AI in Drug Development

Why in news?

The advent of Artificial Intelligence (AI) has opened up a world of possibilities with respect to fast-tracking drug development.

What is the process of developing the drugs?

- The process of developing a drug starts with identifying and validating a target.
- **Target -** A target is a biological molecule (usually a gene or a protein) to which a drug directly binds in order to work.
- **Druggable proteins -** Proteins are mainly used as targets, proteins with ideal sites where drugs can go and dock to do their business are druggable proteins.
- **Discovery phases -** Target proteins are identified in the discovery phase, wherein a target protein sequence is fed into a computer which looks for the best-fitting drug out of millions in the library of small molecules.
- **Pre- clinical phase -** In pre-clinical phase potential drug candidates are tested outside a biological system, using cells and animals for the drug's safety and toxicity.
- **Human trial-** After this, as part of the clinical phase, the drug is tested on a small number of human patients before being used on more patients for efficacy and safety.
- **Approval phase -** Finally, the drug undergoes regulatory approval and marketing and post-market survey phases.
- **Computational phase-** These methods avoid the need for preliminary laboratory experiments, which are often time-consuming, costly, and have high failure rates. Once a suitable drug-target interaction is identified, the process moves to the pre-clinical phase.

How does AI can help this process?

- **Accelerated target discovery**- AI models can process vast amounts of data quickly, identifying potential targets and predicting their interactions with drugs much faster than traditional methods.
- **Enhanced accuracy**- AI tools, such as AlphaFold and RoseTTAFold, developed by DeepMind and the University of Washington respectively, have made significant strides in predicting the three-dimensional structures of proteins.
- **Forecast dynamic interactions**- The latest versions, AlphaFold 3 and RoseTTAFold All-Atom, go beyond predicting static structures to forecasting dynamic interactions, including those involving small molecules, DNA, RNA, and ions.
- **Increase in accuracy**- In comparative tests, AlphaFold 3 demonstrated a 76% accuracy in predicting interactions between targets and small molecule drugs, significantly higher than the previous versions.
- **Generative diffusion based architecture**- These AI models improve the prediction

of structural complexes, enhancing the understanding of how drugs interact with their targets.

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• **Alpha Fold-** It predicts the 3D structure of proteins based on their amino acid sequence, it can predict protein shape with atomic accuracy almost instantly. • **RoseTTAFold**- It is a "three track" neural network, meaning it simultaneously consider patterns in protein sequences, how a protein's amino acids interact with one another and protein's possible three-dimensional structure • **AlphaFold 3**- It goes beyond proteins to a broad spectrum of biomolecules including DNA, RNA, and even small molecules, also known as ligands, which encompass many drugs. • **RoseTTAFold All-Atom**- It is a neural network that can biomolecular assemblies that contain proteins, nucleic acids, small molecules, metals and covalent modifications. • It is faster than other models which can make accurate predictions for protein-small molecule complexes and covalent changes to proteins.

What are the advantages?

- **Target identification -** Computer searches a library of small molecules for the best-fitting drug to a target protein sequence.
- **Assay development -** It can help identify targets and develop assays to test compounds.
- **Preclinical testing -** It can help determine the effectiveness of compounds in preclinical testing.
- **Drug delivery -** It can help develop more efficient drug delivery systems and select formulation approaches to improve drug solubility and absorption.
- **Molecular structure prediction -** Generative AI can train models to generate new molecular structures, which scientists can use to predict potential drug candidates.
- **Saving the time & Money -**It can increase the accuracy of prediction of interaction between a drug and its target, and saving money.

What are the limitations?

- **Accuracy limitations-** AI tools can provide up to 80% accuracy in predicting interactions and the accuracy comes down drastically for protein-RNA interaction predictions.
- **Limited scope -** The tools can only aid a single phase of drug development, target discovery and drug-target interaction.
- **Model hallucinations-**AI models, particularly those based on diffusion architectures, can sometimes produce incorrect or non-existent predictions due to insufficient training data.
- **Restricted accessibility-** Unlike AlphaFold, DeepMind has not released the code for AlphaFold 3, restricting its independent verification, broad utilisation and use.
- **Skilled workforce-** There is a shortage of skilled AI scientists in India compared to countries like the U.S. and China, this gap hinders the ability to capitalize on AI advancements in drug development.
- **Computing infrastructure**- Developing sophisticated AI tools requires robust computing infrastructure, particularly high-speed GPUs. These are expensive and

quickly become outdated as new models are released.

What lies ahead?

- India has a growing pharmaceutical industry and a rich history in structural biology fields like protein X-ray crystallography and modeling.
- With investment in infrastructure and training, India has the potential to become a leader in applying AI tools for drug discovery and testing.

References

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3. The Week | How AI is changing drug development