Drug Interaction Modeling and Visualization in R with drugCombo

Maxim Nazarov – *Open Analytics, Belgium*
Nele Goeyvaerts, Luc Bijnens – *Janssen Pharmaceutica, Belgium*

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drugCombo: R package for drug interaction (synergy/antagonism) analysis

Drug interaction

- Two (or more) drugs applied in combination
  - "Drugs work together" ⟶ **synergy**
  - "Drugs work against each other" ⟶ **antagonism**

Modeling

- We extend Harbron (2010) approach based on Loewe (1953) additivity model: estimate interaction index τ with

$$\tau < 1 \longrightarrow \text{synergy}, \quad \tau = 1 \longrightarrow \text{additivity}, \quad \tau > 1 \longrightarrow \text{antagonism}$$

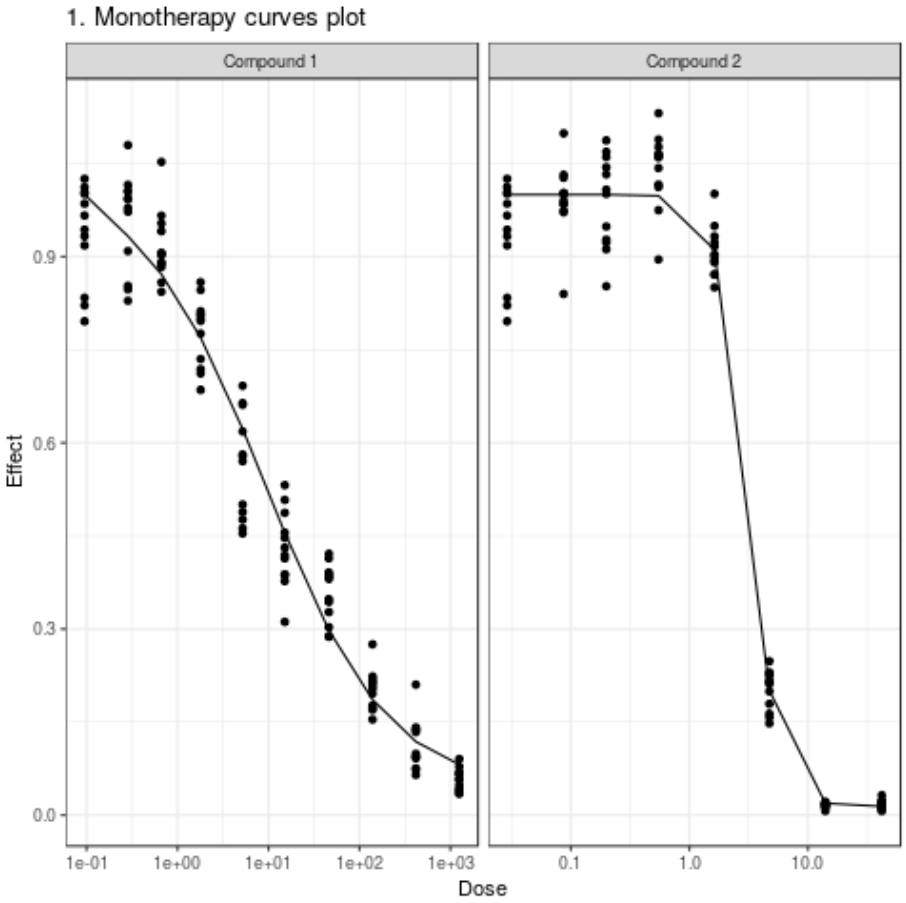
R package

- Freely available on CRAN: https://cran.r-project.org/package=drugCombo

drugCombo — Workflow

1. Monotherapy curve fitting
2. Combination model fitting
3. Model selection
4. Interaction index (τ) estimation

Summary and visualization throughout all stages



3D plot of the τ estimates

Thank you!

Give it a try

```
install.packages("drugCombo")
vignette("userGuide", package = "drugCombo")
```

→

Get in touch

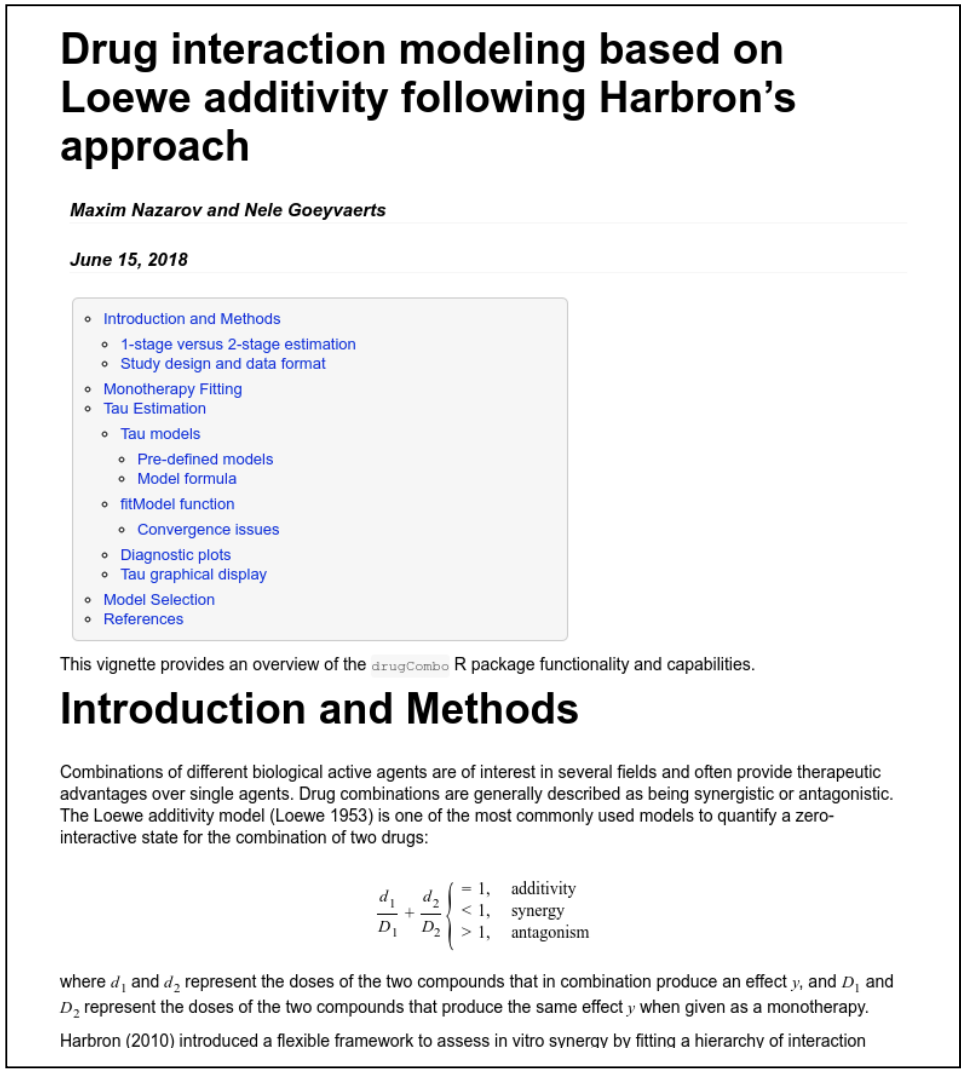
- maxim.nazarov@openanalytics.eu
- ngoeyvae@its.jnj.com

References

Harbron, Chris. 2010. "A Flexible Unified Approach to the Analysis of Pre-Clinical Combination Studies." *Statistics in Medicine* 29 (16). Wiley Online Library: 1746–56.

Loewe, S. 1953. "The Problem of Synergism and Antagonism of Combined Drugs." *Arzneimittelforschung* 3: 285–90.

https://cran.r-project.org/package=drugCombo



Drug interaction modeling based on Loewe additivity following Harbron's approach

Maxim Nazarov and Nele Goeyvaerts

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This vignette provides an overview of the `drugCombo` R package functionality and capabilities.

Introduction and Methods

Combinations of different biological active agents are of interest in several fields and often provide therapeutic advantages over single agents. Drug combinations are generally described as being synergistic or antagonistic. The Loewe additivity model (Loewe 1953) is one of the most commonly used models to quantify a zero-interactive state for the combination of two drugs:

$$\frac{d_1}{D_1} + \frac{d_2}{D_2} \begin{cases} = 1, & \text{additivity} \\ < 1, & \text{synergy} \\ > 1, & \text{antagonism} \end{cases}$$

where d_1 and d_2 represent the doses of the two compounds that in combination produce an effect y, and D_1 and D_2 represent the doses of the two compounds that produce the same effect y when given as a monotherapy.

Harbron (2010) introduced a flexible framework to assess in vitro synergy by fitting a hierarchy of interaction