INTERNATIONAL CONSORTIUM for INNOVATION & QUALITY in PHARMACEUTICAL DEVELOPMENT

Machine Intelligence for Quantitative Modeling in Drug Discovery & Development Applications

A Virtual Workshop

15-16 September 2022

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AI/ML-enabled Analytics & Pharmacometrics Workflow

Key applications: ML for exposure-response; ML for covariate selection; DL for PK/PD

Explainable ML for Disease Progression/Digital Twins

Key applications: Supporting clinical trial design (enrichment, stratification, and reducing the size of clinical trials); enable decision making by predicting long term clinical outcomes from early longitudinal data (e.g., biomarkers or tumor size).

NLP in Quantitative Pharmacology Modeling

Key applications: literature selection, data extraction and use of knowledge graphs.

AI/ML Utilization in Drug Discovery

Key applications: Improve DMPK and safety end points and influence large molecule design

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While there is significant interest from both industry & regulatory agencies on applying Artificial Intelligence (AI) and Machine Learning (ML) to quantitative modeling for drug development applications, several challenges remain: these include the generalizability, interpretability and data requirement of such models. To help address these issues, within the IQ Consortium the AI/ML Working Group was formed with the aim to foster scientific dialogue on AI/ML applications and identify a set of good-practices, so as to enable broader impacts in drug development. With this IQ Workshop, we aim to bring together experts from industry, academia and the FDA to initiate a scientific dialogue and collaboration across disciplines to elevate the impact of ML.

Thursday, 15 September Agenda

Welcome & Keynote: Application of Machine Learning in Drug Development

Start: 10:00 AM ET \ **Presentation:** 30 minutes

Speaker

- **Qi Liu**, US Food & Drug Administration

Session 1: AI/ML-enabled Analytics & Pharmacometrics Workflows

Start: 10:35 AM ET \ **Presentations**: 90 minutes \ **Panel:** 30 minutes

The advent of AI/ML provides opportunities for increased automation, resulting in more efficiency and/or accuracy in data analytics. However, compared to existing analytics approaches, AI/ML can potentially overfit data and magnify difference in results drawn from the train versus the test set. Furthermore, the generalizability of AI/ML models (eg, to new dosing schedule) needs to be considered. Overall, the model should aim to have clinical relevance and be explainable. Currently, there is a need for general guiding principles to be considered in applying AI/ML to workflows.

Presentations

- **Meng Hu** (US Food & Drug Administration) **Use of AI/ML technologies to enhance regulatory efficiency**
- **Nadia Terranova** (Merck Serono) **Machine Learning-empowered Fast Screening of Covariates in Population Modeling**
- **James Lu** (Genentech) **Neural-PK/PD as a Pharmacology-Informed Deep Learning Architecture**
- **Kamrine Poels** (Pfizer) **A Machine Learning Based Approach for Toxicity Predictions in Immuno-Oncology**

Panelists

- **Jonathan French** (Metrum)
- **Sarah Kim** (University of Florida)
- **Qi Liu** (US Food & Drug Administration)

Moderators

- **Kumpal Madrasi** (Merck Serono)
- **Didier Renard** (Novartis)
- **Pavan Vaddady** (Daiichi Sankyo)

Session 2: **Explainable ML for Disease Progression/Digital Twins**

Start: 1:35 PM ET \ **Presentations:** 90 minutes \ **Panel:** 30 minutes

Advances in AI/ML and the increasing availability of high-content clinical data have given rise to the possibility of constructing computational models that are able to predict patients' disease progression, at either the clinical trial and/or the individual level. While the use of Digital Twins to enhance the quantification of treatment effects offers much potential value, there is a need to understand the predictors driving the AI/ML models so as to ensure the generalizability of the findings and assess the potential risks of model applications. This session will cover a brief overview of the current state-of-the-art methods that improve ML models' explainability and highlight the value of using digital twins in clinical trials. The speakers will highlight lessons learned and best practices based on different case studies using explainable ML and Digital Twins in drug development. They will also provide lessons learned and best practices from formulating models that enhance interpretability and generalizability.

Presentations

- **Michaela van der Schaar** (University of Cambridge) TBD
- **James Kozloski** (IBM Research) **Constructing Virtual Cohorts and Coherent Data Distributions with Generative Adversarial Networks**
- **Nadia Terranova** (Merck Serono) **Explainable Machine Learning for Disease Progression in Multiple Sclerosis Patients: Application to Mavenclad Trials**
- **James Lu** (Genentech)**: Explainable Deep Learning for Tumor Dynamic Modeling and Overall Survival Prediction Using Neural-ODE**

Panelists

- **Yaning Wang** (Createrna)
- **James Lu** (Genentech)
- **Nadia Terranova** (Merck Serono)

Moderators

- **Mohamed Shahin** (Pfizer)
- **Sujatha Menon** (Pfizer)

Session 3: **NLP in Quantitative Pharmacology Modeling**

Start: 4:05 PM ET \ **Presentations:** 60 minutes \ Panel**:** 30 minutes

Natural Language Processing (NLP) is one of the most active areas in AI/ML, particularly the deep-learning approaches has revolutionized NLP in recent years. PubMed as a biomedicine-focused public text database contains over 30 million published abstracts and papers. It provides an untapped unstructured data source of biomedical knowledge and can potentially be leveraged to aid in drug development. Biomedical NLP that has been actively developing in past the few years is addressing this opportunity and the challenges.

In this session, the speakers will talk about 3 key aspects of biomedical NLP application to address questions in quantitative pharmacology modeling. Specifically, (1) literature selection: how to select relevant literature for meta-analysis, which can be used for Model-Based Meta-Analysis (MBMA), (2) data extraction: how to extract data (e.g. PK parameters) from literature, and (3) knowledge graph: how to infer relationship among recognized entities, which can be further leveraged to aid in QSP model development. Following the presentations, a panel discussion will focus on how NLP can help inform decision-making in drug development: challenges and opportunities.

Presentations

- **Jenny Ding** (Merck) **Using Deep Learning NLP Technique to Streamlining Meta-Analysis**
- **Frank Kloprogge** (University College London) **An Automated Approach to Extract Pharmacokinetic Parameters from Scientific Publications**
- **Jinfeng Zhang** (Insilicom/Florida State University) **Constructing a Biomedical Knowledge Graph for All PubMed Articles and Its Applications**

Panelists

- **Youfang Cao** (Eisai)
- **Frank Kloprogge** (University College London)
- **Hoifung Poon** (Microsoft)
- **Jiang Bian** (University of Florida)

Moderators

- **Thomas Tensfeldt** (Pfizer)
- **James Lu** (Genentech)

Friday, 16 September

Session 4: AI/ML Utilization in Drug Discovery

Start: 10:00 AM ET \ **Presentations:** 90 minutes \ **Panel:** 30 minutes

The use of AI/ML approaches has accelerated both drug discovery and development. In this session, we hope to highlight recent promising approaches happening in the preclinical and early discovery area where utilization of in silico tools has been shown to augment decision-making in the selection of the most promising molecules, even at the stage of initial compound design, across a variety of disciplines. Specific presentations will be included to highlight research on leveraging AL/ML tools that improve DMPK and Safety endpoints, as well as highlight approaches being leveraged to influence large molecule modalities. Ultimately, it is hoped that these efforts will allow us to accelerate drug discovery from years to months helping to identify the most promising medicines for patients at lower costs. This session will be critical to initiating a robust dialogue and identifying novel opportunities across participating groups.

Presentations

- **John Sanders** (Merck)**: In vivo QSAR ADME Tools to Augment Drug Discovery Efforts**
- **Rich Bonneau** (Prescient/Genentech)**: Use of AI/ML to Design Antibodies**
- **Nigel Greene** (AstraZeneca)**: Use of AL/ML in Discovery Toxicology**

Panelists

- **Prashant Desai** (Eli Lilly)
- **Fabio Broccatelli** (Bristol Myers Squibb)
- **Beth Joshi** (Bristol Myers Squibb)

Moderators

- **Nicholas Ellinwood** (Eli Lilly)
- **Marcel Hop** (Genentech)

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This material was developed with the support of the International Consortium for Innovation and Quality in Pharmaceutical Development (IQ, www.iqconsortium.org). IQ is a not-for-profit organization of pharmaceutical and biotechnology companies with a mission of advancing science and technology to augment the capability of member companies to develop transformational solutions that benefit patients, regulators and the broader research and development community.