, leading to significant advancements in nutrition and food science [132]. Consequentially, the AI technology may have a positive effect on the health-care system by assisting medical professionals with quick diagnosis, modified medicine, drug design, disease assessment, intensive care, and diseases linked to diet [133]. During the COVID-19 pandemic, advancements have been achieved through the utilization of telematic tools for remote nutrition assessments and devices that enable patients to self-assess various nutrition-related health metrics, including glucose level in the blood, body weight, rate of heart, percentage of fat in the body, BP, tracking activity, calorie tracking, and quality of diet [134]. In this regard, artificial intelligence (AI) and digital technologies can be advantageous tools, particularly when it comes to chronic diseases that can be quite incapacitating, such as obesity, diabetes mellitus, and metabolic illnesses, which are frequently tough to handle and can show non-optimal results [135].

Numerous applicability for tracking weight-loss and food designs have been widely utilized and researched in the field of nutrition and here the utilization of AI is important for fast advancements with the huge data science in this important for better survival (Figure 7). For instance, those who utilized weight loss mobile apps had a significant decrease in their body mass index (BMI) of about 0.43 kg/m2, as the apps offered nonstop actual feedback on the health measures they adhered to [136]. Notably, research on a variety of probiotic effects can aid in the development of probiotic combinations and formulations that are more successful or in the synthesis of probiotics using synthetic biology techniques [137, 138]. Compared to a control diet, this AI-assisted food plan successfully improved symptoms associated with irritable bowel syndrome in a clinical pilot investigation [139]. It's interesting to note that the application of AI-powered algorithms, which include gut bacteria, significantly improved cardiovascular risk prediction models [140]. AI and bioinformatics can find biomarkers linked to particular dietary treatments or health outcomes [141].

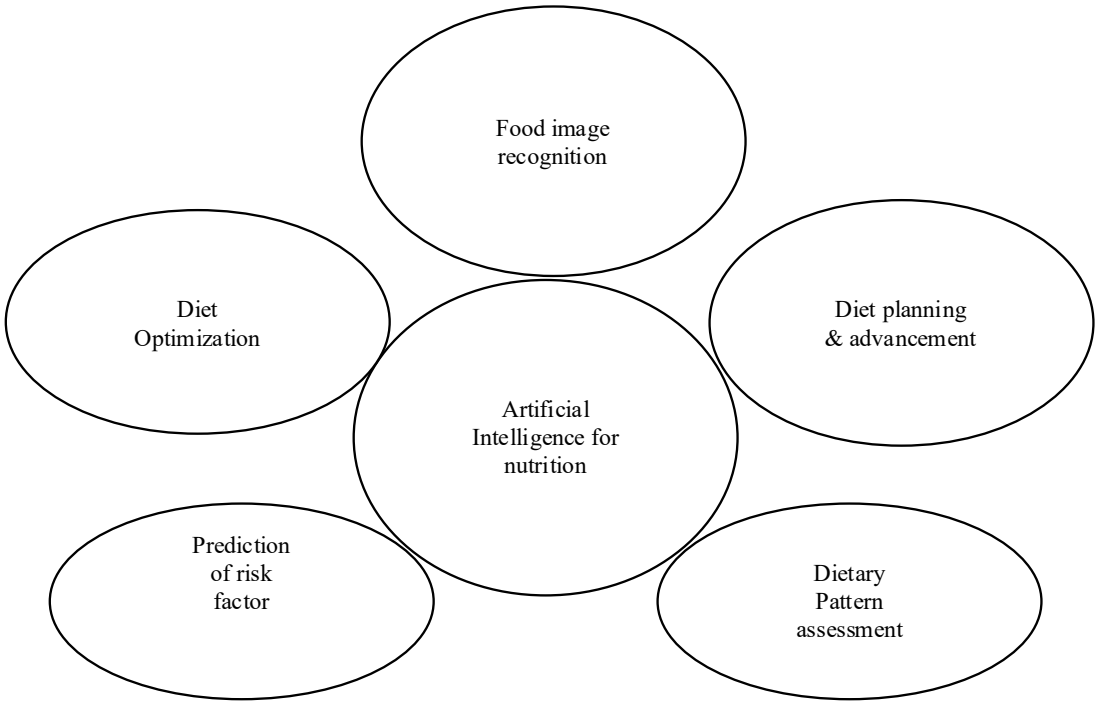

Figure 7. Implementation of AI in food and science

Artificial neural networks (ANN) successfully forecast the chemical makeup of peach fruit in a recent study, showing that AI application in the food industry is both practical and efficient [142]. Similar to these findings, ANN estimates the phenolic and flavonoid content of garlic more accurately than response surface approach [143]. With the help of deep learning techniques, food picture recognition is regarded as a revolutionary technique that will get more capable as food databases expand [144]. In this regard, the "NutriNet" tool was introduced and put through an intense testing phase using over 225,000 images of 520 different nutrients and drinks whereas the GoCARB program was just as efficient at estimating carbohydrates as dieticians [145, 146]. With smartphone photographs, the goFOODTM app can estimate a meal's calorie and macronutrient content [147]. Additionally, AI can help dieticians and other medical experts provide better nutrition and healthcare [148]. Adoption of AI may eventually pave the way for the creation of tailored diet plans and the improvement of the support care infrastructure, which may improve health for individuals as well as society.

ARTIFICIAL INTELLIGENCE IN NANOSCIENCE AND NANOTECHNOLOGY

Nanotechnology leverages principles from physics, chemistry, and engineering, while AI is inspired by biological mechanisms such as neural networks and evolutionary algorithms. By establishing a connection between current advancements in nanoscience and AI, researchers can enhance exploration in these areas and create a new wave of information and communication technologies that may revolutionize society through the integration of technology and biology towards the sustainable smart applications [149]. Nanoscience deals with the material manipulation in molecular, atomic, and macromolecular scale, where properties are substantially different from those at larger scales. Designing, characterization, manufacture and application of structures, devices and schemes by regulating the shape and size at nanoscale is known as nanotechnology [150]. Numerous applications of nanotechnology, such as drug delivery to imaging, being explored in the subject of nanomedicine. Although the physical limitations of nanotechnology limit its potential applications, a wide range of nanomedicine have been examined for imaging and drug delivery applications [151]. Drug synergism can be promoted by tailoring combinations of drugs to improve the clinical effectiveness of cancer treatment. However, optimization is still a challenging task since it necessitates selection of appropriate

drug combination, dosage, and dosing rate to boost potency with lowering of undesirable toxicities [152]. Even if multifunctional nanomedicines in particular have increased therapeutic effectiveness, they still have the similar optimization problems. Achieving synergy and enhancing combination therapy are important factors in this discipline [153].

A new field of study known as computational nanotechnology or computational nanoscience [154], has emerged as a result of the creation and application of algorithms and computational tools to the advancement of nanoscience and nanotechnology (N&N). Algorithms for classification were created to increase the accuracy of medical diagnosis [155]. Eventually, the development of computational tools offers a feasible opportunity to fully realize the future potential of combinatorial nanomedicine [156]. The reason for this is that combination parameters defined by AI can achieve globally optimal therapeutic outcomes, independent of comprehensive information on disease mechanisms. Creating a connection between the current state of nanoscience and artificial intelligence can further study in both fields and lead to the development of new information and communication techniques that will significantly influence our society, potentially even paving the way for the fusion of technology and biology [157]. In this context, techniques as machine learning paradigms might be extremely important for developing scientific findings and for the advancement of future nano applications [158]. The combination of AI with nanotechnology finds useful and effective applications in information science, bioengineering, neuroscience, etc (Figure 8).

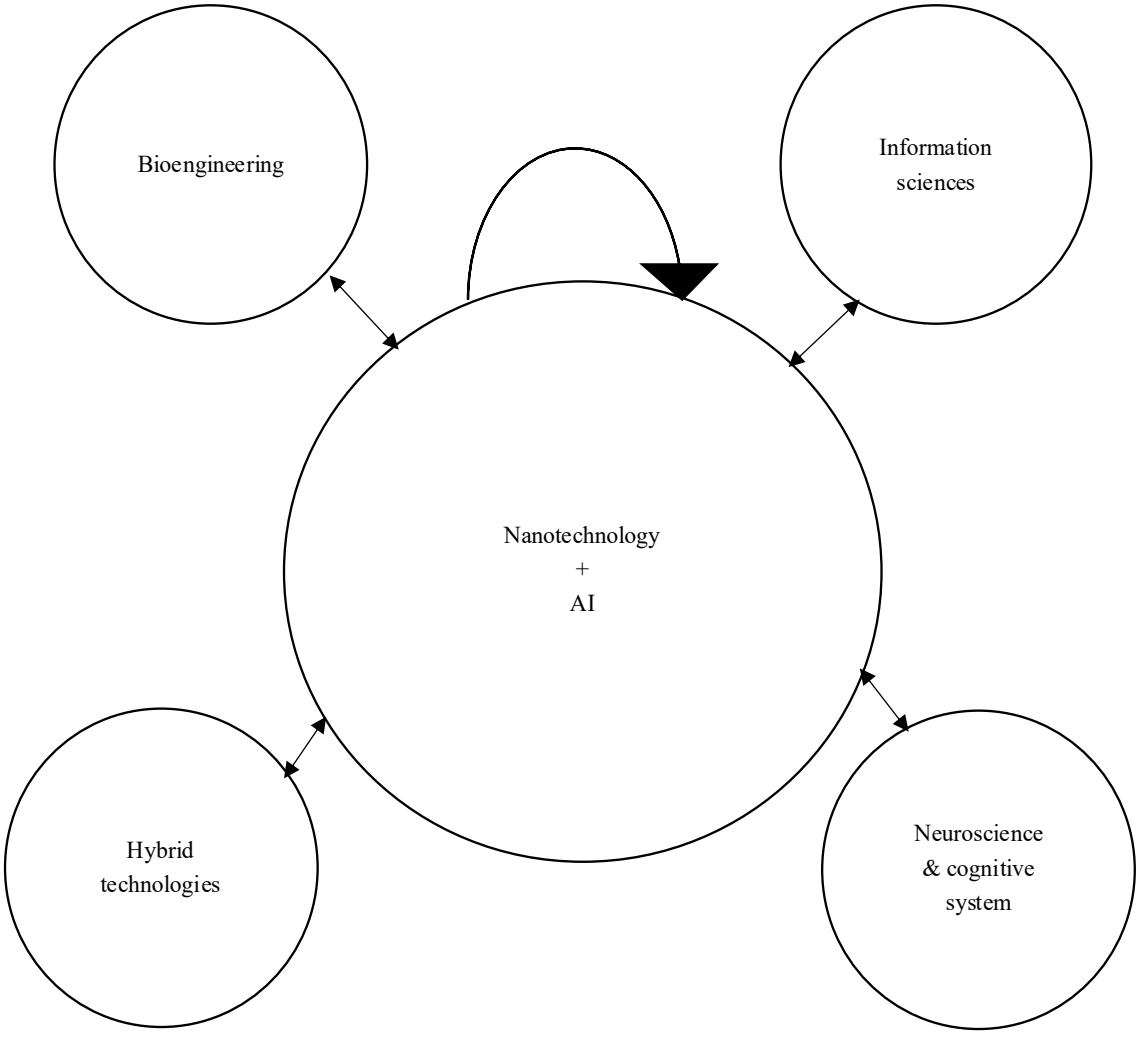

Figure 8. Impact of combined effect of nanotechnology and AI.

Research on nanotechnology focuses on creating things from the bottom up, whereas research on artificial intelligence usually takes a top-down approach to problem-solving. Many complicated problems requiring several description levels and interactions will have solutions when these two disciplines are combined [159]. Understanding information processing in the nervous system, where intricate calculations are carried out at various but interacting timescales from the molecular level to the level of the entire brain, is one such challenge [160]. The convergence of nanotechnology and AI has the potential to influence a wide range of information sciences technological advancements, including hybrid techniques that combine biological entities and nanotechnology, bioengineering, neuroscience, and many other related disciplines, as well as new computer architectures and data representations. Wang et al. recently established feedback system control, a popular platform for therapeutic advances that are both unmodified and modified by nanotechnology [161]. The authors employed artificial intelligence for the standardization of drug dose groupings that would result in extreme cytotoxicity. The combinations that were employed to study the effects on several breast-cancer cell lines consisted of nanodiamond-doxorubicin, nanodiamond-bleomycin, nanodiamond-mitoxantrone, and unmodified paclitaxel. Based on this technique, the results demonstrated that combinations of drugs for nanomedicines performed better than combinations of drugs chosen at random [162].

The field of nanorobotics, a cutting-edge technology in nanoscience, involves the creation of robots or machines at the nanoscale dimension (10^{-1}). These nanorobots are equipped with unique sensors for identifying target molecules and are programmed to diagnose and treat life-threatening diseases, such as cancer [163]. The use of nanorobots in cancer treatment is a promising area of research, with the potential to revolutionize therapy [164]. By delivering medication directly to cancer cells, nanorobots aim to reduce the side effects of chemotherapy and improve treatment outcomes. Furthermore, nanorobots have the potential to advance personalized medicine and enhance health monitoring through their intravascular therapeutic capabilities [165, 166]. In the realm of small-scale technology, nanotechnology emerges as the harbinger of the future. To unlock its full potential, the incorporation of Artificial Intelligence (AI) becomes indispensable. By harnessing AI's data analytics prowess, nanotechnology can effectively gather and analyze information, equipping us with the ability to make more decisive and knowledgeable decisions [167]. In the near future, AI-based strategies and particular nanoscience-related problems will continue to be useful tools in the pharmaceutical industry.

Artificial Intelligence In Waste Water Treatment

The treatment of wastewater plays a vital role in reducing the release of pollutants and preserving the value of water resources [168]. However, different types of pollutants are progressively diverse and challenging to treat in wastewater through the development of novel industrial products, such as medicinal and personal care products, by-products caused by disinfection, and per- and polyfluoroalkyl materials [169, 170]. To resolve these complicated issues, the scientific community is using artificial intelligence to treat wastewater (Figure 9). Artificial intelligence has been extensively used in the process and management of wastewater, quality monitoring and estimation, and process optimization [171, 172]. For example, using the AI, the electricity consumption of the pumping stations for wastewater is reduced to 16.7% [173]. Also, in troubleshooting procedures, AI is used to solve problems like sludge bulking, sensor faults, and membrane contamination problems [174]. Lotfi et al. reported a mixed process, like linear and nonlinear, to precisely predict the elimination of predictable pollutants from wastewater, such as BOD and COD [175]. For the exclusion of organic micro-pollutants, Vakili and his group used artificial neural networks (ANNs) and the response surface methodological process (RSM) [176].

The water quality index (WQI) serves as a fundamental indicator for evaluating the efficiency of a water treatment plant, taking into consideration essential water quality variables like dissolved oxygen (DO), temperature, turbidity, TSS, BOD, calcium, COD, and pH [177]. Various artificial intelligence (AI) models, including artificial neural networks (ANN), multi-linear regression (MLR), genetic algorithms (GA), radial basis function (RBF), particle swarm optimization (PSO), and support vector machines (SVM), have been utilized in scientific studies for the prediction and monitoring of water

quality parameters, demonstrating satisfactory results [178]. Notably, neural networks (NNs) have been widely used in research to monitor and assess the quality of surface water but practical applications face numerous challenges and categorized as (a) Insufficient data effectiveness in wastewater treatment plants (WWTP), (b) the robustness of the models, (c) the assignment of hyper-parameters, and (d) the determination of initial weight parameters [179]. Another aspect that needs to be addressed in future research is the quantitative evaluation of the influence of predicting wastewater parameters on the reduction of energy consumption in wastewater treatment plants and limitation should be considered during the future investigation on waste water treatment [180].

Recent advances in artificial intelligence in chemical and allied science

Recently, numerous review papers have been reported on the application of artificial intelligence to managing wastewater. As such, Bhagat et al. reported an analysis of the recent status and upcoming potential of artificial intelligence to simulate the removal of heavy metals from wastewater [181]. Also, Niu and his group presented an application of several AI approaches to membrane fouling prediction [182].

Thakkar et al. introduced a ML based technique that enables the classification of whether a synthetic route can be determined for a particular compound using the CASP tool AiZynthFinder. The ML models developed in this research provide a retrosynthetic accessibility score (RA score, Figure 10) for any molecule of interest. Remarkably, these models exhibit a computational efficiency that is at least 4500 times faster than the retrosynthetic analysis performed by the underlying CASP tool [183].

Grzybowski group described the limitation of artificial intelligence in real life practical organic synthetic chemistry. Emphasizing the intricacies and biases present within the realm of synthetic chemistry, they suggest leveraging the unique capabilities of AI by incorporating the knowledge base and reasoning methodologies of domain experts through the active engagement of synthetic chemists, who represent the end users of synthesis planning software, in the development process [184].

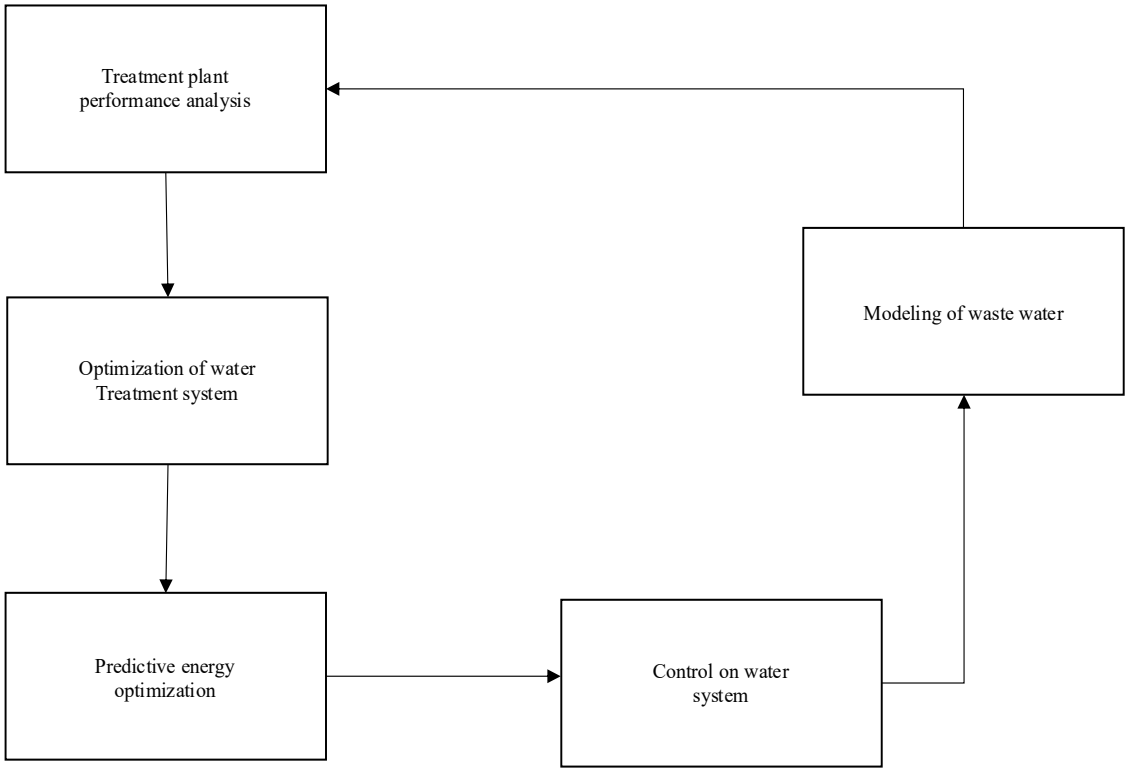

Figure 9. Utilization of AI in wastewater treatment.

Srinivasan et al. have devised an innovative strategy for molecular design that employs artificial intelligence (AI) to identify novel therapeutic agents against SARS-CoV-2 (Figure 11). The approach involves an iterative search and retrain process, combining a Monte Carlo tree search algorithm with a multitask neural network surrogate model for conducting computationally expensive docking simulations. Additionally, recurrent neural networks are utilized for rollouts. By utilizing Vina scores as the target objective to evaluate binding to either the isolated spike protein (S-protein) at its host receptor region or the S-protein/angiotensin converting enzyme 2 receptor interface, they also have successfully generated a substantial number of new therapeutic agents (~100's). These agents demonstrate superior performance over both Food and Drug Administration (FDA) and non-FDA molecules [185].

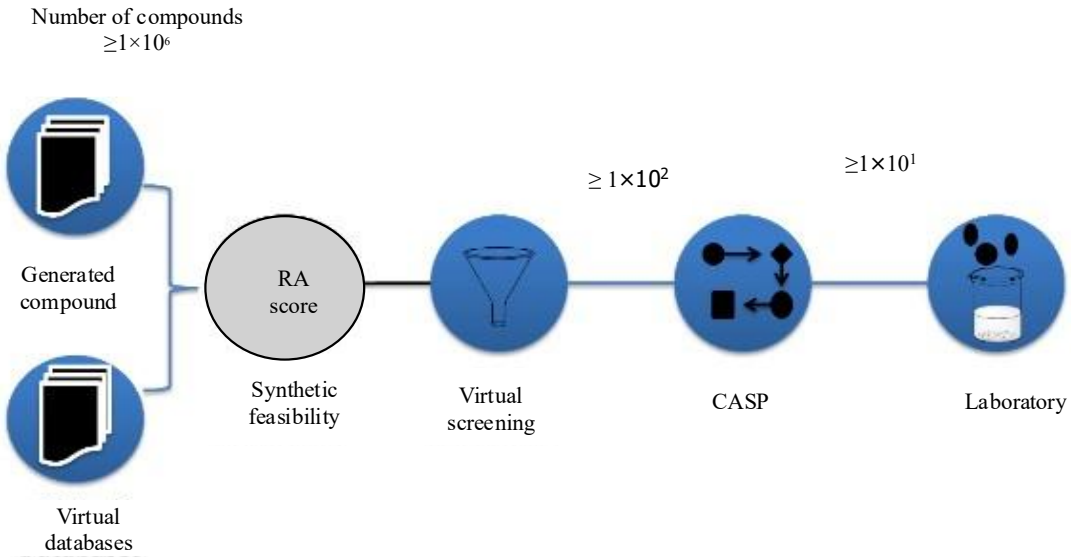

Figure 10. Schematic diagram for RA Score and CASP

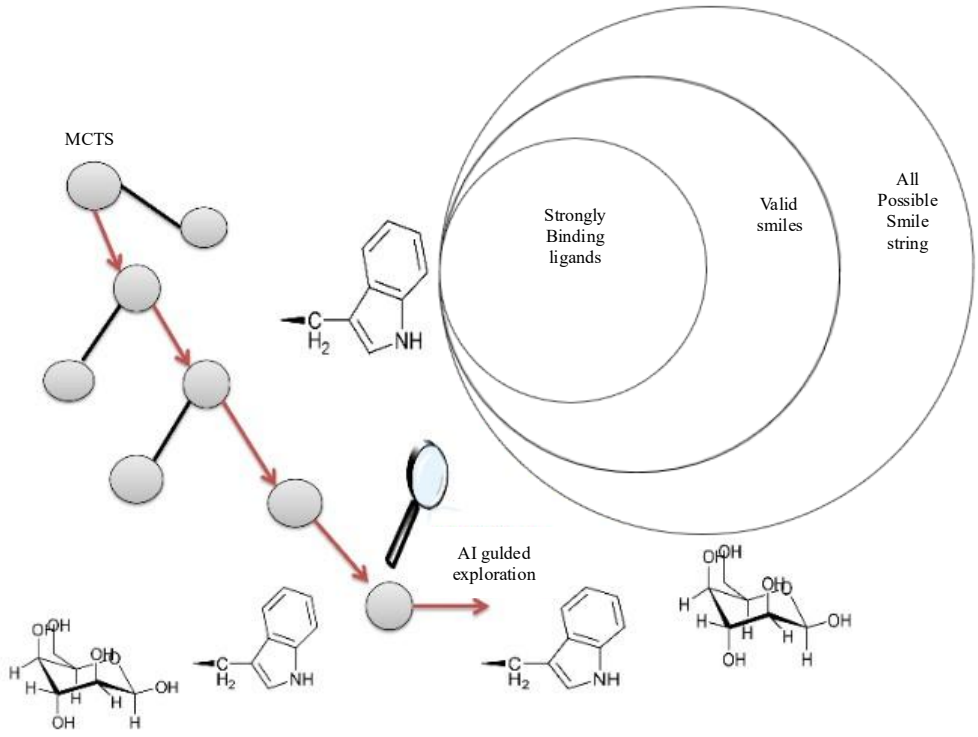

Figure 11. AI guided exploration of therapeutic agents.

Adir et al. recently presented a review on the utilization of nanomaterials with the significant support of AI in advancing omics, diagnostics, and treatment technologies for the field of precision cancer medicine (Figure 12). They also discussed the unique role played by AI in the analysis of precision medicine data and the design of nanomedicine [186].

Hsu et al. in very recent reported the fusion of metalens technology with artificial intelligence models for significant a groundbreaking development in optimizing the functionality of full-colour metalens-based imaging systems [187]. In this work the optical response of a GaN-based metalens was analyzed in conjunction with the use of two successive artificial intelligence (AI) models to address issues such as blurriness and color cast in images. It was determined that the color cast in the images was a result of the optical loss of the metalens in the blue spectral range. To rectify this, the Autoencoder and CodeFormer sequential models were employed for color correction and image reconstruction, respectively.

In 2024, Wang et al. demonstrated the XGboost algorithm as the premier predictive tool for forecasting polymer viscosities in different phases. According to the authors, this revelation is set to yield significant information for the assessment of polymers screening for utilization in medicine and the chemical industry [188].

Another work in 2024, by Zhang and co-workers reported the artificial intelligence-assisted multiparameter technique showcased remarkable efficacy in swiftly achieving precise size discrimination of nanoparticles at the individual particle level, thereby providing valuable guidance for their practical implementation [189]. In their report an intriguing advancement with the combination of multiparameter analysis and artificial intelligence, a powerful tool for processing multidimensional data was implemented. Significantly, the successful utilization of artificial intelligence-assisted multiparameter size discrimination facilitated the intelligent distinction of mixed Ag NPs, yielding an optimal accuracy rate surpassing 95%.

Gulbalkan et al. have demonstrated the fusion of molecular simulations with AI and practical experiments for the development of exceptional MOFs and MOF-based composites that excel over traditional porous materials in CO_2 capture. The future directions are elucidated by examining the current opportunities and hurdles in the realm of utilizing experiments, theory, and AI for the rapid exploration of porous materials for CO_2 capture [190].

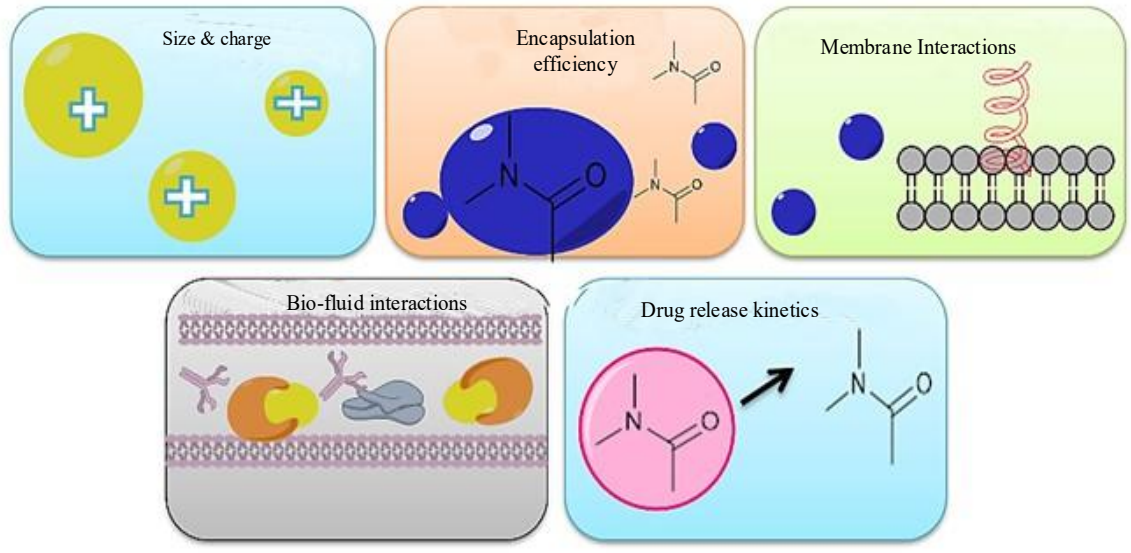

Figure 12. AI in the analysis of precision medicine.

In 2023, Lia et al. presented a practical demonstration on AI workflow application to enhance catalyst synthesis for ammonia production. The results strongly emphasize the workflow's ability to streamline the catalyst development process, offering a resource-efficient and highly accurate alternative to the conventional methods. Their approach integrates advanced language comprehension with robust optimization techniques, efficiently converting information gathered from various sources into practical parameters for experimental and optimization purposes [191].

Another work in 2023, by Yu group reported the practicable models with the potential to offer valuable insights for the rapid identification of compounds that exhibit organ-level toxicity in humans during the process of drug discovery [192]. This research revealed that the graph-based deep learning approach exhibited superior performance over the conventional machine learning models, particularly in predicting human organ toxicity endpoints. Moreover, the utilization of transfer learning algorithm significantly enhanced model accuracy for skin sensitization endpoint by incorporating data from in vivo acute toxicity experiments and in vitro assays conducted in the Tox21 project.

CONCLUSION AND OUTLOOK

In recent years, applicability and acceptance of artificial intelligence in chemistry have gradually increased, as supported by the growing volume of relevant journal publications. So far, it is striking that the progress has not even been dilated much in the various fields of chemistry. In the various areas of chemistry and chemical biology, artificial intelligence is much more with the familiar hype cycle of evolving techniques than the others techniques. In analytical chemistry and life sciences, adoption of AI is probably passed the so-called “highest inflated hopes” and “trough of disenchantment”. The usefulness of artificial intelligence in a given area is fundamentally connected to the number and quality of its information, also the chances to gain the inner form from its investigation. Artificial intelligence can help to gain the deep knowledge that would extend beyond the established data. It is also beneficial for extracting inner visions from huge amount of obstinate data, also aiding in the robotics of repetitive jobs. To keep in attention clear, it is not an astonishment to see a surge in artificial intelligence adaptation in analytical chemistry, where huge physical activity sets are easily attained, or in the field of bio-chemistry, this comprises a large amount of data sets for macro-molecules, their structural associations are not clear to scientists. Yet, the achievements in these conventionally data-intensive field is being emulated in other branches of chemistry and biochemistry. The current implementation of AI software suffers from a flawed delivery system that lacks the capacity to effectively integrate knowledge and diverse methodologies, while also failing to evaluate the cost-effectiveness of data-driven technology. The disadvantages of AI, including exorbitant costs, insufficient experiential advancements, and the potential for job displacement, will continue to persist till recent future. Also, to improve the reliability and attractiveness of predictions for chemist users, it is essential to integrate a wide range of chemical knowledge modalities. By incorporating diverse sources of information, the quality of predictions can be enhanced, providing chemist users with more accurate and appealing results. A general aim should be to bridge the gap between computer algorithms and the real practical complex nature of chemical synthesis.

REFERENCES

1. Abedsoltan, H. COVID-19 and the Chemical Industry: Impacts, Challenges, and Opportunities. J. Chem. Technol. Biotechnol. 2023; 98 (12): 2789–2797.
2. Heo, S.; Chan, A. Y.; Diaz Peralta, P.; Jin, L.; Pereira Nunes, C. R.; Bell, M. L. Impacts of the COVID-19 Pandemic on Scientists’ Productivity in Science, Technology, Engineering, Mathematics (STEM), and Medicine Fields. Humanit. Soc. Sci. Commun. 2022; 9 (1): 1–11p.
3. Sanderson K. Automation: chemistry shoots for the Moon. Nature 2019; 568(7753): 577–9p.
4. Porwol L, Kowalski DJ, Henson A, et al. An autonomous chemical robot discovers the rules of inorganic coordination chemistry without prior knowledge. Angew. Chem., Int. Ed. Engl. 2020; 59(28): 11256–61p.
5. Bedard AC, Adamo A, Aroh KC, et al. Reconfigurable system for automated optimization of diverse chemical reactions. Science 2018; 361(6408): 1220–5p.

6. Coley CW, Thomas IIIDA, Lummiss JAM, et al. A robotic platform for flow synthesis of organic compounds informed by AI planning. Science 2019; 365(6453): 1566.
7. Mullin, R. The Lab of the Future Is Now. Chem. Eng. News 2021; 28.
8. Khatod, R. G., & Sakhale, C. N. Design and Fabrication of Liquid Dispensing Machine Using Automatic Control for Engg. Industry. International journal of innovative technology and exploring engineering (IJITEE) 2012; 1(5): 38-44p.
9. Joshi, R. P.; Kumar, N. Artificial Intelligence for Autonomous Molecular Design: A Perspective. Molecules 2021; 26 (22): 6761p.
10. Dias, A. L.; Rodrigues, T. Large Language Models Direct Automated Chemistry Laboratory. Nature 2023; 624 (7992): 530–531p.
11. Gaulton A, Hersey A, Nowotka M, et al. The ChEMBL database in 2017. Nucleic Acids Res. 2017; 45: 945–954p.
12. Wang Y, Cheng T, Bryant SH. PubChem BioAssay: a decade's development toward open high-throughput screening data sharing. SLAS Discov. 2017; 22(6): 655–666p.
13. Loeffler, H. H.; He, J.; Tibo, A.; Janet, J. P.; Voronov, A.; Mervin, L. H.; Engkvist, O. Reinvent 4: Modern AI–Driven Generative Molecule Design. J. Cheminform. 2024; 16:1-16p.
14. Gómez-Bombarelli, R.; Wei, J. N.; Duvenaud, D.; Hernández-Lobato, J. M.; Sánchez-Lengeling, B.; Sheberla, D.; Aguilera-Iparraguirre, J.; Hirzel, T. D.; Adams, R. P.; Aspuru-Guzik, A. Automatic Chemical Design Using a Data-Driven Continuous Representation of Molecules. ACS Cent. Sci. 2018; 4 (2): 268–276p.
15. Kai, L.; Wei, Z.; Ming, G. Molecular Design Method Based on New Molecular Representation and Variational Auto-Encoder. In Natural Language Processing, Information Retrieval and AI; Academy and Industry Research Collaboration Center (AIRCC), 2023.
16. Jabbar, R.; Jabbar, R.; Kamoun, S. Recent Progress in Generative Adversarial Networks Applied to Inversely Designing Inorganic Materials: A Brief Review. Comput. Mater. Sci. 2022, 213, 111612p.
17. Gupta, A.; Müller, A. T.; Huisman, B. J. H.; Fuchs, J. A.; Schneider, P.; Schneider, G. Generative Recurrent Networks for DE Novo Drug Design. Mol. Inform. 2018; 37:1–2p.
18. Liu, X.; Ye, K.; van Vlijmen, H. W. T.; IJzerman, A. P.; van Westen, G. J. P. DrugEx v3: Scaffold-Constrained Drug Design with Graph Transformer-Based Reinforcement Learning. J. Cheminform. 2023; 15 (1): 1-14p.
19. Olivecrona, M.; Blaschke, T.; Engkvist, O.; Chen, H. Molecular De-Novo Design through Deep Reinforcement Learning. J. Cheminform. 2017; 9 (1): 1-14p.
20. Blaschke, T.; Arús-Pous, J.; Chen, H.; Margreitter, C.; Tyrchan, C.; Engkvist, O.; Papadopoulos, K.; Patronov, A. REINVENT 2.0: An AI Tool for DE Novo Drug Design. J. Chem. Inf. Model. 2020; 60 (12): 5918–5922p.
21. Ross, J.; Belgodere, B.; Chenthamarakshan, V.; Padhi, I.; Mroueh, Y.; Das, P. Large-Scale Chemical Language Representations Capture Molecular Structure and Properties. Nat. Mach. Intell. 2022; 4 (12): 1256–1264p.
22. He, J.; Nittinger, E.; Tyrchan, C.; Czechtizky, W.; Patronov, A.; Bjerrum, E. J.; Engkvist, O. Transformer-Based Molecular Optimization beyond Matched Molecular Pairs. J. Cheminform. 2022; 14 (1): 1-14p.
23. Shi, C.; Xu, M.; Zhu, Z.; Zhang, W.; Zhang, M.; Tang, J. GraphAF: A Flow-Based Autoregressive Model for Molecular Graph Generation. arXiv [cs.LG], 2020.
24. Plehiers, P. P.; Coley, C. W.; Gao, H.; Vermeire, F. H.; Dobbelaere, M. R.; Stevens, C. V.; Van Geem, K. M.; Green, W. H. Artificial Intelligence for Computer-Aided Synthesis in Flow: Analysis and Selection of Reaction Components. Front. Chem. Eng. 2020; 2: 1-19p.
25. Yang, L.; Zhang, Z.; Song, Y.; Hong, S.; Xu, R.; Zhao, Y.; Zhang, W.; Cui, B.; Yang, M.-H. Diffusion Models: A Comprehensive Survey of Methods and Applications, arXiv. 2022.
26. Hoogeboom, E.; Satorras, V. G.; Vignac, C.; Welling, M. Equivariant Diffusion for Molecule Generation in 3D. arXiv. 2022.
27. Xu, M.; Powers, A.; Dror, R.; Ermon, S.; Leskovec, J. Geometric Latent Diffusion Models for 3D Molecule Generation. arXiv. 2023; 1-18p.

28. Luu, R. K.; Wysokowski, M.; Buehler, M. J. Generative Discovery of de Novo Chemical Designs Using Diffusion Modeling and Transformer Deep Neural Networks with Application to Deep Eutectic Solvents. Appl. Phys. Lett. 2023; 122 (23): 234103-(1-9).
29. Bradshaw, J.; Paige, B.; Kusner, M. J.; Segler, M. H. S.; Hernández-Lobato, J. M. A Model to Search for Synthesizable Molecules. arXiv. 2019; 1-20p.
30. Bilodeau, C.; Jin, W.; Jaakkola, T.; Barzilay, R.; Jensen, K. F. Generative Models for Molecular Discovery: Recent Advances and Challenges. Wiley Interdiscip. Rev. Comput. Mol. Sci. 2022; 12 (5): 1-17p.
31. Polykovskiy, D.; Zhebrak, A.; Sanchez-Lengeling, B.; Golovanov, S.; Tatanov, O.; Belyaev, S.; Kurbanov, R.; Artamonov, A.; Aladinskiy, V.; Veselov, M.; et al. Molecular Sets (MOSES): A Benchmarking Platform for Molecular Generation Models. Front. Pharmacol. 2020; 11: 1-10p.
32. Brown, N.; Fiscato, M.; Segler, M. H. S.; Vaucher, A. C. GuacaMol: Benchmarking Models for de Novo Molecular Design. J. Chem. Inf. Model. 2019; 59 (3): 1096–1108p.
33. Ivanenkov, Y. A.; Polykovskiy, D.; Bezrukov, D.; Zagribelnyy, B.; Aladinskiy, V.; Kamya, P.; Aliper, A.; Ren, F.; Zhavoronkov, A. Chemistry42: An AI-Driven Platform for Molecular Design and Optimization. J. Chem. Inf. Model. 2023; 63 (3): 695–701p.
34. Coley, C. W.; Rogers, L.; Green, W. H.; Jensen, K. F. Computer-Assisted Retrosynthesis Based on Molecular Similarity. ACS Cent. Sci. 2017; 3 (12): 1237–1245p.
35. Judson P. Knowledge-Based Expert Systems in Chemistry: Not Counting on Computers. Cambridge: Royal Society of Chemistry; 2009.
36. Sun Y, Sahinidis NV. Computer-Aided Retrosynthetic Design: Fundamentals, Tools, and Outlook. Curr. Opin. Chem. Eng. 2022; 35: 100721p.
37. Corey EJ, Wipke WT, Cramer IIIRD, et al. Computer-Assisted Synthetic Analysis. Facile Man-Machine Communication of Chemical Structure by Interactive Computer Graphics. J. Am. Chem. Soc. 1972; 94(2): 421–430p.
38. Johnson PY, Burnstein I, Crary J, et al. Designing an Expert System for Organic Synthesis: The Need for Strategic Planning. ACS Symposium Series; Washington, DC: American Chemical Society 1989; 102–123p.
39. Gelernter HL, Sanders AF, Larsen DL, et al. Empirical Explorations of SYNCHEM: The Methods of Artificial Intelligence Are Applied to the Problem of Organic Synthesis Route Discovery. Science 1977; 197(4308): 1041–1049p.
40. Warr WA. A Short Review of Chemical Reaction Database Systems, Computer-aided Synthesis Design, Reaction Prediction and Synthetic Feasibility. Mol. Inform. 2014; 33(6-7): 469–476p.
41. Cook A, Johnson AP, Law J, et al. Computer-aided Synthesis Design: 40 Years On. Wiley Interdiscip. Rev. Comput. Mol. Sci. 2012; 2(1): 179–107p.
42. Latendresse M, Malerich JP, Herson J, et al. SynRoute: A Retrosynthetic Planning Software. J. Chem. Inf. Model. 2023; 63(17): 5484–5495p.
43. Wang Y, Pang C, Wang Y, et al. Retrosynthesis Prediction with an Interpretable Deep-Learning Framework Based on Molecular Assembly Tasks. Nat. Commun. 2023; 14(1): 1–15p.
44. Zhong Z, Song J, Feng Z, et al. Recent advances in deep learning for retrosynthesis. Wiley Interdisciplinary Reviews. Comput. Mol. Sci. 2024; 14(1): 1-27p.
45. Cadeddu, A.; Wylie, E. K.; Jurczak, J.; Wampler-Doty, M.; Grzybowski, B. A. Organic Chemistry as a Language and the Implications of Chemical Linguistics for Structural and Retrosynthetic Analyses. Angew. Chem. Int. Ed Engl. 2014; 53 (31): 8108–8112p.
46. Proudfoot, J. R. Molecular Complexity and Retrosynthesis. J. Org. Chem. 2017; 82 (13): 6968–6971p.
47. Corey, E. J. General Methods for the Construction of Complex Molecules. Pure Appl. Chem. 1967; 14 (1): 19–38p.
48. Rogers D, Hahn M. Extended-Connectivity Fingerprints. J. Chem. Inf. Model. 2010; 50(5): 742–754p.
49. Braams BJ, Bowman JM. Permutationally Invariant Potential Energy Surfaces in High Dimensionality. Int. Rev. Phys. Chem. 2009; 28(4): 577–606p.

50. Schwaller P, Laino T, Gaudin T, et al. Molecular Transformer: A Model for Uncertainty-Calibrated Chemical Reaction Prediction. ACS Cent. Sci. 2019; 5(9): 1572–1583p.
51. Lin K, Xu Y, Pei J, et al. Automatic Retrosynthetic Route Planning Using Template-Free Models. Chem. Sci. 2020; 11(12): 3355–3364p.
52. Wei JN, Duvenaud D, Aspuru-Guzik A. Neural Networks for the Prediction of Organic Chemistry Reactions. ACS Cent. Sci. 2016; 2(10): 725–732p.
53. Segler MHS, Waller MP. Neural-symbolic Machine Learning for Retrosynthesis and Reaction Prediction. Chemistry (Weinheim an Der Bergstrasse, Germany). 2017; 23(25): 5966–5971p.
54. Coley CW, Rogers L, Green WH, et al. SCScore: Synthetic Complexity Learned from a Reaction Corpus. J. Chem. Inf. Model. 2018; 58(2): 252–261p.
55. Segler MHS, Preuss M, Waller MP. Planning Chemical Syntheses with Deep Neural Networks and Symbolic AI. Nature 2018; 555(7698): 604–610p.
56. Thakkar A, Kogej T, Reymond JL, et al. Datasets and Their Influence on the Development of Computer Assisted Synthesis Planning Tools in the Pharmaceutical Domain. Chem. Sci. 2020; 11(1): 154–168p.
57. Jiang Y, Yu Y, Kong M, et al. Artificial Intelligence for Retrosynthesis Prediction. Engineering (Beijing) 2023; 25: 32–50p.
58. Jeong J, Lee N, Shin Y, et al. Intelligent Generation of Optimal Synthetic Pathways Based on Knowledge Graph Inference and Retrosynthetic Predictions Using Reaction Big Data. J. Taiwan Inst. Chem. Eng. 2022; 130: 103982p.
59. Szymkuc S, Gajewska EP, Klucznik T, et al. Computer-assisted synthetic planning: the end of the beginning. Angew. Chem. Int. Ed. 2016; 55(20): 5904-5937p.
60. de Almeida, A. F.; Moreira, R.; Rodrigues, T. Synthetic Organic Chemistry Driven by Artificial Intelligence. Nat. Rev. Chem. 2019; 3 (10): 589–604p.
61. Kowalik M, Gothard CM, Drews AM, et al. Parallel optimization of synthetic pathways within the network of organic chemistry. Angew. Chem. Int. Ed. 2012; 51(32): 7928-7932p.
62. Bort W, Baskin II, Gimadiev T, et al. Discovery of novel chemical reactions by deep generative recurrent neural network. Sci. Rep. 2021; 11(1): 1-15p.
63. Nam J, Kim J: Linking the Neural Machine Translation and the Prediction of Organic Chemistry Reactions. 2016arXiv:1612.09529. 2016; 1-19p.
64. Tetko IV, Karpov P, Van Deursen R, et al. State-of-the-art augmented nlp transformer models for direct and single-step retrosynthesis. Nat. Commun. 2020; 11(1): 1-11p.
65. Mo Y, Guan Y, Verma P, et al. Evaluating and clustering retrosynthesis pathways with learned strategy. Chem. Sci. 2021; 12(4): 1469-1478p.
66. Bai R, Zhang C, Wang L, et al. Transfer learning: making retrosynthetic predictions based on a small chemical reaction dataset scale to a new level. Molecules 2020; 25(10): 2357 (1-14)p.
67. Katare S, Caruthers JM, Delgass WN, et al. An intelligent system for reaction kinetic modeling and catalyst design. Ind Eng Chem Res. 2004; 43(14): 3484-3512p.
68. Sun, R.; Dai, H.; Li, L.; Kearnes, S.; Dai, B. Energy-Based View of Retrosynthesis. 2020; 1-15p.
69. Staszak, M. Artificial intelligence in the modeling of chemical reactions kinetics. Phys. Sci. Rev. 2023; 8(1): 51–72p.
70. Caruthers J, Lauterbach JA, Thomson K, et al. Catalyst design: knowledge extraction from high-throughput experimentation. J Catal. 2003; 216(1-2): 98-109p.
71. Qureshi R, Irfan M, Gondal TM, et al. AI in Drug Discovery and its Clinical Relevance. Heliyon 2023; 9(7): e17575p.
72. Jiménez-Luna J, Grisoni F, Weskamp N, et al. Artificial intelligence in drug discovery: recent advances and future perspectives. Expert Opin Drug Discov . 2021; 16(9): 949-59p.
73. Vemula D, Jayasurya P, Sushmitha V, et al. AI and ML in drug discovery: A comprehensive review. Eur. J. Pharm. Sci. 2023; 181: 106324p.
74. Paul D, Sanap G, Shenoy S, et al. Artificial intelligence in drug discovery and development. Drug Discov. Today 2021; 26(1): 80–93p.

75. Lavecchia, A. Deep learning in drug discovery: opportunities, challenges and future prospects. Drug Discov. Today 2019; 24(10): 2017-32p.
76. Liu Z, Roberts RA, Lal-Nag M, et al. AI-based language models powering drug discovery and development. Drug Discov. Today 2021; 26(11): 2593-2607p.
77. Zhuang D, Ibrahim AK. Deep Learning for Drug Discovery: A Study of Identifying High Efficacy Drug Compounds Using a Cascade Transfer Learning Approach. Appl. Sci. (Basel) 2021; 11 (17): 7772p.
78. Pu L, Naderi M, Liu T, et al. eToxPred: A Machine Learning-Based Approach to Estimate the Toxicity of Drug Candidates. BMC Pharmacol. Toxicol. 2019; 20 (1): 1-15p.
79. You J, McLeod RD, Hu P. Predicting drug-target interaction network using deep learning model. Comput. Biol. Chem. 2019; 80: 90–101p.
80. Niazi SK. The Coming of Age of AI/ML in Drug Discovery, Development, Clinical Testing, and Manufacturing: The FDA Perspectives. Drug. Des. Devel. Ther. 2023; 17: 2691-2725p.
81. Xu Y, Liu X, Cao X, et al. Artificial intelligence: A powerful paradigm for scientific research. Innovation 2021; 2(4): 100179p.
82. Beneke F, Mackenrodt M.-O. Artificial intelligence and collusion. IIC Int. Rev Int Rev Ind Prop Copyr Law. 2019; 50(1): 109–134p.
83. Bender A, Cortés-Ciriano I. Artificial intelligence in drug discovery: what is realistic, what are illusions? Part 1: Ways to make an impact, and why we are not there yet. Drug Discov. Today 2021; 26(2): 511-524p.
84. Blanco-González A, Cabezón A, Seco-González A, et al. The role of AI in drug discovery: Challenges, opportunities, and strategies. Pharmaceuticals (Basel, Switzerland) 2023; 16(6): 891p.
85. Xu Y, Liu X, Cao X, et al. Artificial intelligence: A powerful paradigm for scientific research. The Innovation 2021; 2(4): 100179p.
86. Zhuang D, Ibrahim AK. Deep learning for drug discovery: a study of identifying high efficacy drug compounds using a cascade transfer learning approach. Appl. Sci. 2021; 11(17): 7772p.
87. Stumpfe, D.; Bajorath, J. Current Trends, Overlooked Issues, and Unmet Challenges in Virtual Screening. J. Chem. Inf. Model. 2020; 60 (9): 4112–4115p.
88. Schneider, P.; Walters, W. P.; Plowright, A. T.; Sieroka, N.; Listgarten, J.; Goodnow, R. A., Jr; Fisher, J.; Jansen, J. M.; Duca, J. S.; Rush, T. S.; et al. Rethinking Drug Design in the Artificial Intelligence Era. Nat. Rev. Drug Discov. 2020; 19 (5): 353–364p.
89. Boström, J.; Brown, D. G.; Young, R. J.; Keserü, G. M. Expanding the Medicinal Chemistry Synthetic Toolbox. Nat. Rev. Drug Discov. 2018; 17 (10): 709–727p.
90. Strokach, A.; Becerra, D.; Corbi-Verge, C.; Perez-Riba, A.; Kim, P. M. Fast and Flexible Protein Design Using Deep Graph Neural Networks. Cell Syst. 2020; 11 (4): 402-411p.
91. Rynazal R, Fujisawa K, Shiroma H, et al. Leveraging explainable AI for gut microbiome-based colorectal cancer classification. Genome Biol. 2023; 24(1): 1-3p.
92. Mak, K.-K.; Pichika, M. R. Artificial Intelligence in Drug Development: Present Status and Future Prospects. Drug Discov. Today 2019; 24 (3): 773–780p.
93. Hughes, J. P.; Rees, S.; Kalindjian, S. B.; Philpott, K. L. Principles of Early Drug Discovery. Br. J. Pharmacol. 2011; 162 (6): 1239–1249p.
94. Katsila, T.; Spyroulias, G. A.; Patrinos, G. P.; Matsoukas, M.-T. Computational Approaches in Target Identification and Drug Discovery. Comput. Struct. Biotechnol. J. 2016; 14: 177–184p.
95. Mohs, R. C.; Greig, N. H. Drug Discovery and Development: Role of Basic Biological Research. Alzheimers Dement. (N. Y.) 2017; 3 (4): 651–657p.
96. Emig, D.; Ivliev, A.; Pustovalova, O.; Lancashire, L.; Bureeva, S.; Nikolsky, Y.; Bessarabova, M. Drug Target Prediction and Repositioning Using an Integrated Network-Based Approach. PLoS One 2013; 8 (4): e60618p.
97. Duch, W.; Swaminathan, K.; Meller, J. Artificial Intelligence Approaches for Rational Drug Design and Discovery. Curr. Pharm. Des. 2007; 13 (14): 1497–1508p.
98. Bain, E. E.; Shafner, L.; Walling, D. P.; Othman, A. A.; Chuang-Stein, C.; Hinkle, J.; Hanina, A. Use of a Novel Artificial Intelligence Platform on Mobile Devices to Assess Dosing Compliance in a Phase 2 Clinical Trial in Subjects with Schizophrenia. JMIR MHealth UHealth 2017; 5 (2): e18p.

99. Perez-Gracia, J. L.; Sanmamed, M. F.; Bosch, A.; Patiño-Garcia, A.; Schalper, K. A.; Segura, V.; Bellmunt, J.; Tabernero, J.; Sweeney, C. J.; Choueiri, T. K.; et al. Strategies to Design Clinical Studies to Identify Predictive Biomarkers in Cancer Research. Cancer Treat. Rev. 2017; 53: 79–97p.
100. Deliberato, R. O.; Celi, L. A.; Stone, D. J. Clinical Note Creation, Binning, and Artificial Intelligence. JMIR Med. Inform. 2017; 5 (3): e24p.
101. Lozano-Diez, A.; Zazo, R.; Toledano, D. T.; Gonzalez-Rodriguez, J. An Analysis of the Influence of Deep Neural Network (DNN) Topology in Bottleneck Feature Based Language Recognition. PLoS One 2017; 12 (8): e0182580p.
102. Aliper, A.; Plis, S.; Artemov, A.; Ulloa, A.; Mamoshina, P.; Zhavoronkov, A. Deep Learning Applications for Predicting Pharmacological Properties of Drugs and Drug Repurposing Using Transcriptomic Data. Mol. Pharm. 2016; 13 (7): 2524–2530p.
103. Kadurin, A.; Nikolenko, S.; Khrabrov, K.; Aliper, A.; Zhavoronkov, A. DruGAN: An Advanced Generative Adversarial Autoencoder Model for de Novo Generation of New Molecules with Desired Molecular Properties in Silico. Mol. Pharm. 2017; 14 (9): 3098–3104p.
104. Ozerov, I. V.; Lezhnina, K. V.; Izumchenko, E.; Artemov, A. V.; Medintsev, S.; Vanhaelen, Q.; Aliper, A.; Vijg, J.; Osipov, A. N.; Labat, I.; et al. In Silico Pathway Activation Network Decomposition Analysis (iPANDA) as a Method for Biomarker Development. Nat. Commun. 2016; 7 (1): 1–11p.
105. Ryu, J. Y.; Kim, H. U.; Lee, S. Y. Deep Learning Improves Prediction of Drug–Drug and Drug–Food Interactions. Proc. Natl. Acad. Sci. U. S. A. 2018; 115 (18): E4304-E4311p.
106. Reddy, A. S.; Zhang, S. Polypharmacology: Drug Discovery for the Future. Expert Rev. Clin. Pharmacol. 2013; 6 (1): 41–47p.
107. Ding H, Wu J, Zhao W, et al. Artificial intelligence in dentistry—A review. Front. Dent. Med. 2023; 4: 1085251p.
108. Harel, S.; Radinsky, K. Prototype-Based Compound Discovery Using Deep Generative Models. Mol. Pharm. 2018; 15 (10): 4406–4416p.
109. Chen CC, Wu YF, Aung LM, et al. Automatic recognition of teeth and periodontal bone loss measurement in digital radiographs using deep-learning artificial intelligence. J. Dent. Sci. 2023; 18(3): 1301-1309p.
110. Shen J, Nicolaou CA. Molecular property prediction: recent trends in the era of artificial intelligence. Drug Discov. Today Technol. 2019; 32: 29-36p.
111. Zhavoronkov, A. Artificial Intelligence for Drug Discovery, Biomarker Development, and Generation of Novel Chemistry. Mol. Pharm. 2018; 15 (10): 4311–4313p.
112. Walters WP, Barzilay R. Applications of deep learning in molecule generation and molecular property prediction. Acc. Chem. Res. 2020; 54(2): 263-270p.
113. Deng J, Yang Z, Wang H, et al. A systematic study of key elements underlying molecular property prediction. Nat. Commun. 2023; 14(1): 6395 (1-20)p.
114. Wang Z, Liu M, Luo Y,et al. Advanced graph and sequence neural networks for molecular property prediction and drug discovery. Bioinform. 2022; 38(9): 2579-2586p.
115. Wieder O, Kohlbacher S, Kuenemann M, et al. A compact review of molecular property prediction with graph neural networks. Drug Discov. Today Technol. 2020; 37: 1-2p.
116. Li, Z.; Jiang, M.; Wang, S.; Zhang, S. Deep Learning Methods for Molecular Representation and Property Prediction. Drug Discov. Today 2022, 27 (12), 103373p.
117. Nigam A, Pollice R, Hurley MF, et al. Assigning confidence to molecular property prediction. Expert Opin Drug Discov. 2021; 16(9): 1009-23p.
118. Heinonen, M.; Shen, H.; Zamboni, N.; Rousu, J. Metabolite Identification and Molecular Fingerprint Prediction through Machine Learning. Bioinformatics 2012, 28 (18), 2333–2341p.
119. Rao J, Zheng S, Lu Y, et al. Quantitative evaluation of explainable graph neural networks for molecular property prediction. Patterns 2022; 3(12): 100628p.
120. Walters WP, Barzilay R. Critical assessment of AI in drug discovery. Expert Opin Drug Discov. 2021; 16(9): 937-947p.

121. Yang, C. C. Explainable Artificial Intelligence for Predictive Modeling in Healthcare. J. Healthc. Inform. Res. 2022; 6 (2): 228–239p.
122. Wu, H.; Zhao, J. Deep Convolutional Neural Network Model Based Chemical Process Fault Diagnosis. Comput. Chem. Eng. 2018; 115: 185–197p.
123. Shilpa S, Kashyap G, Sunoj RB. Recent Applications of Machine Learning in Molecular Property and Chemical Reaction Outcome Predictions. J. Phys. Chem. A 2023; 127(40): 8253-71p.
124. Zhang XC, Wu CK, Yang ZJ, et al. leveraging unsupervised atomic representation learning for molecular property prediction. Brief. Bioinformatics 2021; 22(6): bbab152p.
125. Bond A, Mccay K, Lal S. Artificial Intelligence & Clinical Nutrition: what the future might have in store. Clinical nutrition ESPEN 2023.
126. Hacker, P. A Legal Framework for AI Training Data—from First Principles to the Artificial Intelligence Act. Law Innov. Technol. 2021; 13 (2): 257–301p.
127. Wang, Y.; Xiao, J.; Suzek, T. O.; Zhang, J.; Wang, J.; Bryant, S. H. PubChem: A Public Information System for Analyzing Bioactivities of Small Molecules. Nucleic Acids Res. 2009; 37: W623–W633p.
128. Kim, S.; Thiessen, P. A.; Bolton, E. E.; Chen, J.; Fu, G.; Gindulyte, A.; Han, L.; He, J.; He, S.; Shoemaker, B. A.; et al. PubChem Substance and Compound Databases. Nucleic Acids Res. 2016, 44: D1202–D1213p.
129. Gaulton, A.; Bellis, L. J.; Bento, A. P.; Chambers, J.; Davies, M.; Hersey, A.; Light, Y.; McGlinchey, S.; Michalovich, D.; Al-Lazikani, B.; et al. ChEMBL: A Large-Scale Bioactivity Database for Drug Discovery. Nucleic Acids Res. 2012; 40: D1100–D1107.
130. Holzinger, A.; Langs, G.; Denk, H.; Zatloukal, K.; Müller, H. Causability and Explainability of Artificial Intelligence in Medicine. Wiley Interdiscip. Rev. Data Min. Knowl. Discov. 2019; 9 (4): e1312p.
131. Maity, S. Identifying Opportunities for Artificial Intelligence in the Evolution of Training and Development Practices. J. Manag. Dev. 2019; 38 (8): 651–663p.
132. Salinari A, Machì M, Armas Diaz Y, et al. The Application of Digital Technologies and Artificial Intelligence in Healthcare: An Overview on Nutrition Assessment. Diseases 2023; 11(3): 97p.
133. Noorbakhsh-Sabet, N.; Zand, R.; Zhang, Y.; Abedi, V. Artificial Intelligence Transforms the Future of Health Care. Am. J. Med. 2019; 132 (7): 795–801p.
134. de Moraes Lopes MHB, Ferreira DD, Ferreira AC, et al. Use of artificial intelligence in precision nutrition and fitness. In Artificial Intelligence in Precision Health 2020; 465-496p.
135. Rashid, J.; Batool, S.; Kim, J.; Wasif Nisar, M.; Hussain, A.; Juneja, S.; Kushwaha, R. An Augmented Artificial Intelligence Approach for Chronic Diseases Prediction. Front. Public Health 2022; 10: 795-801p.
136. Ramakrishnan R, Xing T, Chen T, et al. Application of AI in Nutrition. arXiv preprint arXiv:2312.11569. 2023.
137. Kumar P, Sinha R, Shukla P. Artificial intelligence and synthetic biology approaches for human gut microbiome. Crit. Rev. Food Sci. Nutr. 2022; 62(8): 2103-2121p.
138. Karakan T, Gundogdu A, Alagözlü H, et al. Artificial intelligence-based personalized diet: A pilot clinical study for irritable bowel syndrome. Gut Microbes 2022; 14(1): 2138672-2138674p.
139. Vilne B, Ķibilds J, Siksna I, et al. Could artificial intelligence/machine learning and inclusion of diet-gut microbiome interactions improve disease risk prediction? Case study: coronary artery disease. Front. microbiol. 2022; 13: 627892p.
140. Feng J, Liu H, Mai S, et al. Protocol of a parallel, randomized controlled trial on the effects of a novel personalized nutrition approach by artificial intelligence in real world scenario. BMC Public Health 2023; 23(1): 1700p.
141. Panagoulias DP, Sotiropoulos DN, Tsihrintzis GA. Biomarker-based deep learning for personalized nutrition. In2021 IEEE 33rd International Conference on Tools with Artificial Intelligence (ICTAI) 2021; 306-313p.
142. Abdel-Sattar M, Al-Obeed RS, Aboukarima AM, et al. Development of an artificial neural network as a tool for predicting the chemical attributes of fresh peach fruits. Plos one. 2021; 16(7): e0251185p.

143. Behkami S, Zain SM, Gholami M, et al.Classification of cow milk using artificial neural network developed from the spectral data of single-and three-detector spectrophotometers. Food Chem. 2019; 294: 309-15p.
144. Matusheski NV, Caffrey A, Christensen L, et al. Diets, nutrients, genes and the microbiome: recent advances in personalised nutrition. Br. J. Nutr. 2021; 126(10): 1489-1497p.
145. Cai Q, Li J, Li H, et al. BTBUFood-60: Dataset for object detection in food field. In2019 IEEE International Conference on Big Data and Smart Computing 2019; 1-4p.
146. Dias SB, Oikonomidis Y, Diniz JA, et al. Users' Perspective on the AI-Based Smartphone PROTEIN App for Personalized Nutrition and Healthy Living: A Modified Technology Acceptance Model (mTAM) Approach. Front. Nutr. 2022; 9: 898031p.
147. Detopoulou P, Voulgaridou G, Moschos P, et al. Artificial intelligence, nutrition, and ethical issues: A mini-review. Clin. Nutr. Open Sci. 2023; 50: 46-56p.
148. Miyazawa, T.; Hiratsuka, Y.; Toda, M.; Hatakeyama, N.; Ozawa, H.; Abe, C.; Cheng, T.-Y.; Matsushima, Y.; Miyawaki, Y.; Ashida, K.; et al. Artificial Intelligence in Food Science and Nutrition: A Narrative Review. Nutr. Rev. 2022, 80 (12), 2288–2300p.
149. Sacha GM, Varona P. Artificial intelligence in nanotechnology. Nanotechnology. 2013; 24(45): 452002p.
150. Whitesides, G. M. Nanoscience, Nanotechnology, and Chemistry. Small 2005; 1 (2): 172–179p.
151. Ho, D.; Wang, P.; Kee, T. Artificial Intelligence in Nanomedicine. Nanoscale Horiz 2019; 4 (2): 365–377p.
152. Tsigelny, I. F. Artificial Intelligence in Drug Combination Therapy. Brief. Bioinform. 2019; 20 (4): 1434–1448p.
153. Rani, P.; Dutta, K.; Kumar, V. Artificial Intelligence Techniques for Prediction of Drug Synergy in Malignant Diseases: Past, Present, and Future. Comput. Biol. Med. 2022; 144: 105334p.
154. Neto, O. P. V. Intelligent Computational Nanotechnology: The Role of Computational Intelligence in the Development of Nanoscience and Nanotechnology. J. Comput. Theor. Nanosci. 2014; 11 (4): 928–944p.
155. Liu C, Sun J. AI in measurement science. Annu. Rev. Anal. Chem. 2021; 14: 1-9p.
156. Singh, A. V.; Ansari, M. H. D.; Rosenkranz, D.; Maharjan, R. S.; Kriegel, F. L.; Gandhi, K.; Kanase, A.; Singh, R.; Laux, P.; Luch, A. Artificial Intelligence and Machine Learning in Computational Nanotoxicology: Unlocking and Empowering Nanomedicine. Adv. Healthc. Mater. 2020; 9 (17): 1901862p.
157. Brown KA, Brittman S, Maccaferri N, et al. Machine learning in nanoscience: big data at small scales. Nano Lett. 2019; 20(1): 2-10p.
158. Liu, C., & Sun, J. AI in measurement science. Annu. Rev. Anal. Chem. 2021; 14:1–19p.
159. Epps RW, Abolhasani M. Modern nanoscience: Convergence of AI, robotics, and colloidal synthesis. Appl. Phys. Rev. 2021; 8(4): 041316p.
160. Rawat B, Bist AS, Supriyanti D, et al. AI and Nanotechnology for Healthcare: A survey. APTISI Transactions on Management (ATM) 2023; 7(1): 86-91p.
161. Adir O, Poley M, Chen G, et al. Integrating artificial intelligence and nanotechnology for precision cancer medicine. Adv. Mater. 2020; 32(13): 1901989p.
162. Wang H, Lee DK, Chen KY, et al. Mechanism-independent optimization of combinatorial nanodiamond and unmodified drug delivery using a phenotypically driven platform technology. ACS nano 2015; 9(3): 3332-3344p.
163. Luo, M.; Feng, Y.; Wang, T.; Guan, J. Micro-/Nanorobots at Work in Active Drug Delivery. Adv. Funct. Mater. 2018; 28 (25): 1706100p.
164. Tripathi, R.; Kumar, A. Application of Nanorobotics for Cancer Treatment. Mater. Today 2018; 5 (3): 9114–9117p.
165. Glécia Virgolino da Silva Luz; Barros, K. V. G.; Fábio Vladimir Calixto de Araújo; Silva, G. B. da; Pedro Augusto Ferreira da Silva; Condori, R. C. I.; Brasil, L. M. Nanorobotics in Drug Delivery Systems for Treatment of Cancer: A Review. J. Mater. Sci. Eng. A. 2016; 6 (3): 167-180p.
166. Mir, U. B.; Sharma, S.; Kar, A. K.; Gupta, M. P. Critical Success Factors for Integrating Artificial Intelligence and Robotics. Digit. Pol. Regul. Gov. 2020; 22 (4): 307–331p.

167. Bahman, Z.; Farhang, M.-R. A Model to Forecast Future Paradigms: Volume 1: Introduction to Knowledge Is Power in Four Dimensions; Apple Academic Press: Includes bibliographical references and index. | Contents: Volume 1. Introduction to knowledge is power in four dimensions, 2019.
168. Modin O, Fuad N, Abadikhah M, et al. A relationship between phages and organic carbon in wastewater treatment plant effluents. Water Res. X 2022; 16: 100146p.
169. Cantwell MG, Katz DR, Sullivan JC, et al. Spatial patterns of pharmaceuticals and wastewater tracers in the Hudson River Estuary. Water research 2018; 137: 335-43p.
170. Long S, Zhao L, Liu H, et al. A Monte Carlo-based integrated model to optimize the cost and pollution reduction in wastewater treatment processes in a typical comprehensive industrial park in China. Sci. Total Environ. 2019; 647: 1-10p.
171. Jawad J, Hawari AH, Zaidi SJ. Artificial neural network modeling of wastewater treatment and desalination using membrane processes: A review. Chem. Eng. J. 2021; 419: 129540p.
172. Zhu J, Jiang Z, Feng L. Improved neural network with least square support vector machine for wastewater treatment process. Chemosphere 2022; 308: 136116p.
173. Filipe J, Bessa RJ, Reis M, et al. Data-driven predictive energy optimization in a wastewater pumping station. Appl. Energy. 2019; 252: 113423p.
174. Cheng H, Wu J, Liu Y, et al. A novel fault identification and root-causality analysis of incipient faults with applications to wastewater treatment processes. Chemometr Intell Lab Syst. 2019; 188: 24-36p.
175. Lotfi K, Bonakdari H, Ebtehaj I,et al. Predicting wastewater treatment plant quality parameters using a novel hybrid linear-nonlinear methodology. J. Environ. Manage. 2019; 240: 463-474p.
176. Vakili M, Mojiri A, Kindaichi T, et al. Cross-linked chitosan/zeolite as a fixed-bed column for organic micropollutants removal from aqueous solution, optimization with RSM and artificial neural network. J. Environ. Manage. 2019; 250: 109434p.
177. Yaseen, Z. M.; Ramal, M. M.; Diop, L.; Jaafar, O.; Demir, V.; Kisi, O. Hybrid Adaptive Neuro-Fuzzy Models for Water Quality Index Estimation. Water Resour. Manage. 2018; 32 (7): 2227–2245p.
178. Singh, N. K.; Yadav, M.; Singh, V.; Padhiyar, H.; Kumar, V.; Bhatia, S. K.; Show, P.-L. Artificial Intelligence and Machine Learning-Based Monitoring and Design of Biological Wastewater Treatment Systems. Bioresour. Technol. 2023; 369: 128486p.
179. Wang, G.; Jia, Q.-S.; Zhou, M.; Bi, J.; Qiao, J.; Abusorrah, A. Artificial Neural Networks for Water Quality Soft-Sensing in Wastewater Treatment: A Review. Artif. Intell. Rev. 2022; 55 (1): 565–587p.
180. Aghdam, E.; Mohandes, S. R.; Manu, P.; Cheung, C.; Yunusa-Kaltungo, A.; Zayed, T. Predicting Quality Parameters of Wastewater Treatment Plants Using Artificial Intelligence Techniques. J. Clean. Prod. 2023, 405: 137019p.
181. Bhagat SK, Tung TM, Yaseen ZM. Development of artificial intelligence for modeling wastewater heavy metal removal: State of the art, application assessment and possible future research. J. Clean. Prod. 2020; 250: 119473p.
182. Niu C, Li X, Dai R, et al. Artificial intelligence-incorporated membrane fouling prediction for membrane-based processes in the past 20 years: A critical review. Water Res. 2022; 216: 118299p.
183. Thakkar, A.; Chadimová, V.; Bjerrum, E. J.; Engkvist, O.; Reymond, J.-L. Retrosynthetic Accessibility Score (RAscore) – Rapid Machine Learned Synthesizability Classification from AI Driven Retrosynthetic Planning. Chem. Sci. 2021; 12 (9): 3339–3349p.
184. Strieth-Kalthoff, F.; Szymkuć, S.; Molga, K.; Aspuru-Guzik, A.; Glorius, F.; Grzybowski, B. A. Artificial Intelligence for Retrosynthetic Planning Needs Both Data and Expert Knowledge. J. Am. Chem. Soc. 2024; 16: 11005–11017p.
185. Srinivasan, S.; Batra, R.; Chan, H.; Kamath, G.; Cherukara, M. J.; Sankaranarayanan, S. K. R. S. Artificial Intelligence-Guided DE Novo Molecular Design Targeting COVID-19. ACS Omega 2021; 6 (19): 12557–12566p.
186. Adir, O.; Poley, M.; Chen, G.; Froim, S.; Krinsky, N.; Shklover, J.; Shainsky-Roitman, J.; Lammers, T.; Schroeder, A. Integrating Artificial Intelligence and Nanotechnology for Precision Cancer Medicine. Adv. Mater. 2020; 32 (13): 1-15p.

187. Hsu, W.-L.; Huang, C.-F.; Tan, C.-C.; Liu, N. Y.-C.; Chu, C. H.; Huang, P.-S.; Wu, P. C.; Yiin, S. J.; Tanaka, T.; Weng, C.-J.; et al. High-Resolution Metalens Imaging with Sequential Artificial Intelligence Models. Nano Lett. 2023; 23 (24): 11614–11620p.
188. Wang, S.; Sadowski, G.; Ji, Y. Strategy of Coupling Artificial Intelligence with Thermodynamic Mechanism for Predicting Complex Polymer Viscosities. ACS Sustain. Chem. Eng. 2024; 12 (11): 4631–4643p.
189. Xu, Y.; Jiang, W.-J.; Bai, Y.-Y.; Yang, Y.-J.; Zhang, Z.-L. Artificial Intelligence-Assisted Multiparameter Size Discrimination of Silver Nanoparticles through Electrochemical Collision. Anal. Chem. 2024; 96 (16): 6195–6201p.
190. Gulbalkan, H. C.; Aksu, G. O.; Ercakir, G.; Keskin, S. Accelerated Discovery of Metal–Organic Frameworks for CO_2 Capture by Artificial Intelligence. Ind. Eng. Chem. Res. 2024; 63 (1): 37–48p.
191. Lai, N. S.; Tew, Y. S.; Zhong, X.; Yin, J.; Li, J.; Yan, B.; Wang, X. Artificial Intelligence (AI) Workflow for Catalyst Design and Optimization. Ind. Eng. Chem. Res. 2023; 62 (43): 17835–17848p.
192. Hu, Y.; Ren, Q.; Liu, X.; Gao, L.; Xiao, L.; Yu, W. In Silico Prediction of Human Organ Toxicity via Artificial Intelligence Methods. Chem. Res. Toxicol. 2023; 36 (7): 1044–1054p.

