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Future of chemistry in the presence of artificial intelligence

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ABSTRACT

Science-related subjects including chemistry, physics, mathematics, engineering, and medicine have all benefited greatly from advanced technology, particularly Artificial Intelligence (AI). Recently, the significance of AI in promoting chemistry research to improve the chemical industry has evolved. The goal of the researchers is to advance drug development by creating novel medications at a minimal cost. AI assists in achieving this goal. Other areas of chemistry that will benefit from AI include compound solubility, optimizing reaction conditions, and providing production methods for challenging target molecules. Researchers from Massachusetts Institute of Technology (MIT) have discovered a potent new antibiotic molecule using a machine-learning system. Typically, AI may produce ten times more antibody sequence clusters than a lab-based approach alone. Systems containing hundreds of interacting ions and electrons can now be modeled using an approximation of the physical laws. This is because modern algorithms and supercomputers make these applications possible.

KEYWORDS

AI, designing molecules, detection of molecules, drug discovery, molecule, properties of molecules

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INTRODUCTION

AI has enabled computers to function and think like human by creating software or machines that are based on human intelligence. Google Maps is among the most useful examples of AI.[1] The AI has developed into a helpful tool in many sectors since the early 2000s. The development stages have ranged from developing games and speech recognition to autonomous vehicle operation and spaceships. As reported, the idea of AI started in the middle on 20th century. The notion of creating an artificial brain sparked discussions among scientists from a variety of disciplines, including mathematics, psychology, engineering, biology, etc., in the first half of the 20th century, which led to a rise in popularity for this fascinating concept. John McCarthy first used the phrase "Artificial Intelligence" in 1956 at the Dartmouth conference, which served as the official birthplace of AI as a field of study. Nine notable AI-driven biotech companies were established in 2021.[2] Recently, the application of artificial intelligence in chemistry has developed dramatically. This can be a surprise for many people to know that AI and chemistry have very strong connection. Drug discovery and the development of the healthcare industry are major applications of artificial intelligence in the field of chemistry. Due to the highly developed technology and equipment employed by scientists, this technology has also been a result of cutting-edge pharmaceutical industry research and development. AI can be effectively applied to a variety of tasks, because complex correlations frequently exist in datasets. For instance, theoretical calculations or equations based on empirical data can both be used to forecast the solubility of a new molecule. An AI software that has learned structure-solubility connections through training on a large number of molecules with known solubilities may also predict solubility.[2] AI is now commonly employed for tasks like property prediction because of the quick rise in processing capacity, the accessibility of open-source machine learning frameworks, and chemists' developing data literacy. By facilitating laboratory automation, forecasting the biological effects of novel medications, enhancing reaction conditions, and offering production techniques for specific target molecules.[3-10] AI implementations have demonstrated their ability to significantly reduce design and experimental effort.[11] In the areas of Analytical Chemistry, Synthetic Chemistry, and Physical Chemistry, new methods using AI have been developed to complement analytical data, automate flow chemistry, improve retrosynthetic planning, and predict reaction outcomes. Additionally, it was reported that a technique combining AI with physics-based approaches such density functional theory may improve calculation accuracy. User-friendly computing tools were also developed. According to the McKinsey Global Institute, society's workplace culture will undoubtedly undergo significant changes as a result of the rapid breakthroughs in AI-guided automation.[12,13] Systems with hundreds of interacting ions and electrons can now be represented using approximations to the physical rules that govern the world on the atomic scale, this is due to contemporary algorithms and supercomputers.[14-17] The field of computational chemistry has expanded in the 21th century, and its applications include the creation of catalysts for the conversion of greenhouse gases, the identification of materials for energy harvesting and storage, and the development of computer-aided pharmaceuticals.[18] Chemical engineers have also utilized machine learning to speed up and conserve resources by searching the solution space of potential reactions.[19-23] Shields et al.'s study demonstrates how Bayesian optimization can be utilized in synthetic chemistry to fine-tune neural networks. In this study, they show how Bayesian optimization can be viewed as a self-sufficient technique for reducing human biases.[24] Gale and Durand's assessment of reaction prediction techniques demonstrates how machine learning in chemistry has a lot of room for improvement and is actively being researched in practically every field.[25] They discuss a number of significant issues, including the requirement for datasets to produce both negative outcomes and error-free responses. They talk about how challenging it is to encode chemical information in a way that is machine-readable. An encoder and decoder type neural network can be utilized to represent a continuous chemical latent space, as demonstrated by the work of Iovanac et al. To forecast the features of distinct pKa predictions of moderately sized molecular species, their research employs both actual and projected models from density functional theory.[26]

AI APPLICATIONS IN CHEMISTRY

Although AI has many applications in the area of technology, it also has many applications in the field of chemical science.[2] By searching the features of molecules included in existing databases, the AI can

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find combinations that may be promising as drugs. Machine learning techniques may transform the search for novel medications because they can operate faster and cheaper than people.[1] The sequence of data, experience and learning represents machine learning. This sequence and reasoning represent AI.[27] This means that machine learning serves AI to complete the tasks. Researchers from the University of Toronto and the Hong Kong-based Insilico Medicine reported that AI algorithms had selected roughly 30 000 previously unknown chemical combinations, eventually narrowing that list down to six promising novel pharmaceutical molecules.

AI AND DRUG DISCOVERY

It is stated that the process of drug discovery is one of the top applications of AI in chemistry.[1] MIT researchers have discovered a potent new antibiotic molecule using a machine-learning algorithm. Many of the most troublesome disease-causing bacteria in the world, including some types that are resistant to all known antibiotics, were destroyed by the medication in laboratory experiments. There is a wide application of AI technology in various ways, such as entire drug pipeline, novelty design of drug, evaluation of drug activity, etc..[28] It is noticeable that collaborations in the field of research and development that include major pharmaceutical companies and emerging drug discovery companies that rely on artificial intelligence are increasing, as shown in the figure 1.[2] The specialized companies in this area have a comprehensive AI-augmented drug discovery platform, which is based on AI, big data, and machine learning, increases the hits, diversity, delivery speed, and profit margin in drug discovery projects, making clients more competitive.

Big data and machine learning-based antibody design has also extensively utilized AI technologies. Additionally, a variety of AI models can assess and optimize the biophysical characteristics of potential antibodies, such as stability, solubility, and chemical properties, to lower costs and boost therapeutic effectiveness. As reported, the number of antibody clusters for HIV GP140 has increased 13-fold thanks to research that uses AI to boost discovery.[28] Typically, AI can produce 10 times more antibody sequence clusters than a lab-based method by itself. The expansion of antibody diversity by AI results in the identification of novel binding mechanisms and perhaps novel therapeutic modes-of-action.

The lack of advanced technologies affects the production of medicines, and this costs pharmaceutical companies large sums of money and a long time, and all of this can be solved to reduce money and time by using artificial intelligence.[28-30] Researchers from the University of Toronto and the Hong Kong-based Insilico Medicine reported that AI algorithms had selected roughly 30 000 previously unknown chemical combinations, eventually narrowing that list down to six promising novel pharmaceuticalmolecules.[1] It is reported that the discovery of new medicine requires about 13 years or more, and it needs to screen thousands of chemical compounds. The number of potential drug-like compounds has been estimated to be between 1023 and 1060, while there have only been around 108 different chemicals created through synthetic processes. Also, the new medicine requires to spend about 1 billion USD to produce it. The typical period from discovery to commercial production outside of the pharmaceutical industry can be significantly longer; for example, the period for energetic compounds is 25 years.[31-33] All these steps to produce new medicine is time consuming too. Accordingly, AI has significantly advanced the R&D process for accelerating drug discovery. However, as stated in a recent study, there are other uses for AI in chemistry besides drug discovery.[34]

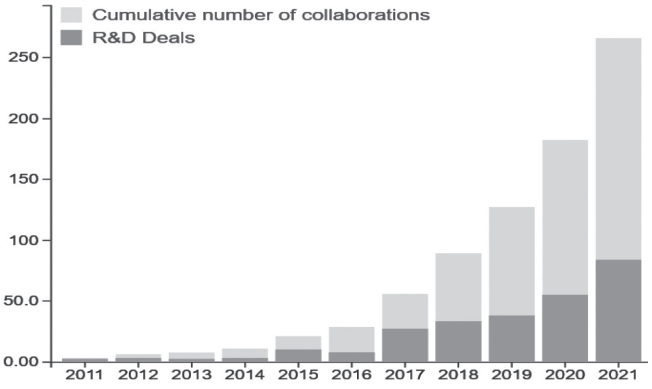

Figure 1: "big pharma" and AI-driven drug discovery companies collaborate on research and development.[2]

MOLECULAR PROPERTIES AND AI

The first and most important application of AI in chemistry is the discovery of molecular properties. Scientists perform the process of manually revealing the chemical properties of molecules because characterizing a molecule is a lengthy process.[1] However, this process has been made easier by AI, which has allowed researchers to learn about molecular characteristics. This made chemical processes more effective while also simplifying the manual detection process. Additionally, identifying molecular characteristics has made it possible for researchers to assess the potential of a hypothetical substance. Chemistry has benefited from the use of AI algorithms since past data enables computers to assess current data. It is reported that large databases of known compounds and their characteristics can now be explored by machine learning techniques, which then use the data to suggest new possibilities, as shown in Figure 2. The search for novel medicine options might become easier and more affordable as a result. AI helps researchers to synthesize only the most promising chemicals and avoid synthesizing and testing several molecules that don't have the desired qualities.[31] As shown in Figure 3, the AI predicts new similar molecules. Machine learning methods can also be used to predict chemical properties, as shown in Figure 2. Numerous other types of attributes, including, solubility of compounds, melting point of compounds, bioactivity of compounds, toxicity of compounds, atomization energies, HOMO/LUMO molecular orbital energies, and many others, have also been predicted using these algorithms.

STRUCTURING OF MOLECULES

While the characterization of compounds is extremely useful in the field of chemistry, the discrete use of artificial intelligence in molecular design has led to groundbreaking discoveries. Scientists have been able to gather historical information and establish chemical relationships by building molecules. Researchers have advanced in

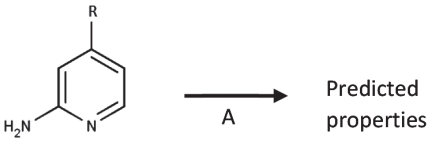

Figure 2: AI application predicting chemical properties.

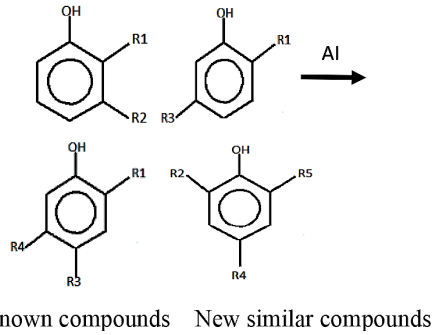

Figure 3: Example of AI application to predict new molecules.

finding compounds by incorporating AI algorithms, and this has undoubtedly assisted them in making ground-breaking discoveries in AI chemical synthesis.[1] The designing new molecule needs to do two steps, step 1 is to find the right chemical structure for the molecule and step 2 is to determine the exact chemical reaction which will bond the right atoms to form the required molecule.[35]

An AI programe created by German researchers at the University of Münster, for instance, can plan a multistep synthetic route 30 times faster than a person can by continuously simulating the 12.4 million known single-step chemical processes.[35,36] Computer-aided synthesis planning can help chemists find better methods faster. The missing ingredient can also be found in new virtual design and robot systems that perform molecular design, synthesis, and test cycles.[37-39] Games or automated theorem proving are examples of sequential choice problems with large branching factors that can be solved using Monte Carlo tree search (MCTS), a universal search approach.[40-42] As stated, to create new materials, the sequential steps of molecular design, property prediction, synthesis of chemicals, and experimental assessment are routinely repeated until adequate performance is reached.[43]

REACTANTS AND PRODUCTS PREDICTION

Synthesis of new chemical compounds by using conventional methods take a lot of time, this is because of experiment trying and errors to find suitable reactants, and to produce the required products, as shown in Figure 4. The researchers stay days and nights in the laboratories for testing and searching to synthesis new molecules. AI has made a significant change in this issue. It shortens the steps to synthesis new molecules. The process of reactants prediction is called retrosynthesis.

FUTURE OF AI AND CHEMISTRY

In fact, the relationship between chemistry and AI still has a long way to go, because AI is still a work in progress, but it can be said that artificial intelligence can contribute to the development of the chemical industry in the future. The world experiences more and more illnesses arising, accordingly, AI in chemistry rashly assists researchers in the production of potentially ground-breaking scientific discoveries. It can be expected that the future use of artificial intelligence is anticipated to greatly expand the field of chemical sciences.[1] Although more of these improvisations are likely to occur in the future, it is still important to make sure that the scientific community is aware of the technological developments being made in artificial intelligence. This combination will aid researchers in the coming decades not just in gathering vast amounts of data and creating algorithms for better usage, but also in enabling discoveries in a variety of areas that will have remarkable effects on humanity. It is important to notice that there is an increase in the number of publications about AI and chemistry. It is stated that since 2015, it has been observed that the number of scientific publications in journals and patents has increased dramatically, and the most significant has been in the fields of analytical chemistry and biochemistry, because both fields integrate AI to the maximum extent and with the highest growth rates.[3] According to a study, from 2000 to 2020, the CAS Content Collection had 17500 patents and roughly 70 000 academic publications.[3] According to reports, China and USA have provided the most journal articles and patents. The majority of commercial patent assignees for AI chemical research are medical diagnostic developers and technology corporations.[3] Jennifer Newton questioned when an AI would be named as an author on a scientific article in January. It turns out that the response was actually quite brief. Recently, ChatGPT, the generating text algorithm that has quickly gained notoriety, was recognized as a co-author on a number of papers.[44]

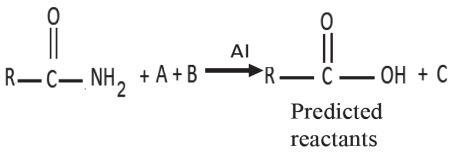

Figure 4: Prediction of reactants of the chemical reaction.

SAVING MONEY AND TIME

It is reported that AI can save money and time, particularly the process of discovery of drug. It is estimated that 85% of drugs projects have been failed within the period 2000 and 2015.[44] Therefore, there is a cooperation between drug companies and AI developers. As mentioned, in 2022, Sanofi teamed up with Exscientia and gave an upfront payment of US$ 100 million (GB£ 80 million) to support the development of 15 brand-new small molecule candidates for oncology and immunology. Sanofi might pay up to US$ 5.2 billion if the research reaches its development milestones. Recursion, a Utah-based AI biotech company, and Roche and Genentech have agreed to work together to find compounds using AI for neurological and cancer applications. Recursion will receive US$ 150 million up front, and Roche and Genentech will provide up to US$ 300 million more in performance milestone payments. Additionally, AstraZeneca and Benevolent AI expanded their drug research partnership last year to include heart failure and lupus.[45] It is stated that we must alter the pharmaceutical industry's economy. We must alter how medications are created. A cooperative initiative between Bayer and Google Cloud to use machine learning to enhance Bayer's quantum chemistry calculations was announced in January 2023. This should increase the modelling of biological and chemical systems in silico and aid in the identification of therapeutic candidates. On the other hand, Alphabet, the parent company of Google, said in late January 2023 that it will eliminate 12 000 jobs globally, many of them in its teams that support drug discovery. For GB£ 362 million at the same time, BioNTech purchased the AI firm InstaDeep to aid in the creation of vaccines and immunotherapies.[45] Faster discovery is regarded as a key benefit of AI. A 2019 paper from Insilico developed a deep generative model for small molecules that maximizes synthetic feasibility, novelty, and biological activity for fibrosis and other illnesses. It is mentioned that because of the artificial intelligence, the company carried out experiments in a short period of time, which is 21 days, and the compound that reached the mice was produced in only 46 days. In fact, this in itself is considered an achievement of its kind, as time and money were saved.[45] There is a study to artificially produce continuous datasets. As reported, a Variational AutoEncoder (VAE)-based artificial intelligence model has been created and studied. This method by using AI produces nearly 7 million novel reactions from a training dataset of only 7 000 reactions, the created approach is put to the test. As observed, larger and more varied molecular species than those in the training set are present in the created reactions.[46]

LABORATORY AUTOMATION BY AI

Some organizations, such as InSilico organization and Exscientia, are rapidly merging AI methods with laboratory automation.[45] It is reported that chemical reaction mechanisms can be classified. This classification depends on concentration data to predict that are 99.6% accurate with realistically noisy data. A model has been developed to help progress fully automated organic reaction discovery and development.[47,48] As known, we need about 15 years and try thousands of chemical compounds to produce normal medicine. Also, about 25 years and thousands of chemical compounds are required to produce antibiotics. Nowadays, AI can produce a drug in less than a year. It is reported by Exscientia that AI helps to produce a novel cancer inhibitor called CDK7 in less than one year, and just 136 chemical compounds are fabricated and tested. This is incredible achievement. It will facilitate producing many drugs for diseases treatment within few years.[45] Similar achievement was done to produce immune-oncology for tumor treatment and only 176 chemical compounds were tested to produce this drug. Schrödinger, a conventional method of producing

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pharmaceuticals that is described as utilising a physics-based platform, was computationally evaluated for 8.2 billion molecules. Only 78 compounds out of 8.2 billion were fabricated within a period of 10 months. This process was applied before selecting a compound for anticancer treatment, which was approved to involve in a clinical trail in patients with lymphoma. Idiopathic pulmonary fibrosis is an ongoing lung disease, and Insilico has developed a small molecule therapeutic candidate after using AI to find a new target for the condition. Only by drawing on vast volumes of information was this made possible. As mentioned, a company has close to two million chemicals, 40 million publications, 10 million data samples, and biological data covering structure, activity, safety, and AI platform for drug discovery. New method has applied to generate chemical compounds. Although limited to gas-phase processes, AGoRaS has wide-ranging applications. The purpose of AGoRaS was to eliminate bias that exists in all training data.[45] As reported, 7 million reactions were produced by the AGoRaS programme. Only about 7 000 reactions and 2 000 compounds made up the core dataset used to generate these reactions.

AI PLATFORMS AND CHEMICAL REACTIONS

Since the evolution of AI, there have been a number of AI platforms developed to facilitate the process of chemical reactions and their complex conditions.[49] Table 1 shows a summary of some AI platforms and their useful applications in chemistry.

In reality, there are additional platforms that have already been established and will be produced in the future in addition to those listed in table 1. One such combination involves the platforms TS-EMO, Phoenics, Gryffin, and Chimaera. This combination is to add more advantages and functions for chemical reactions and compound formation. The developing of aforementioned platforms and other platforms have been done by Aspuru-Guzik's group.[60] As reported, the combination of platforms is to make autonomous optimization of manufacturing of thin films multicomponent polymer OPV blends, and reaction conditions of stereoselective of Suzuki coupling.[61-63]

ADVANTAGES AND LIMITATIONS OF AI

AI has a number of advantages, such as accelerating data analysis, making accurate predictions of chemical reactions and properties, providing support in adapting the exact period of the research project, minimizing errors in chemical reactions, reducing repetitive experiments of researchers, allowing the automation of synthesis of compounds, and saving money on the production process.[49, 64]

As usual, new applications are applied without paying much attention to drawbacks or limitations. In fact, there are a number of limitations for AI applications. AI cannot replace humans, especially human judgement in chemistry. AI cannot perform critical thinking or contextual comprehension in the same way that humans can. These are thought to be crucial for making complicated judgements in chemistry and drug discovery. The data must be reliable and accurate in order to be used in the AI process for decision making and prediction. Any mistake or inaccuracy in the data can result in erroneous results, limiting the efficiency of AI. It is necessary to mention the complexities of various chemical reactions. This intricacy includes modifications in the experimental circumstances, which must be tried numerous times to achieve the optimal reaction conditions. Also, some conditions such as, toxicity, safety of the materials, environmental impact, need to adapted by human. This intricacy will provide a challenge for AI, but with appropriate algorithmic computations, some of these conditions may be addressed. According to a real example, my research in the synthesis and intercalation of layered materials, MPS_3, (where M is a transition element), revealed a number of parameters that must be met in order to achieve the optimum results.[65] Although AI can recommend reaction conditions, in my opinion, AI will be unable to conduct such human work effectively and will not be able to achieve the level of human crit-

Table 1: AI platforms for chemical reactions and experimental conditions.

AI platforms	Main idea	Applications
1. Bayesian optimization algorithms (BOA). It is developed to the algorithms below.	It is a derivative free global stochastic optimization method for the automatic optimization of multi-objective experimental parameters in chemistry, materials, and other fields.[50, 51]	a. Achieving optimization for processing single or multi-objective reaction parameters.[50, 52]
2. Thompson Sampling Efficient Multi-Objective (TS-EMO)	It aims at offering better solutions and better data efficiency. Therefore, it performs well on a set of mathematical test functions for a given budget.	a. It makes self-optimization for the following reactions: Sonogashira reaction, Claisen-Schmidt condensation reaction, N-benzylation reaction, and N-benzylation reaction with flow chemistry systems.[53, 54] b. Identification of optimal reaction conditions. c. It helps making balance between yield, cost, space-time yield, and E-factor in a data efficient manner.[55]
3. Phoenics platform	It was developed to avoid the problem of classical Bayesian algorithms that select data in the order of parameter points.[56-58]	a. It uses Bayesian neural networks (BNNs) to construct kernel density estimates of the objective function. b. It is applied to optimize temperature and concentration as continuous parameters. c. It can optimize chemical reaction conditions, and properties of materials.
4. Gryffin platform	It was developed to address the drawback of conventional Bayesian algorithms, which select data based on parameter values.[56-58]	a. It applies to optimize experimental parameters, such as solvent selection. b. It uses categorical kernel densities that can be relaxed to continuous ones. c. It is successfully used for the optimization of chemical reaction conditions.
5. Chimera platform	It is developed to avoid the problem of classical Bayesian algorithms that select data in the order of parameter points.[56-58]	a. It allows for defining a hierarchy of objective preferences that are combined into a single function optimized with any chosen algorithm.
6. NEXTorch platform	It uses BOA state of the arts to enable continuous variables sampling and subtypes discrete values.[59]	a. It helps chemical synthesis of compounds in lab. Experiments. b. Multiscale computational tasks from molecular scale design to reactor scale optimization.

ical thinking during the actual trial. Furthermore, throughout experiments, the researcher may discover new results that AI cannot. For example, as shown in table 2, we discovered that the nanosize of the layered materials might alter during phase transformation in open air for 36 days.[66]

AI cannot detect nanosize variations unless there is human intervention. Human skills, talent, critical thinking, observation, trial and error, and so on cannot be totally acquired by AI, even if some elements, such as trial and error, can be done by AI while still lacking the human mind and sensibility. As previously stated, AI can recommend certain conditions, but it is only capable of recommending a single reaction class.[67,68] The fundamental cause of such constraints is a scarcity of high-quality data. Future challenges face AI applications in the field of chemistry include: (1) there is a need to develop in-line and online analysis, especially in terms of accuracy of measurements, tool response speed, and compatibility with heterogeneous synthesis; (2) the cost of automated equipment is still high where developing countries can't purchase it. As is usual, every new technology is first quite expensive, but the cost will reduce with time. For example, mobile phones and the internet were initially prohibitive in price, but as technology advanced, their costs fell.[49] They are now available to millions of individuals all around the world. The same is true for AI and automated tools for chemical reactions and pharmaceutical industrial processes; it will take time for them to be available in all universities, research institutes, chemical enterprises, and pharmaceutical companies worldwide.

CONCLUSION

In conclusion, reading about how AI found molecules is a groundbreaking subject. Nevertheless, it is not impossible to see chemical sciences working with AI to improve results and data. The R&D method for accelerating drug discovery has greatly improved due to AI. The missing CASP component is absent from modern virtual design and robotic systems that perform molecular design, synthesis, and testing cycles. This might speed up the process of helping chemists discover better techniques. There are a number of AI platforms have been developed to automate and optimize chemical reaction and experimental conditions. AI application in chemistry and drug discovery is a reality, and it will never end, especially, it saves a lot of money, time and jobs. If you can't keep up with 21st century technology, you will be back in the 19th century and beyond. Although we need many years to produce any drugs, AI helps to produces drugs in less than a year. This saves money, and time.

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Table 2: Estimated crystallite size of $MnPS_3$ during phases transformation in open air.[66]

Time left in open air	Pure MnPS3 (d-spacing = 6.4 Å)		d10 (d-spacing = 10. 84 Å)		d9 (d-spacing = 9.7 Å)		d7 (d-spacing = 7.34 Å)	
	CS (nm)	LS (%)	CS (nm)	LS (%)	CS (nm)	LS (%)	CS (nm)	LS (%)
0	889	0.155	-	-	-	-	-	-
1/2 hr	-	-	85	1.089	121	0.718	27	1.568
3 hrs	-	-	30	2.137	24	2.221	27	1.585
1 day	-	-	80	1.054	-	-	34	1.289
2 days	-	-	105	0.883	-	-	32	1.368
7 days	-	-	103	0.886	443	0.343	38	1.204
9 days	-	-	100	0.900	285	0.438	43	1.099
17 days	-	-	103	0.882	199	0.535	41	1.142
21 days	-	-	91.5	0.956	190	0.551	43	1.095
24 days	-	-	39	1.722	38	1.613	29	1.47
26 days	-	-	33	1.99	42	1.491	25	1.648
30 days	-	-	26	2.375	51	1.286	-	-
36 days	-	-	-	-	85	0.905	-	-

N.B. CS is the crystallite size and LS is the lattice strain.

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