**Introduction**

Drug discovery and development demands versatile and efficient prediction and optimisation tools which can effectively handle complex and multi-variant problems (van de Waterbeemd et al., 2003). Currently, almost all of the data analysis and optimisation software used in PK/PD studies are based on either gradient-based (e.g. Gauss-Newton and Newton-Raphson) or direct/random search (e.g. Nelder-Mead) optimisation methods. However, these methods cannot effectively tackle such complex problems.

Recently, evolutionary optimisation algorithms have been developed and Genetic Algorithms (GAs) are amongst the most popular algorithms. The latter have not been used in PK/PD data analysis. The aim of this study was to demonstrate that GAs can be used as alternatives to conventional methods in PK/PD data analysis.

**Genetic Algorithms Principles**

GAs mimic natural selection (Goldberg, 1989) and have been applied successfully in various fields, including chemistry, biology, and many engineering disciplines. They are based on Darwin's theory of evolution whose principles can be summarised as follows:

- Personality of parents is passed onto offspring during reproduction;
- Fittest individuals are liable to have more offspring and thus drive the population towards their favourable characters;
- Offspring's traits are partly inherited from their parents and partly generated through mutation.

The following figure represents the relationship between an optimisation problem and the evolution of a population.

**Optimisation Problem**

- **Evolution of a Population**
  - The problem
  - A potential solution
  - Decision parameters
  - Superiority

**Fitness**: Chances for survival to the next generation and reproduction

Generally, there are three main steps in a GA, namely: fitness evaluation of the individuals in the population, selection of parents for mating and recombination of offspring to survive to the next generation. This process of evolution continues until predefined criteria are met. A schematic diagram of GA is shown below.

**Case Studies**

In order to assess the performance of GA in PK/PD studies, we applied GAs to different problems including:

- **PK/PD Fitting**;
- **Mechanism-Based Inhibition (MBI) Parameter Estimation**;
- **Physiologically-Based Pharmacokinetic (PBPK) Modelling**.

In the following case, the performance of GA was compared with that of WinNonLin in a PK fitting problem.

**Conclusions**

Using different case studies, we have shown that GAs are plausible alternatives to conventional optimisation methods. GAs have shown superior performances in multi-modal and multi-variant optimisation problems. However, they should not be used where the conventional optimisation methods are efficient enough. The use of GA in other PK/PD problems warrants further investigation.

**References**