SIMPLE CURVE FITTING
instead of EXPENSIVE EQUIPMENT

HU-MATHS-IN
Hungarian Service Network for Mathematics in Industry and Innovations

CHALLENGES

Health, demographic change and wellbeing

The Industrial Problem

Determination of concentration of biologically active substances, including drugs and drug candidates, may be challenging in the different compartments of living tissues. However, in the drug development, it is important to collect reliable concentration-effect data about drug candidates that may require expensive equipment.

Biomedicine and Health Care

Research group

Pharmacological Work Team
(in: Industrial Mathematics Research Group of the University of Debrecen)

UNIVERSITY of DEBRECEN

An academic work team with a research topic of quantitative modelling of receptor function

Company

Kéri Pharma Hungary Kft.

KÉRI PHARMA® Csoport

A limited company dealing with market and public opinion research, focused on drug development, production and distribution

SZÉCHENYI 2020
MAGYARORSZÁG KORMÁNYA
Európai Unió
Európai Strukturális és Beruházási Alapok
BEFEKTETÉS A JÖVŐBE

SIMPLE CURVE FITTING
instead of EXPENSIVE EQUIPMENT

HU-MATHS-IN
Hungarian Service Network for Mathematics in Industry and Innovations

H2020 SOCIETAL CHALLENGES: Health, demographic change and wellbeing

Challenges & Goals

Challenges

- The microenvironment of the binding sites of a given receptor (sub)type in a tissue is a crucial compartment in terms of the biological mechanisms involving the given receptors. However, this compartment is difficult to assess in a living (and, especially, moving) organ. It is particularly true for agonists with short half-life.
- In the case of an acute increase in the concentration of an agonist at its receptors), this issue has been addressed with the receptorial responsiveness method (RRM). However, this method should be optimized, and the use of RRM should be fashioned to be as comfortable as possible.

Goals

- To find the best assumption about the distribution of concentration-effect data to fit
- To find the best assumption about the scedasticity of concentration-effect data to fit
- To find the best manner of fitting (individual or global).

SIMPLE CURVE FITTING
instead of EXPENSIVE EQUIPMENT

HU-MATHS-IN
Hungarian Service Network for Mathematics in Industry and Innovations

Mathematical and computational methods and techniques applied

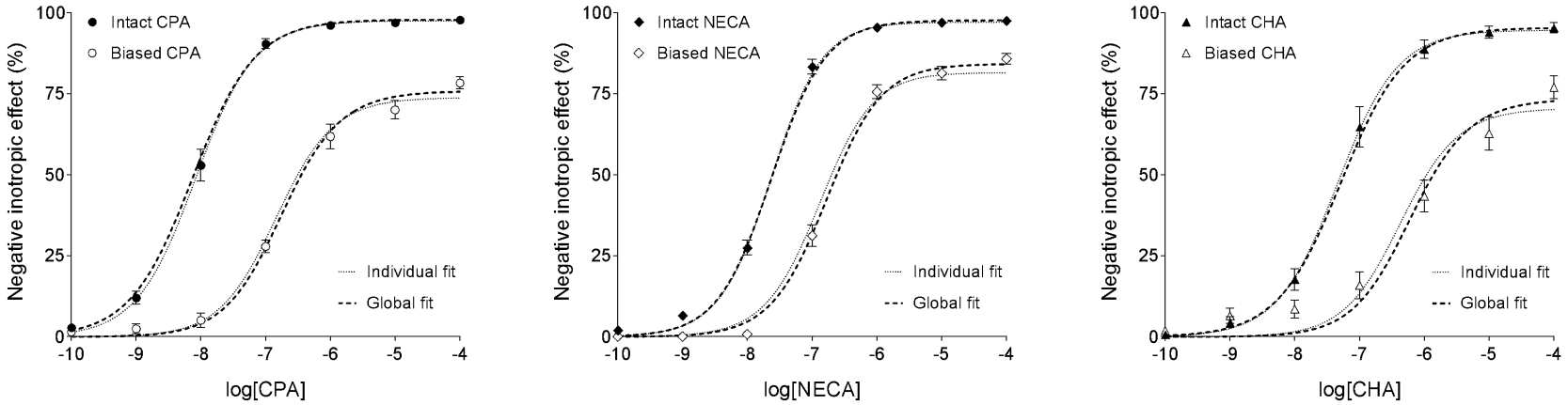
- To produce an appropriate *ex vivo* experimental system to test RRM /using isolated, paced guinea pig left atria and three stable synthetic A_1 adenosine receptor agonists (CPA, NECA, CHA)/, two types of concentration-effect curves were generated: an intact one and a biased one that contained a known extra agonist concentration to be determined
- RRM was implemented by combining different fitting approaches and setting options:
  - individual vs. global fitting
  - ordinary vs. robust fitting
  - three weighting options (no weighting vs. weighting by $1/Y^2$ vs. weighting by $1/SD^2$)
- The known concentrations of the three agonists were estimate with RRM
- The estimates were compared to the known agonist concentrations to assess the accuracy of RRM
- The 95% confidence limits of the estimates were considered to evaluate the precision of RRM

SIMPLE CURVE FITTING
instead of EXPENSIVE EQUIPMENT

HU-MATHS-IN
Hungarian Service Network for Mathematics in Industry and Innovations

Results & Benefits to the company

- Results
  - both Gaussian and Lorentzian distributions may be assumed
  - homoscedasticity may be assumed
  - individual fitting should be preferred over the global one – when performing RRM.
- Benefit
  - a cost-effective resolution of a well-circumscribed pharmacological problem.



Fitting of the model of RRM to concentration-effect curves generated with CPA, NECA and CHA, three A_1 adenosine receptor agonists, in two manners (individually and globally). Regression parameters provided by this curve fitting estimate the agonist concentrations that bias the concentration-effect curves (as compared to the intact ones).

A new point of application to determine an increase in concentration of agonists using a simple functional assay