Aim for the Stars

Streamlining Drug Development with AI

Industry 4.0 is sweeping across the globe. Bringing in its wake revolutionary developments such as the internet of things (IoT), augmented reality, and digital simulations, it has become abundantly clear that the world will never be the same again.

In the pharma industry specifically, the dramatic expansion in digitalized healthcare data has motivated the use of artificial intelligence (AI) to process large and complex datasets. By applying AI, it may be possible to generate useful insights which, for example, could guide the use of personalized medicine for patients through real-world evidence (RWE) or improve the design of clinical trials. Similarly, in silico methods could enable computational libraries of drug compounds to be screened virtually to provide a faster selection of lead drug compounds with less expenditure, or to identify opportunities for drug repurposing.

De-risking Drug Development

The potential of AI to optimize decision-making by predicting the drug candidates most likely to be successful is of particular importance in the context of the low success rates and enormous expense in drug development.

The price tag associated with bringing a single therapeutic to market is often in the range of $1 billion, spread over 10–15 years. Meanwhile, approximately 90% of therapeutic molecules fail in clinical trials and never obtain regulatory approval. The time and expense sunk into drugs that often ultimately fail during clinical trials have led to the development of AI algorithms that can virtually screen drug compounds, allowing resources to be allocated more effectively.

For example, algorithms, such as Nearest-Neighbor classifiers, support vector machines, and deep neural networks (DNNs) are used to screen drug compounds based on synthesis feasibility and can also predict in vivo activity and toxicity. Different AI-based tools, such as machine learning approaches, can also be used to predict physicochemical properties—including solubility and intrinsic permeability. These properties can influence pharmacokinetics, or the movement of drugs in the body, and thus play an important role in determining the success of a drug compound.

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The Need to Enhance Solubility and Bioavailability

Poor solubility, and consequently poor bioavailability, is perhaps the greatest hurdle that drug candidates need to overcome. A trend toward increasingly complex and, consequently, more hydrophobic pharmaceuticals means that poor solubility is a leading cause of failure in clinical trials. Approximately 60–70% of new drug candidates are poorly soluble in water. Poor aqueous solubility leads to poor absorption of oral therapies in the gastrointestinal (GI) tract and poor bioavailability, preventing the therapeutic from reaching its target area in a sufficient concentration to achieve the desired effect.

It is no surprise, therefore, that there is an increasing spotlight on how technologies that can improve bioavailability can be implemented to allow more drugs to reach the market. Nanoparticle engineering approaches, in which the size of drug particles is reduced to the nanoscale, are among these technologies. These work by increasing the active surface area of the drug particles, thereby increasing interaction with solvent particles and enhancing solubility.

Nanoparticle Engineering in the Industry

There are a number of examples of nanoparticle engineering technologies in the industry, including nanomilling and spray drying. The former involves milling drug particles in a wet medium, while the latter approach transforms a fluid material into a dried powder by spray drying active pharmaceutical ingredients (APIs) with a polymer to create an amorphous solid.

Controlled Expansion of Supercritical Solutions (CESS) is another nanoparticle engineering approach that has emerged to control the size of drug particles. CESS reduces particle size by dissolving the drug particles in supercritical carbon dioxide and recrystallizing under controlled temperature and pressure, and can generate uniform nanoparticles as small as 10 nm in some cases. Reducing particle size to this extent opens up exciting possibilities for both dramatically improving solubility (and thus bioavailability) and even facilitating new drug delivery routes by enabling transport across biological

membranes that would ordinarily be impassable.

Combining AI and Advanced Nanoparticle Engineering

Each nanoparticle engineering technique has its own technical challenges, a common one being a lack of predictive capability for success. However, in order to implement predictive technologies in conjunction with nanoparticle engineering a key challenge must be overcome: the vast number of potential different drug molecules. This makes the available physicochemical data from existing molecules inevitably sparse in the universe of possible molecules. This, in turn, adversely impacts the predictive ability of generic AI algorithms that are built within the realm of nearly unlimited amounts of training data.

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Sparse-data AI-based approaches can provide a solution. For example, the CESS approach can work in tandem with STARMAP 2.0, a bespoke sparse-data AI engine that predicts the success of the CESS process. STARMAP 2.0 has run predictions on every molecule ever disclosed. It augments sparse-data AI with detailed expert knowledge to overcome the challenge associated with an inherently limited amount of data and make reliable predictions regarding CESS-powered nanoforming success.

Predicting the Winning Drug Candidates

AI is a powerful tool for predicting successful drug candidates. The best results will be achieved when the latest AI-based approaches are used in harmony with new solubility-enhancing technologies, such as CESS, to maximize success rates.

For instance, STARMAP can quickly and efficiently screen thousands of compounds, allowing the rapid identification of the best candidates for CESS. In addition, the STARMAP evaluation of a specific molecule to be nanoformed using CESS provides practical guidance for setting the optimal process parameters. An example of this is a collaborative study between TargTex and Nanoform to process TargTex's glioblastoma multiforme drug candidate. The results from the STARMAP evaluation of the drug candidate helped identify the processing conditions required to produce nanoparticles with the desired characteristics.

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Using predictive AI, the process of applying new technology to a candidate struggling to achieve the necessary bioavailability can be de-risked. At the same time, opportunities are created for libraries of previously undruggable molecules to be reassessed. This can potentially enable failed assets to be brought back to life again and in general accelerate the cycle of APIs from drug discovery to a pre-clinical and further to a clinical phase.

AI-powered Nanoparticle Engineering of the Future

Ultimately, the value in applying AI in Pharma is in making new and better drugs available faster than would be possible otherwise. By augmenting sparse-data AI with expert knowledge and applying it to the latest nanoparticle engineering techniques, opportunities are created to eliminate the risk associated with new techniques and give therapeutics a second chance to reach the patients who need them.

Meanwhile, AI-based techniques could be used to screen all known drug molecules for drug repurposing potential to help combat challenging diseases. The possibility of identifying 505(b)(2) opportunities using AI also opens up exciting opportunities for enabling swift patient-centric innovation. In the midst of Industry 4.0, it is a highly exciting time to be working in the field and ensuring patients also benefit from the remarkable leaps in AI-based technology.

References to this article can be requested from the authors.

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