AI could speed up discovery of new medicines

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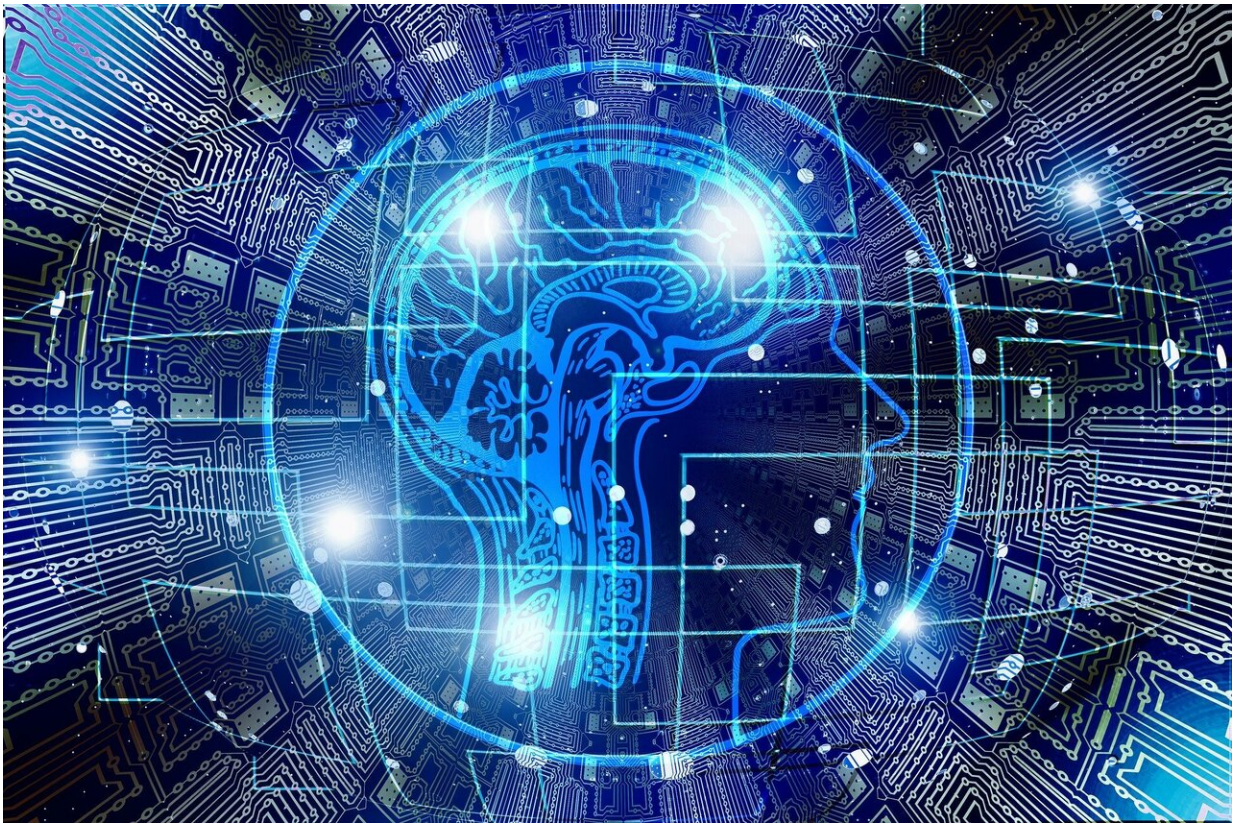

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Artificial intelligence that could reduce the cost and speed-up the discovery of new medicines has been developed as part of a collaboration between researchers at the University of Sheffield and AstraZeneca.

The new technology, developed by Professor Haiping Lu and his Ph.D. student Peizhen Bai from Sheffield's Department of Computer Science, with Dr. Filip Miljković and Dr. Bino John from AstraZeneca, is described in a new study published in *Nature Machine Intelligence*.

The study demonstrates that the AI, called DrugBAN, can predict whether a candidate drug will interact with its intended target protein molecules inside the human body.

AI that can predict whether drugs will reach their intended targets already exists, but the technology developed by the researchers at Sheffield and AstraZeneca can do this with greater accuracy and also provide useful insights to help scientists understand how drugs engage with their protein partners at a molecular level, according to the paper published on February 2, 2023.

AI has the potential to inform whether a drug will successfully engage an intended cancer-related protein, or whether a candidate drug will bind to unintended targets in the body and lead to undesirable side-effects for patients.

The AI is trained to learn the substructures of proteins in the human body as well those of drug compounds. The technology then learns how these substructures can interact with each other, which it draws on to make predictions on how new medicines will likely behave.

Haiping Lu, Professor of Machine Learning at the University of Sheffield, said, "We designed the AI with two primary objectives. Firstly, we want the AI to capture how drugs interact with their targets at a finer scale, as this could provide useful biological insights to help researchers understand these interactions on a molecular level. Secondly, we want the tool to be able to predict what these interactions will be with new drugs or targets to help accelerate the overall prediction process.

The study we've published today shows our AI model does both of these."

Key to the AI's design is how the model learns pairwise substructure interactions—the multiple interactions that can take place between substructures of drug compounds and proteins in the body. Whereas most existing drug prediction AI on the market learn from whole representations of drugs and proteins, which don't capture their substructures and so provide less useful insights.

In the next stage of the AI's development, the team plans to use more in-depth data on the structure of compounds and proteins to make the AI even more accurate.

Dr. Bino John, Director of Data Science, Clinical Pharmacology and Safety Sciences (CPSS), at AstraZeneca, said, "A key novelty of DrugBAN is its reliance on a bilinear attention network that allows it to learn interactions from substructures of both drugs and their targets simultaneously. We have also made the source code freely available to the public, which hopefully will support more AI approaches that will continue to accelerate drug discovery."

Drug discovery and development using traditional methods can be incredibly difficult, with lengthy development times and huge sums of money in expenditure. However, drug discovery processes have the potential to be significantly accelerated; with advances in AI and digital technology, researchers are finding new ways to pinpoint which proteins a drug may interact with in our body.

Nick Brown, head of imaging and data analytics, CPSS, AstraZeneca, said "I am really excited to see this paper, particularly because unlike other approaches, DrugBAN simultaneously learns from candidate drugs and their targets using a bilinear attention network, and is explicitly

designed to generalize the problem."

Professor Guy Brown, head of the University of Sheffield's Department of Computer Science, added, "Our research at Sheffield is strongly motivated by a desire to make a positive difference to people's lives, and we see interaction with industry leaders such as AstraZeneca as crucial to that mission.

"This is exciting research which will hopefully allow significant advances in the design of therapeutics. The approach is also distinctive for its focus on interpretability, enabling human experts to benefit from insights generated by the AI system."

More information: Peizhen Bai et al, Interpretable bilinear attention network with domain adaptation improves drug–target prediction, *Nature Machine Intelligence* (2023). DOI: 10.1038/s42256-022-00605-1

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