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BIOSIMULATION EDITION

Applied BioMath

MATHEMATICAL APPROACH FOR PREDICTING RISKS EARLY-ON IN DRUG R&D

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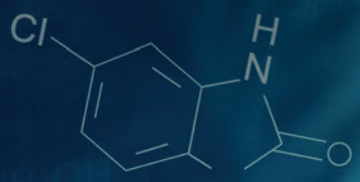
BIOSIMULATION SOLUTION PROVIDERS - 2021



Applied BioMath

MATHEMATICAL APPROACH FOR PREDICTING RISKS EARLY-ON IN DRUG R&D

Discovering a new drug or therapeutic candidate, going through regulatory approval, and bringing it to market is complicated and time-consuming. Developing a therapeutic requires an understanding of human biology, underlying causes of diseases, the interactions between drugs and the body, and several other factors. Moreover, the attrition rates are often high towards the later stages of the R&D pipeline as many promising candidates prove ineffective or toxic. What makes R&D projects even more sensitive is the amount of money and effort invested along with the crucial responsibility of health safety and compliance to medical guidelines. Predicting the complexities or risks is essential to eliminating the failures earlier and accelerating the winners into the clinic.

Applied BioMath offers biosimulation services and software to biotech and pharmaceutical companies, assisting them throughout the pipeline to help understand such complexities and identify risks early on. Applied BioMath integrates math, biology, and

high-performance computing to help answer their partner's critical go/no-go decisions. "Our aim is to help our partners develop therapeutics more efficiently and quickly, leveraging an engineering approach that incorporates the therapeutic's mechanism-of-action and high-performance computing to provide the most accurate and effective modeling supplement to traditional R&D," mentions John Burke, PhD, Co-founder, President, and CEO of Applied BioMath.

Applied BioMath's decades of cumulative industry experience, iterative collaborations, and breadth of experience make them a unique player in the industry. Their team is composed of biologists, mathematicians, physicists, computer scientists, pharmacometricians, and engineers. With such a cross-disciplinary team, Applied BioMath can seamlessly work with teams just as varied. The founders are also dedicated to creating a culture of scientific integrity and respect, which has resulted in a high repeat business rate and several multi-year strategic collaborations. To date, they have partnered with over 55 companies and completed over 160 projects.

While every project is unique, a collaboration with Applied BioMath typically involves determining the right modeling approach and building a fit-for-purpose solution as a result of their partner's scientific questions, data, and timelines. Applied BioMath's expertise spans various modeling approaches such as quantitative systems pharmacology (QSP), mechanistic or translational PK/PD, classical PK/PD, PBPK, population PK, and exposure response modeling, to name a few. A critical component to each project is determining what type of modeling or combination of modeling approaches is best suited to answer the questions at hand. Their models help project teams answer many questions, such as 1) Is it possible to develop this therapeutic given the target dosing requirements? 2) What are optimal drug properties? 3) What is the predicted efficacious dose for my therapeutic? 4) How do we differentiate our candidate from competitors?

Once a modeling approach has been selected, Applied BioMath will build a model in close collaboration with the client based on a variety of inputs, including public knowledge, the client's proprietary knowledge, and any available data. Applied BioMath is then able to vary parameters and simulate different experimental conditions. Since Applied BioMath's models are based on mechanism-of-action, the models are more easily and accurately adapted to help facilitate translation through various stages, such as from preclinical to clinical or from mouse to cyno to human.

One factor driving the increased adoption of such modeling approaches is the increased complexity of novel therapies. By using mechanistic modeling and high-performance computing, Applied BioMath is able to analyze all of the various possibilities or scenarios being considered much more quickly than could be achieved with traditional methods.

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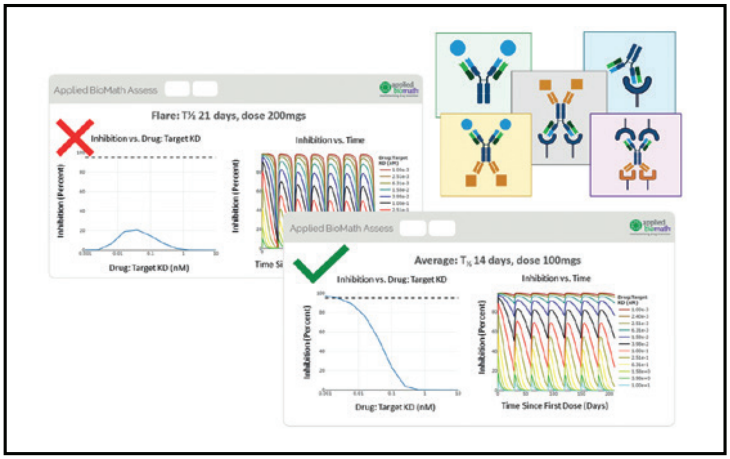
This enables teams to prioritize their resources and plan experiments more efficiently. One example is highlighted in a recent publication with CSL Behring about a systems pharmacology model developed for gene therapy in sickle cell disease. This publication illustrates just how effective modeling can be for even the most complex therapies. The team at Applied BioMath can represent all ranges of biological complexity in their models to quantitatively answer their partner's questions and help them understand the delivery of the therapeutic, amount of therapeutic needed on board, the different half-life instabilities, or even the changing patterns of protein synthesis.

Another common application of Applied BioMath's modeling and software services is early feasibility assessment (EFA), helping project teams answer go/no-go questions very early on in their project. Their recently launched software, Applied BioMath Assess™, brings this EFA service directly to project teams that otherwise would not have access to such a quantitative approach. Applied BioMath Assess helps project leaders, protein engineers and chemists, biologists, and modelers assess the risks and challenges involved in developing therapeutics using an intuitive point-and-click interface and interactive plots. Applied BioMath Assess provides a built-in library of common monospecific and bispecific pharmacologies to quickly get the user started. The interface provides an opportunity for the user to systematically modify any parameters to investigate vital characteristics such as the mechanism-of-action, half-life, target expression and turnover. This helps a user quickly explore various 'what if' scenarios to see if it's feasible to attain the desired target profile, including dose regimen, administration, frequency, etc. For instance, a company developing a bispecific needs a value greater than 90 percent for ligand-receptor inhibition for both targets in the entire dosing interval to be effective. Here the client might be required to perform monthly subcutaneous dosing for convenience, competitive reasons, or compliance. Applied BioMath Assess helps determine what parameters would be required to achieve these target dosing requirements, and teams can determine if the project is worth incorporating into their product portfolio.

Substantiating Applied BioMath's expertise in EFA, Dr. Burke mentioned the success story of Sanofi in prioritizing a bispecific project. Sanofi had five biologics listed that could be equally responsive when paired with the anchor molecule. By deploying Applied BioMath Assess, Sanofi could develop these five bispecific projects based on six targets (the anchor plus the five biologics). First, the team set up disease properties for each target, such as the number of cells, sites per cell, ligand concentration, ligand-receptor binding, etc. They could then navigate different drug properties such as affinities for each target, first-order half-life, and evaluate the nonlinear combination of target mediated drug disposition (TMDD) versus target inhibition, dosing frequencies and amounts, etc. This helped Sanofi prioritize and identify the potential winners among the five bispecifics, which can be easily developed as a function of their TPP or preliminary TPP. "This helped them significantly as it is difficult to support five bispecific projects and the opportunities are very complex," adds Dr. Burke.



In addition to partnering with biotech and pharmaceutical companies, Applied BioMath also does their own internal R&D and has received $4.7M in NIH and FDA grant funding. Most recently, they were awarded a grant by the NIH for the development of a software platform called Antibody Drug Conjugate (ADC) Workbench to facilitate efficient knowledge discovery and enable rapid knowledge qualification in support of QSP models for ADC projects. In 2017, the company was awarded a grant for the development of a QSP model of amyloid beta and tau pathways for clinical trial design and decision making in Alzheimer's Disease and Dementia. Their work in Alzheimer's Disease and Dementia has been presented at multiple scientific conferences, including ACoP, ASCPT, and the Alzheimer's Association International Conference®.

Applied BioMath is always evolving their systems modeling services to stay at the forefront of this scientific approach. Recently they expanded their services to include pharmacometrics, clinical pharmacology, bioinformatics, and ML/AI offerings. Applied BioMath software offering will also continue to evolve, including improvements to existing models and adding new drug modality models and tools. Applied BioMath's exciting roadmap stays true to their mission of helping biotech and pharmaceutical companies make better therapeutics more quickly to help patients. Ph

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Applied BioMath

The annual listing of 10 companies that are at the forefront of providing Biosimulation solutions and transforming businesses