Holmusk Galaxis 1.0

Generalized Modeling Framework for Disease Progression in Chronic & Mental Health

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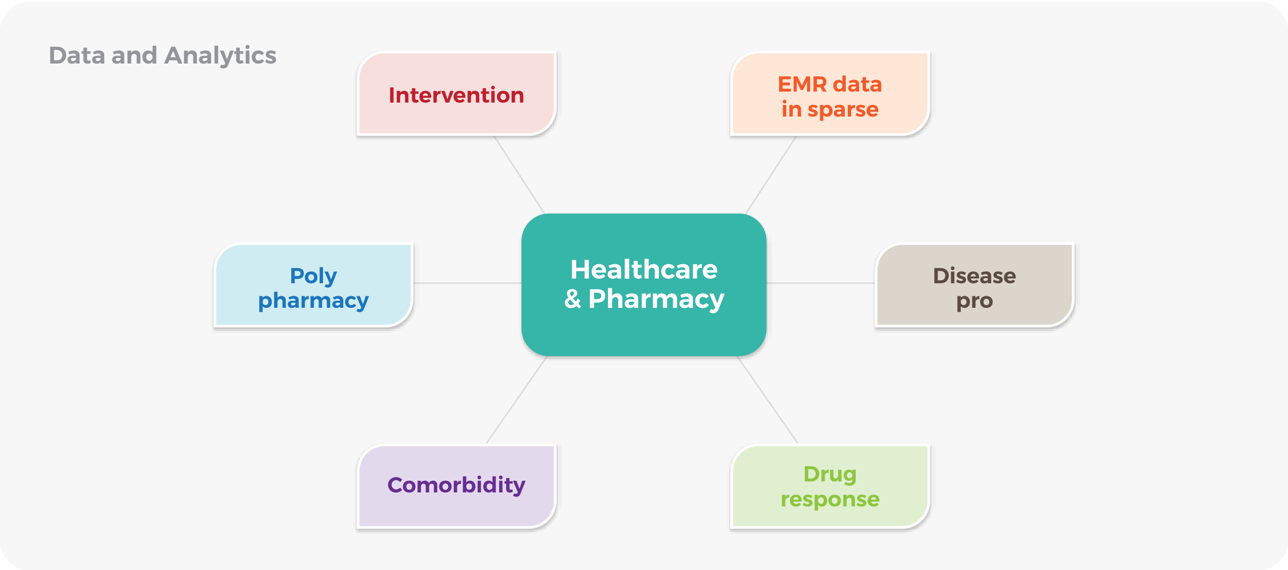
Need For Change

The rising cost of healthcare worldwide is not a new phenomenon. In 2016, healthcare costs increased astronomically to approximately 3.2 Trillion USD. Even in smaller countries like Singapore, the cost of healthcare is expected to increase to $13 Billion by 2020; a 3 fold increase from 2010. In the US, 86% of healthcare costs are accounted for by the treatment of patients with chronic and mental health conditions. Even with the advent of new technologies in treatment, and new drugs for more precise treatment, the number of new patients with such diseases is increasing rapidly. One of the many challenges that clinicians face is the progressive nature of these diseases, and the inability to detect significant heterogeneity in disease trajectory at the onset. The wide variation in drug response makes these conditions particularly difficult to treat. In addition, the problem is further exacerbated by the lack of digital tools used to effectively communicate gaps individual patient's personalized disease progression risk. Gaps in healthcare in itself are hard to detect, and the true effectiveness of new drugs entering the market are equally challenging to assess for pharmaceutical and life sciences (PLS) companies. The healthcare industry as a whole needs innovative solutions to solve the multitude of challenges.

Data in Healthcare

For the first time, the use of electronic health records (EHR) across most developed countries have enhanced the ability to deliver quality care. In the emerging world of AI and machine learning, the ability to conduct a more thorough synthesis has been amplified such that longitudinal records of patients across primary care, secondary care, and tertiary care can be generated as well as the responses to drugs. The assessment of drug efficacies for chronic & mental health conditions is also now far more regularly evaluated in regular healthcare practice rather than clinical trials – now known as real-world evidence (RWE) data. More attention has also been given to early detection, intervention, and improvement of medication adherence. The increased demand for better tools to solve these wideset and deep-rooted problems that plague treatment of chronic and mental health conditions brings advanced analytics to the front & center of the healthcare industry.



Analytics could overcome the many challenges facing healthcare and PLS

Advanced Analytics in Healthcare & PLS

The most common names in the world of advanced analytics in healthcare and life sciences include the likes of statistical models of risk, machine learning (ML), predictive analytics and artificial intelligence (AI). Statistical models of risk have been around for decades and used by clinicians e.g. Framingham risk score, Garvan fracture risk etc. But these models are based on a snapshot of the patient's current condition and do not take into account the longitudinal data. AI applications in healthcare and life sciences are more focused on operations, transcribing unstructured data, diagnosis of diseases etc. ML is unequivocally used to build predictive analytics and is expected to perform significantly better than statistical risk models. However, it is naturally not suited for longitudinal data. Holmusk's own work with cardiovascular risk scores shows significant improvement with ML-based models.

Risk Scores	Purpose	AUC (Statistical Model)	AUC (ML Model)
EuroSCORE II	In-hospital cardiac surgery mortality	80.0%	88.7%
STS*	Cardiac surgery mortality (from discharge up to 30-days)	78.0%	86.0%
ADHERE	In-hospital heart failure mortality	73.0%	88.0%
OPTIMIZE-HF	In-hospital heart failure mortality	75.4%	88.0%

Holmusk machine learning models improve on existing models of risk

Feature engineering of EMR data is one way to incorporate longitudinal data into Deep Learning Neural Networks (DNN) for a better understanding of disease progression. But healthcare data capture is quite spotty and sparse which is not ideal for this way of implementation of DNNs. Feature engineering in chronic and mental health is specifically challenging because of the multitude of co-morbidities present in these patients and ever-changing poly-pharmacy.

Our Solution

Physiology and diseases are characterized by feedback loops that vary over time with a multitude of variables. Our models are designed to capture this and depict it through visualizations. In many diseases, biology tends to precisely explain in detail the causations and correlations; however, this is not always the case. There are many cases where we lack detailed understanding, and mechanistic modeling fails. Mechanistic modeling depends on the causal biological understanding which cannot always explain variability observed in real-world data. Our model encompasses mechanistic modeling principles and artificial neural networks while also incorporating real-world patient datasets to gain a more thorough understanding to explain and understand parts of biology not known or understood.

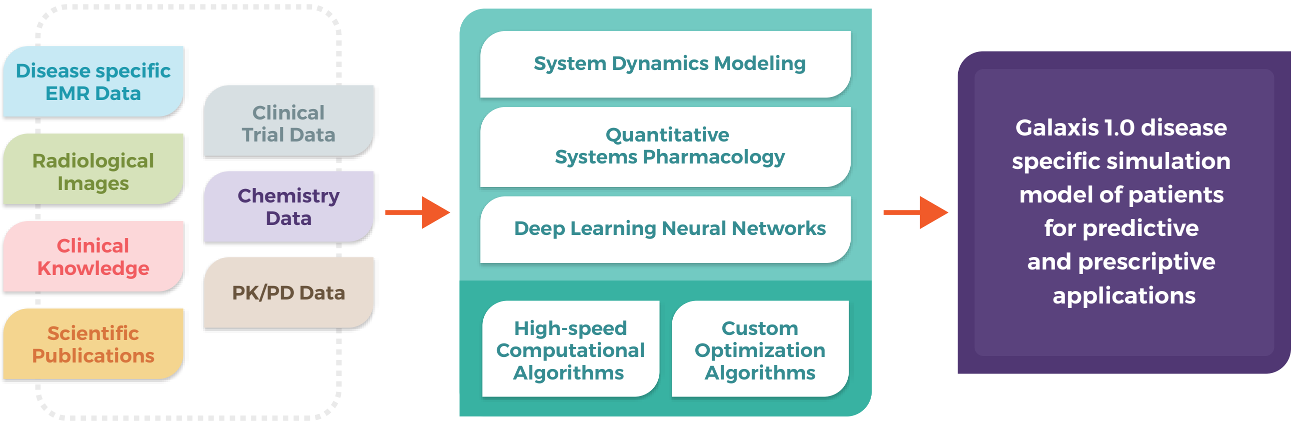
We recognize that relying on datasets as the only source of information is not pragmatic nor beneficial. As such we enhance our capabilities by extracting scientific knowledge from other platforms, thus reducing the reliance solely on real-world data. The combination of data from biology, pharmacokinetics, pharmacology and clinical trials allows for a clearer picture to be formed, amplifying the understanding and explaining capacity of our models, thereby increasing credibility and trust in our models. Because we are not tied to our understanding of physiology, this allows for models to be easily adapted to new measurements and variables as they are introduced as exemplified through the IoT.

Holmusk's data scientists have approached the problem in a way that understands the demands of the solution while knowing the challenges in the data, finding a universal framework or methodology rather than having to redo the process from scratch for every disease, every dataset. Additionally, the team's deep understanding of disease pathophysiology, molecular mechanisms and pathways lead them to seek a method which would lend itself well to the incorporation of biomedical science from published research, studies, clinical trials and emerging data types of the future.

Holmusk's semi-mechanistic simulation framework has been significantly customized based on learning from the world of Quantitative Systems Pharmacology (QSP) used extensively for academic research and drug discovery.

$$\frac{dy}{dt} = NN(\theta, y, t, z) + f\left(C_{drug}, t\right)$$

Holmusk has created custom optimization routines to incorporate scientific information, data from clinical trials etc. into the model training process, a feature not available in the standard training of the largest DNN.



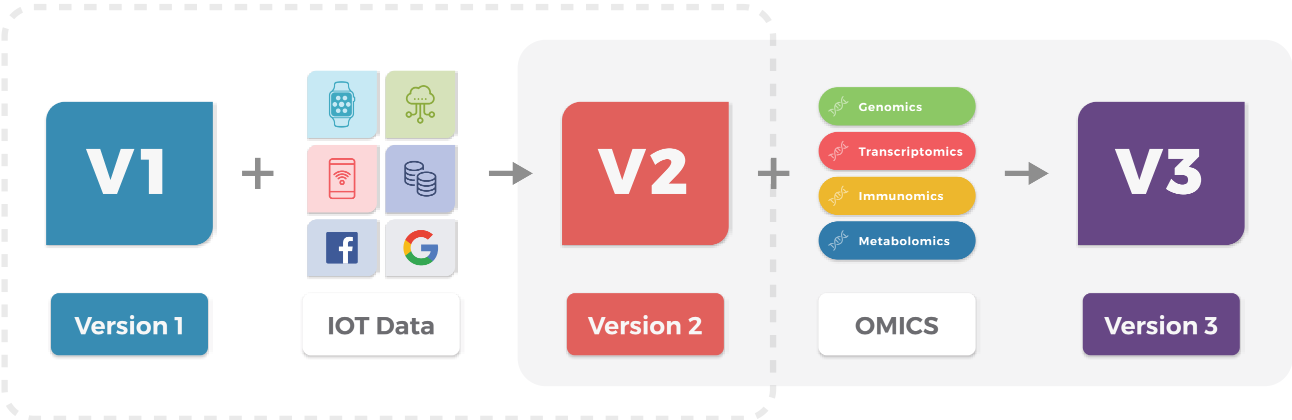
Schematics view of the data inputs and components of Galaxis 1.0

Because the simulation model takes into account that the models can be developed to accept detailed biological interactions for some parts and approximate complex feedback network loops, the simulations have been shown to be significantly more accurate than other models as the predictions move further away from the training dataset. An interesting differentiating factor of the modeling framework is that the models can be developed to accept detailed biological interactions for some parts and approximate, using neural networks for others. Also, the output of the models is not just a risk but the time-varying values of all biomarkers., clinical outputs along with risk scores. This feature makes the outputs particularly useful for interactive visualizations for digital health solutions.

Future

Holmusk is actively engaged with leading healthcare institutions like National Heart Center Singapore (NHCS), Duke University as well leading pharmaceutical companies to develop disease progression models for diabetes, cardiovascular disease, major depressive disorder, schizophrenia. The semi-mechanistic modeling framework is proving to be ideal for analysis of longitudinal patient data from EMRs and answering of different questions from individualized risk sensitivity, patient segmentation, and early diagnosis. Holmusk's goal is to develop lasting partnerships with the keepers of the longitudinal patient data so that its proprietary modeling framework can generate solutions across the spectrum of chronic diseases for all key stakeholders in the healthcare industry.

Future ready design



The current solution is capable of handling large scale EMR data but with the advent of wearable technology,more lifestyle data is made available at a patient level. These not only include activity, heart rate, weight, blood pressure, and sleep, but can also include mobile app based digital technologies for food logging, environmental factors etc. With the cost of sequencing reduced by innovations, there is increasing generation of Omics data (genomics, transcriptomics, immunomics etc) at a patient level. Such Omics data is still mostly collected in funded observational studies and clinical trials and not as regularly as a part of standard healthcare delivery. Many of the data elements in Omics and IoT are known to affect health, but the biological mechanisms are not clearly understood. The framework for Galaxis 1.0 is designed in a way that as more data from IoT infrastructure and Omics are made available on a regular basis, the framework can be extended to ingest such information without redesigning or rethinking from scratch. Holmusk's methodology has a natural advantage because it does not require the biological information and can genuinely learn the inter-relationships that lead to effects on long-term health.

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