

# Coupling Quantitative Systems Pharmacology (QSP) and ML/AI: *pAIns* and *gAIns*

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## Abstract

Quantitative Systems Pharmacology (QSP) has become a powerful tool in the drug development landscape. To ease its continued implementation and to further enhance its applicability, a **symbiotic approach** in which **QSP is combined with artificial intelligence (AI) and machine learning (ML)** is key. The application of a symbiotic approach could unlock new insights from multidimensional data, including real-world data (RWD), potentially leading to **breakthroughs in drug development**. Besides the remarkable **benefits (*gAIns*)** that the symbiosis can offer, it does also carry potential **challenges (*pAIns*)** such as how to assess and quantify uncertainty, bias and error. Hence, to ensure a successful implementation, arising *pAIns* need to be acknowledged and carefully addressed [1].

## Introduction

- **Mechanistic models don't need extensive datasets** for their development (they leverage scientific knowledge) [2]. In addition, in absence of data, they can be used for hypothesis testing, leading to mechanism characterization.
- **Pharmaceutical industry uses QSP models** for many facets [3], e.g., to find optimal doses and schedules – both for monotherapies and drug combinations.
- **QSP model development requires remarkable time and effort commitment:** novel approaches based on ML/AI are expected to facilitate such a process.
- **ML/AI-based models, appropriate for comprehensive datasets**, apply relevant algorithms to identify patterns in the data. They can uncover unreported mechanisms [4].
- Current efforts are focused on **creating a mutualistic symbiosis between the QSP and ML/AI fields** [5], which can be applied to a wide spectrum in the drug research landscape, **ranging from implications at the cellular level to clinical stages**.

## *gAIns*

### Cellular level: multi-omics data integration

Omics data capture multiple facets of cell signalling, e.g. transcriptomics, proteomics and metabolomics. Currently, technological and ML advances allow to extract real time-course information, which allows to infer cell-signalling dynamics on an absolute timescale, compatible with PK data and suitable for QSP models [6]. Since QSP modelling can integrate prior knowledge to contextual data (e.g., efficacy or safety), such a symbiosis can be used to generate synthetic but realistic data for algorithm training.

### Tissue level: image quantification

Biological samples are very valuable but tend to be scarce, so there is a need to optimise their collection time and the information extracted from them. A symbiotic approach can help, as the images can be quantified with ML algorithms (cell labelling), and such data can be used to optimise QSP parameters [7], which can provide insights in the behaviour of the system, especially when data is lacking.

### Clinical level: data heterogeneity

Progresses in ML/AI tools are easing the use of RWD, which holds promising potential. However, clinical data is highly heterogeneous. The difficulty in integrating such data is well exemplified when trying to connect qualitative clinical endpoints to quantitative measurements. A symbiotic approach can draw a link between them [8], obtaining mechanistic understanding of clinical response to treatment, including side effects.

### Bench to bed translation: drug development to precision medicine (see Fig. 1)

Identify new targets → Improve patient selection  
→ Design better treatments

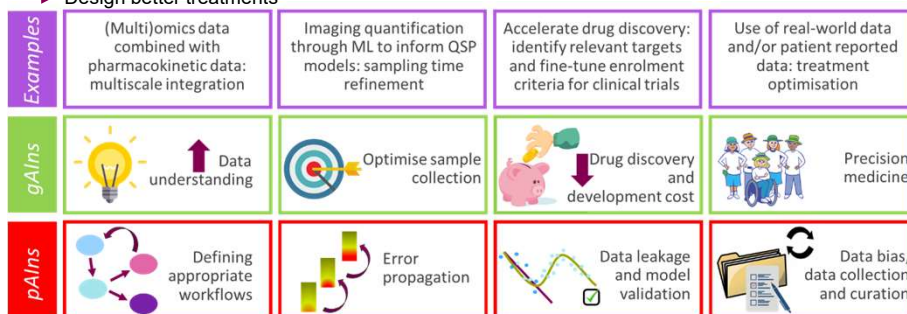


Fig. 1 (below): Schematic representation on the interaction between QSP and ML/AI [1]

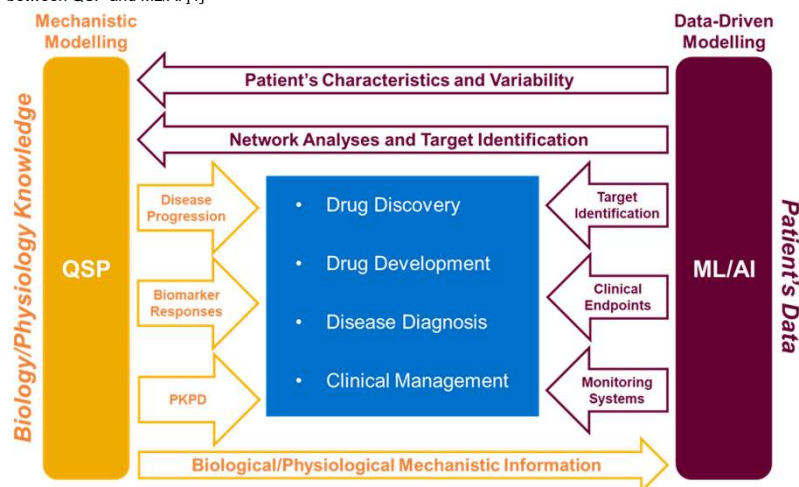


Fig. 2 (above): Case examples where a symbiotic approach could be applied, along with their associated *pAIns* and *gAIns*. [1]

## For the symbiosis to succeed...

QSP modellers and data scientists in the pharmaceutical industry and in academia should work together with drug regulatory agencies (FDA, EMA...) to:

- highlight the symbiotic *gAIns* to encourage its use.
- identify the arising *pAIns*, and plan strategies to overcome them, so as to minimise their effect.

Successful implementation of the symbiotic approach may pave the way for significant advancements in drug development and improved patient outcomes (Fig.2)

## References

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