Statistical Assessment of Optimal Drug Combination

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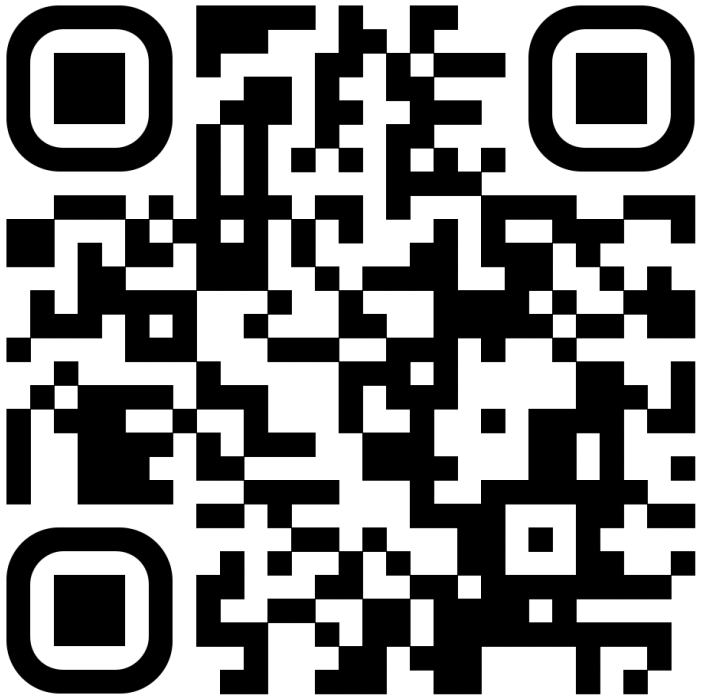
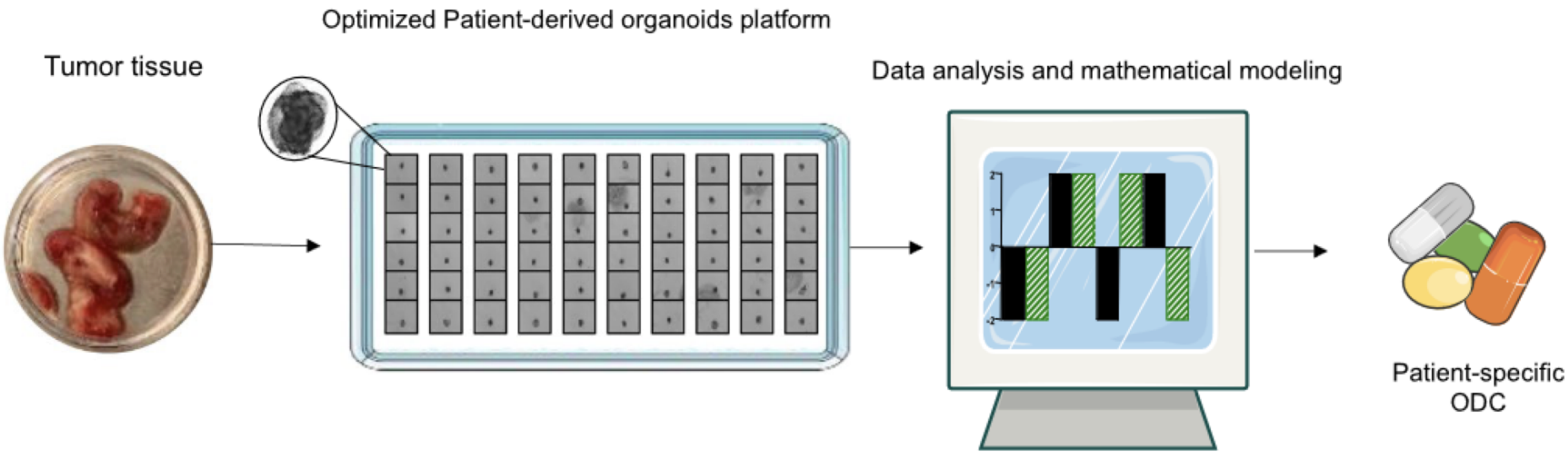
Slides and coding examples

Access the material:



https://github.com/lionelvoirol/stat_modelling_drug_combination

Context



Adapted from Ramzy et al., Journal of Experimental & Clinical Cancer Research, 2023

Drug combination

- Optimized Drug Combination (ODC) for disease treatment.
- The identification of ODC: target disease/malignant cells while causing a minimal harm to healthy cells.
- This is a complicated task from a statistical perspective. Currently no standard statistical procedures exist.
- Example of existing methods: Therapeutically Guided Multidrug Optimization[1,2,3] mainly developed by Prof. Nowak-Sliwinska's group.
- Experiments allow to test a measure of interest (quantifying how well a drug works) for different drug combinations recorded over multiple replicates.

[1] Weiss et al., Cancers, 2019; [2] Zoetemelk et al., Molecular Oncology, 2023; [3] Ramzy et al., Journal of Experimental & Clinical Cancer Research, 2023

Example

- Goal: Investigate the marginal treatment effects of three drugs (i.e., drug A, B and C).
- Record a measure of interest for multiple replicates which have been exposed to one of the treatments.
- As an example, consider 3 replicates per treatment, with only one drug applied in each treatment $\Longrightarrow 3$ replicates $\times$ 3 drugs $= 9$ experiments.

ID	Measure	Treatment	Replicate	Drug A	Drug B	Drug C
1	Y_1	A	1	1	0	0
2	Y_2	A	2	1	0	0
3	Y_3	A	3	1	0	0
4	Y_4	B	1	0	1	0
5	Y_5	B	2	0	1	0
6	Y_6	B	3	0	1	0
7	Y_7	C	1	0	0	1
8	Y_8	C	2	0	0	1
9	Y_9	C	3	0	0	1

Estimating marginal treatment effects

- Intuitive approach: Consider a suitable location estimator (e.g., the sample mean) of the measure for each treatment.
- Estimated effect of drugs:

$$\bar{Y}_A = \frac{Y_1 + Y_2 + Y_3}{3}, \quad \bar{Y}_B = \frac{Y_4 + Y_5 + Y_6}{3}, \quad \bar{Y}_C = \frac{Y_7 + Y_8 + Y_9}{3}.$$

Estimating marginal treatment effects

Alternative approach: linear regression

$$\begin{bmatrix} Y_1 \\ Y_2 \\ \vdots \\ Y_n \end{bmatrix} = \begin{bmatrix} x_{11} & x_{12} & x_{13} \\ x_{21} & x_{22} & x_{23} \\ \vdots & \vdots & \vdots \\ x_{n1} & x_{n2} & x_{n3} \end{bmatrix} \begin{bmatrix} \beta_1 \\ \beta_2 \\ \beta_3 \end{bmatrix} + \begin{bmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \vdots \\ \varepsilon_n \end{bmatrix}$$

$$\boldsymbol{Y} = \boldsymbol{X}\ \boldsymbol{\beta} + \boldsymbol{\varepsilon}$$

- n: number of experiments.
- $\boldsymbol{Y}$: vector of measurements.
- $\boldsymbol{X}$: design matrix, where $x_{ij} = 1$ if drug j is applied in experiment i, and $x_{ij} = 0$ otherwise.
- $\boldsymbol{\beta}$: vector of unknown parameters.
- $\boldsymbol{\varepsilon}$: zero mean random vector which, for example, follows a $\mathcal{N}(\mathbf{0}, \sigma^2 \mathbf{I}_n)$ where σ^2 is an unknown *nuisance* parameter.

Estimating marginal treatment effects

In this example, the model can be written as:

$$\begin{bmatrix} Y_1 \\ Y_2 \\ \vdots \\ Y_9 \end{bmatrix} = \begin{bmatrix} 1 & 0 & 0 \\ 1 & 0 & 0 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 1 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \\ 0 & 0 & 1 \\ 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} \beta_A \\ \beta_B \\ \beta_C \end{bmatrix} + \begin{bmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \vdots \\ \varepsilon_9 \end{bmatrix}$$

$$\boldsymbol{Y} = \boldsymbol{X} \boldsymbol{\beta} + \boldsymbol{\varepsilon}$$

Estimating marginal treatment effects

Define $\hat{\boldsymbol{\beta}}_{\text{OLS}}$ as the Ordinary Least Square (OLS) estimator of $\boldsymbol{\beta}$:

$$\hat{\boldsymbol{\beta}}_{\text{OLS}} = \underset{\boldsymbol{\beta}}{\text{argmin}} \, \|\boldsymbol{Y} - \boldsymbol{X}\boldsymbol{\beta}\|_2^2 = \underset{\boldsymbol{\beta}}{\text{argmin}} \sum_{i=1}^{n} \left(Y_i - \boldsymbol{x}_i^T \boldsymbol{\beta}\right)^2 = (\boldsymbol{X}^T \boldsymbol{X})^{-1} \boldsymbol{X}^T \boldsymbol{Y}.$$

Is this approach equivalent to the sample mean?

Estimating marginal treatment effects

$$\hat{\boldsymbol{\beta}}_{\text{OLS}} = (\boldsymbol{X}^T\boldsymbol{X})^{-1}\boldsymbol{X}^T\boldsymbol{Y} = \left(\begin{bmatrix} 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 1 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 \end{bmatrix} \begin{bmatrix} 1 & 0 & 0 \\ 1 & 0 & 0 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 1 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \\ 0 & 0 & 1 \\ 0 & 0 & 1 \end{bmatrix} \right)^{-1}$$

$$\begin{bmatrix} 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 1 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 \end{bmatrix} \begin{bmatrix} Y_1 \\ Y_2 \\ Y_3 \\ Y_4 \\ Y_5 \\ Y_6 \\ Y_7 \\ Y_8 \\ Y_9 \end{bmatrix} = \begin{bmatrix} \frac{1}{3} & 0 & 0 \\ 0 & \frac{1}{3} & 0 \\ 0 & 0 & \frac{1}{3} \end{bmatrix} \begin{bmatrix} \sum_{i=1}^{3} Y_i \\ \sum_{i=4}^{6} Y_i \\ \sum_{i=7}^{9} Y_i \end{bmatrix}$$

$$= \frac{1}{3} \begin{bmatrix} \sum_{i=1}^{3} Y_i \\ \sum_{i=4}^{6} Y_i \\ \sum_{i=7}^{9} Y_i \end{bmatrix} = \begin{bmatrix} \bar{Y}_A \\ \bar{Y}_B \\ \bar{Y}_C \end{bmatrix}$$

A more realistic design

- In practice: typically more than 3 drugs and consider different dosages.
- Objective: find a combination of k drugs among h drugs. Each drug can have m dosages. (We assume same number of dosages for all drugs for simplicity.)
- Example: Suppose we want to investigate the effect of all treatments composed of $k = 2$ drugs among a total of $h = 3$ drugs (i.e., drug A, B, C), where each drug can be administrated at $m = 2$ dosages (e.g., low dosage encoded as 1 or high dosage encoded as 2).
- How many possible combinations will we consider?

A more realistic design

- 3 possible combinations of drugs (i.e., AB, AC and BC).
- 4 possible combinations of dosages (i.e., $\{1,1\},\{1,2\},\{2,1\},\{2,2\}$).
- Therefore, we have 12 combinations in total (i.e., $A1B1$, $A1B2$, $A2B1$, $A2B2$, $A1C1$, $A1C2$, $A2C1$, $A2C2$, $B1C1$, $B1C2$, $B2C1$, $B2C2$).
- Consider 3 replications for each combination, we obtain the following data structure.

ID	Measure	Combination	Replicate	$A1$	$A2$	$B1$	$B2$	$C1$	$C2$
1	Y_1	$A1B1$	1	1	0	1	0	0	0
2	Y_2	$A1B1$	2	1	0	1	0	0	0
3	Y_3	$A1B1$	3	1	0	1	0	0	0
4	Y_4	$A1B2$	1	1	0	0	1	0	0
5	Y_5	$A1B2$	2	1	0	0	1	0	0
6	Y_6	$A1B2$	3	1	0	0	1	0	0
⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮
33	Y_{33}	$B2C1$	3	0	0	0	1	1	0
34	Y_{34}	$B2C2$	1	0	0	0	1	0	1
35	Y_{35}	$B2C2$	2	0	0	0	1	0	1
36	Y_{36}	$B2C2$	3	0	0	0	1	0	1

A more realistic design

- In general, how many combinations of k drugs based on h drugs at m dosages can we consider?

$$\text{Number of combinations} = \binom{h}{k} m^k.$$

- Suppose $k = 4$, $h = 11$ and $m = 2$, we have

$$\text{number of combinations} = \binom{11}{4} 2^4 = 5,280,$$

with 3 replications this would correspond to $3 \times 5,280 = 15,840$ experiments...

- Hence, it quickly becomes impossible to experimentally test all treatments.

Experimental design

- Experimental design is an area of statistics that involves the random assignment of subjects or treatments to different groups.
- Objective: construct a set of treatments that effectively sample the entire spectrum of possible treatments, optimizing the information extracted from the data.
- Given the number of potential treatments to test and the number of experiments to be performed, an experimental design protocol constructs a design matrix $\boldsymbol{X}$ that explores "at best" the space of possible treatments.
- The theory of experimental design is rather involved and beyond the scope of this presentation. For simplicity, we use the results of Xu, Jaynes and Ding, 2014[4] to construct $\boldsymbol{X}$.

[4] Xu et al., Statistica Sinica, 2014

Parameter estimation

- In our example: we have $5,280$ treatments to test.
- Is it possible to estimate the treatment effects of all combinations?
- Consider a linear regression model with $5,280$ parameters:

$$Y_i = \nu_1 A_{1i} B_{1i} C_{1i} D_{1i} + \nu_2 A_{1i} B_{1i} C_{1i} D_{2i} + \dots + \nu_{5279} H_{2i} I_{2i} J_{2i} K_{1i} + \nu_{5280} H_{2i} I_{2i} J_{2i} K_{2i} + \varepsilon_i$$

where ν_1 the true efficacy of combination A_1 B_1 C_1 D_1 and

$$A_{1i} = \begin{cases} 1 & \text{if drug } A \text{ at dosage 1 is considered in experiment } i \\ 0 & \text{otherwise} \end{cases}$$

- What is the meaning of $H_{2i} I_{2i} J_{2i} K_{2i}$?
- Is this a good approach?

Overparameterized model

- Alternative: consider an overparameterized model allowing to "separate" the effects of each drug and their interactions.
- In our example, we have $k = 4$, $h = 11$, and $m = 2$, so we consider

$$
\begin{aligned}
Y_i = & \underbrace{\beta_1 A_{1i} + \beta_2 A_{2i} + \beta_3 B_{1i} + \ldots + \beta_{21} K_{1i} + \beta_{22} K_{2i}}_{\text{marginal effects}} \\
& + \underbrace{\gamma_1 A_{1i} B_{1i} + \gamma_2 A_{1i} B_{2i} + \ldots + \gamma_{219} J_{2i} K_{1i} + \gamma_{220} J_{2i} K_{2i}}_{\text{first order interactions}} \\
& + \underbrace{\eta_1 A_{1i} B_{1i} C_{1i} + \eta_2 A_{1i} B_{1i} C_{2i} + \ldots + \eta_{1319} I_{2i} J_{2i} K_{1i} + \eta_{1320} I_{2i} J_{2i} K_{2i}}_{\text{second order interactions}} \\
& + \underbrace{\nu_1 A_{1i} B_{1i} C_{1i} D_{1i} + \ldots + \nu_{5279} H_{2i} I_{2i} J_{2i} K_{1i} + \nu_{5280} H_{2i} I_{2i} J_{2i} K_{2i}}_{\text{third order interactions}} \\
& + \varepsilon_i
\end{aligned}
$$

- We define $\boldsymbol{\theta} = [\beta_1, \ldots, \beta_{22}, \gamma_1, \ldots, \gamma_{220}, \eta_1, \ldots, \eta_{1320}, \nu_1, \ldots, \nu_{5280}]$ as the vector of unknown parameters.
- Now we have 1,562 MORE parameters. Why is this a good idea?

How many interactions?

- We should only consider interactions up to $(k-1)$-th order. Why?

$$\text{Total number of interactions} = \sum_{i=2}^{k} \binom{h}{i} m^i$$

- In our example, we consider treatments composed of $k = 4$ drugs, where each drugs can be expressed at $m = 2$ dosages, with a total of $h = 11$ possible drugs. Therefore, there are $\sum_{i=2}^{4} \binom{11}{i} 2^i = 6,820$ interactions (see coding exercise `example_3.R`).
- For the full model with all marginal effects plus all interactions:

$$\text{Total number of parameters} = \sum_{i=1}^{k} \binom{h}{i} m^i$$

Spare estimation

- Generally all drugs expressed at a specific dosage are assumed to have a non-zero treatment effect. However, it is reasonable to think that most interactions have zero effect. But which ones?
- This can be viewed as a model selection problem, where the variables to be chosen are the ones encoding significant interactions and the variables encoding the marginal treatment effects are always included.
- There are 2^p possible models when considering p variables.
- For example, with 3 variables (X_1, X_2 and X_3), we have $2^3 = 8$ models which can be expressed as:
  1. $Y_i = \beta_0 + \varepsilon_i$ (The empty model)
  2. $Y_i = \beta_0 + \beta_1 X_{1i} + \varepsilon_i$
  3. $Y_i = \beta_0 + \beta_1 X_{2i} + \varepsilon_i$
  4. $Y_i = \beta_0 + \beta_1 X_{3i} + \varepsilon_i$
  5. $Y_i = \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \varepsilon_i$
  6. $Y_i = \beta_0 + \beta_1 X_{1i} + \beta_2 X_{3i} + \varepsilon_i$
  7. $Y_i = \beta_0 + \beta_1 X_{2i} + \beta_2 X_{3i} + \varepsilon_i$
  8. $Y_i = \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \beta_3 X_{3i} + \varepsilon_i$

Best subset selection

- When the number of interactions is relatively small, one approach is to consider all possible subsets.
- Procedure:
  - Identify all possible regression models derived from all possible combinations of the interactions.
  - For each model, compute the model performance evaluation metric such as the Akaike information criterion (AIC).
  - Select the *best* model(s) according to the considered criteria.
  - See `example_2.R` for more details.
- In our example: 6,820 interactions $\Longrightarrow 2^{6820}$ possible models.
- As a comparison: $60 \times 60 \times 24 \times 365 \times 2023 = 63797328000 \simeq 2^{36}$.
- NP-hard problem: conventional exhaustive search is impossible. Some hope with mixed integer optimization algorithms (near-optimal solutions)[5].

[5] Bertsimas et al., Annals of Statistics, 2016

Penalized regression

- We are considering high-dimensional settings (in the sense that there are much more parameters p to estimate than observations n, or $p \gg n$).
- Very hot (and very hard) topic in statistics.
- A major aspect of statistical and machine learning methods is to reduce complexity (avoid overfitting) in order to improve prediction accuracy and interpretability.
- A common strategy to control the risk of overfitting and improve predictive accuracy is to use regularization methods. For example, in the linear regression model, we consider:

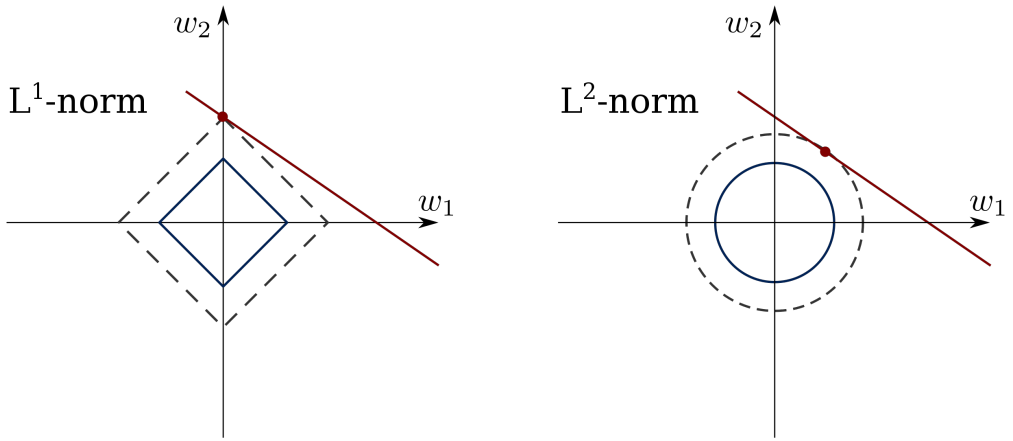
$$\boldsymbol{Y} = \boldsymbol{X}\boldsymbol{\beta} + \boldsymbol{\varepsilon}, \quad \hat{\boldsymbol{\beta}}_{\text{Pen}} = \underset{\boldsymbol{\beta}}{\text{argmin}} \, \|\boldsymbol{Y} - \boldsymbol{X}\boldsymbol{\beta}\|_2^2 + \text{penalty}(\boldsymbol{\beta})$$

- If $\text{penalty}(\boldsymbol{\beta}) = 0 \implies$ OLS estimator.
- If $\text{penalty}(\boldsymbol{\beta}) = \lambda \|\boldsymbol{\beta}\|_1 \implies$ Lasso.

Geometric interpretation

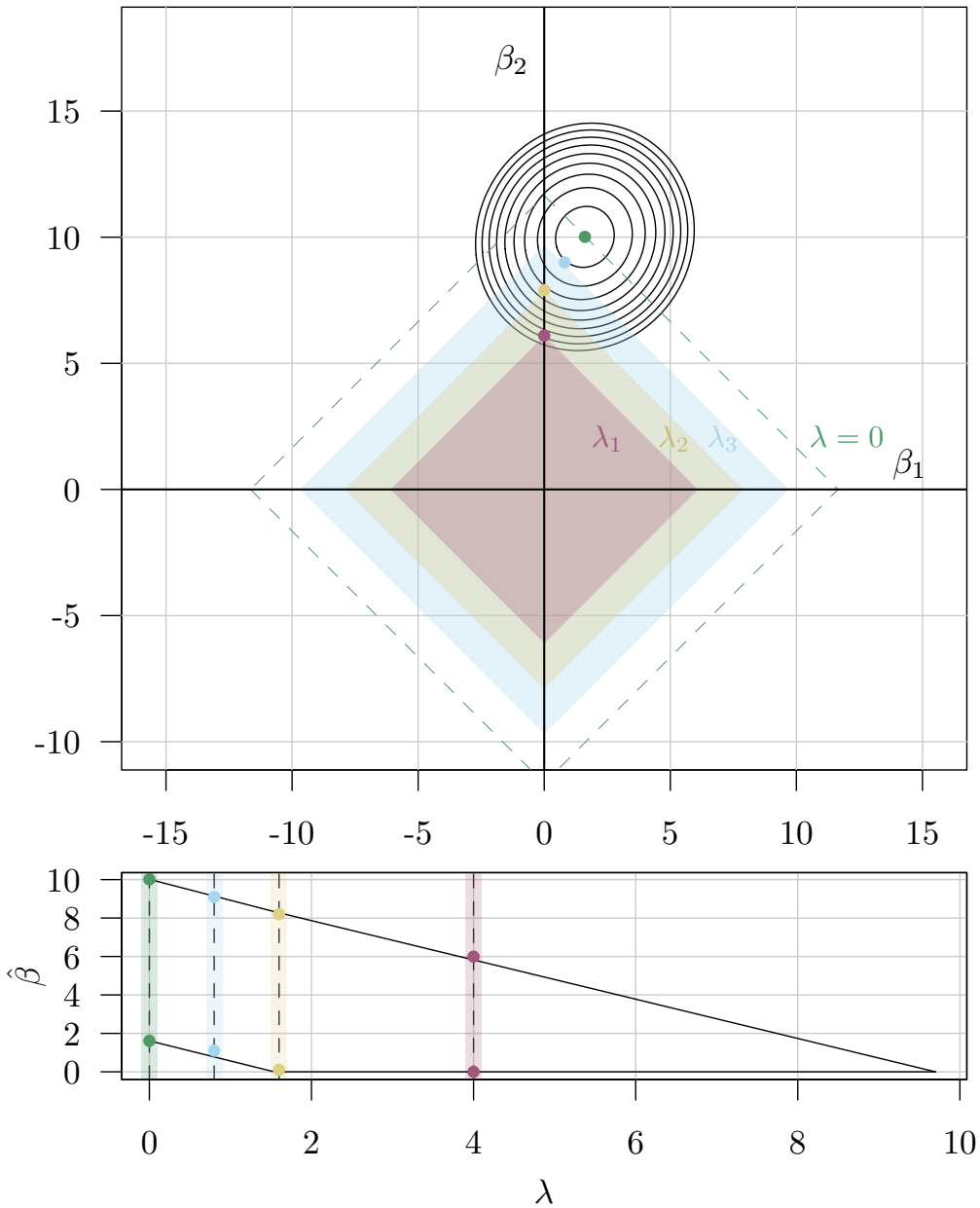
- Lasso (or least absolute shrinkage and selection operator)[6] is a penalization method developed to perform feature selection.
- Lasso considers the ℓ_1 norm multiplied by an hyperparameter λ as the penalty term added to the usual linear regression cost function.
- Procedure shrinks the coefficients toward zero value, hence performing feature selection (often improving predictive performance and interpretability).

$$\hat{\boldsymbol{\beta}}_{\text{Lasso}} = \underset{\boldsymbol{\beta}}{\operatorname{argmin}} \|\boldsymbol{Y} - \boldsymbol{X}\boldsymbol{\beta}\|_2^2 + \lambda \|\boldsymbol{\beta}\|_1$$



[6] Tibshirani, Journal of the Royal Statistical Society Series B, 1996

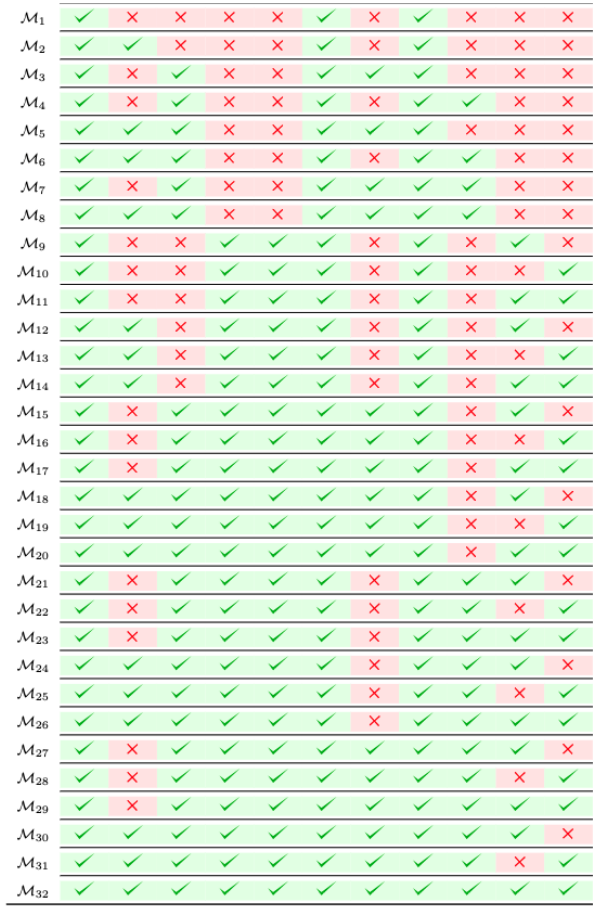
Geometric interpretation



Incorporating domain knowledge: Example in finance

Is it possible to "help" the Lasso by incorporating domain knowledge?

- In finance the No-Arbitrage assumption informally means that there cannot be free investments with a positive payoff.
- This assumption is the core of financial models.
- It can be translated into constraints on the admissible models.
- Penalties $\text{penalty}(\boldsymbol{\beta})$ encoding these constraints can be constructed[7].
- Example: given 11 variables (or $2^{11} = 2048$ models), the penalties result in only 32 models, hence leading to considerable improvements.



[7] Bakalli et al., Journal of Econometrics, 2023

Incorporating domain knowledge

In the context of drug combinations, it is generally believed that:

- All marginal treatment effects of drugs are significant.
- Interactions up to $(k-1)$-th order should be included in the model. Moreover, the proportion of significant covariates associated with interactions decreases as we consider higher order interactions.

To incorporate this information, we consider the adaptive Lasso[8] instead of the Lasso:

$$\hat{\boldsymbol{\beta}}_{\text{AdaLasso}} = \underset{\boldsymbol{\beta}}{\text{argmin}} \, \|\boldsymbol{Y} - \boldsymbol{X}\boldsymbol{\beta}\|_2^2 + \lambda \sum_{j=1}^{p} w_j \, |\beta_j|,$$

where w_j are predetermined (or estimated) weights.

[8] Zou, Journal of American Statistical Association, 2006

Incorporating domain knowledge

- The model we consider can be expressed as:

$$
\begin{aligned}
Y_i = & \underbrace{\beta_1 A_{1i} + \beta_2 A_{2i} + \beta_3 B_{1i} + \ldots + \beta_{21} K_{1i} + \beta_{22} K_{2i}}_{\text{marginal effects}} \\
& + \underbrace{\gamma_1 A_{1i} B_{1i} + \gamma_2 A_{1i} B_{2i} + \ldots + \gamma_{219} J_{2i} K_{1i} + \gamma_{220} J_{2i} K_{2i}}_{\text{first order interactions}} \\
& + \underbrace{\eta_1 A_{1i} B_{1i} C_{1i} + \eta_2 A_{1i} B_{1i} C_{2i} + \ldots + \eta_{1319} I_{2i} J_{2i} K_{1i} + \eta_{1320} I_{2i} J_{2i} K_{2i}}_{\text{second order interactions}} \\
& + \underbrace{\nu_1 A_{1i} B_{1i} C_{1i} D_{1i} + \ldots + \nu_{5279} H_{2i} I_{2i} J_{2i} K_{1i} + \nu_{5280} H_{2i} I_{2i} J_{2i} K_{2i}}_{\text{third order interactions}} \\
& + \varepsilon_i
\end{aligned}
$$

- We can express the penalty term as follows:

$$
\lambda \sum_{j=1}^{p} w_j \left|\theta_j\right| = \frac{\lambda}{W_1} \|\boldsymbol{\beta}\|_1 + \frac{\lambda}{W_2} \|\boldsymbol{\gamma}\|_1 + \frac{\lambda}{W_3} \|\boldsymbol{\eta}\|_1 + \frac{\lambda}{W_4} \|\boldsymbol{\nu}\|_1
$$

Incorporating domain knowledge

- It is not straightforward to determine W_i, with $i = 1, \ldots, 4$.
- A possible (and intuitive) strategy is to use

$$W_i = W_i^{(1)} W_i^{(2)}$$

- $W_i^{(1)}$: Empirical proportion of non-zero effect in the $(i-1)$-th order.
- $W_i^{(2)}$: Average effect of the non-zero effects in the $(i-1)$-th order.

How to assess the efficacy of a drug combination?

- In our example, we have $5,280$ possible treatments (i.e., combinations of drugs at specific dosage).
- The effect of each treatment can be estimated by a linear combination of the estimated parameters. For example, for the treatment composed of drugs A, B, C and D at dosage 1 (i.e., treatment $A1B1C1D1$):

$$\hat{Y}_{A1B1C1D1} = \hat{\beta}_1 + \hat{\beta}_3 + \hat{\beta}_5 + \hat{\beta}_7 + \hat{\gamma}_1 + \ldots + \hat{\eta}_1 + \ldots + \hat{\nu}_1 = \boldsymbol{z}_1^T \hat{\boldsymbol{\theta}}$$

- Here the i-th element of $\boldsymbol{z}_1$ is either 0 or 1, depending on whether the i-th parameter of $\boldsymbol{\theta}$ is associated to treatment 1 (i.e., treatment $A1B1C1D1$).
- We define $\boldsymbol{z}_j$ where $j = 1, ..., 5280$ for all combinations.
- See `example_5.R`.

Best combination or best combinations?

- We define the optimal treatment as:

$$\hat{j} = \underset{j \in \{1,\ldots,5280\}}{\operatorname{argmin}} \quad \boldsymbol{z}_j^T \, \hat{\boldsymbol{\theta}}$$

- Are there other treatments that are non-distinguishable given the data at hand? Probably...
- Since the variance of $\hat{\boldsymbol{\theta}}$, say $\boldsymbol{\Sigma}$, can be estimated by $\hat{\boldsymbol{\Sigma}}$, we have:

$$\operatorname{var}(\boldsymbol{z}_j^T \, \hat{\boldsymbol{\theta}}) = \boldsymbol{z}_j^T \boldsymbol{\Sigma} \boldsymbol{z}_j \approx \boldsymbol{z}_j^T \hat{\boldsymbol{\Sigma}} \boldsymbol{z}_j$$

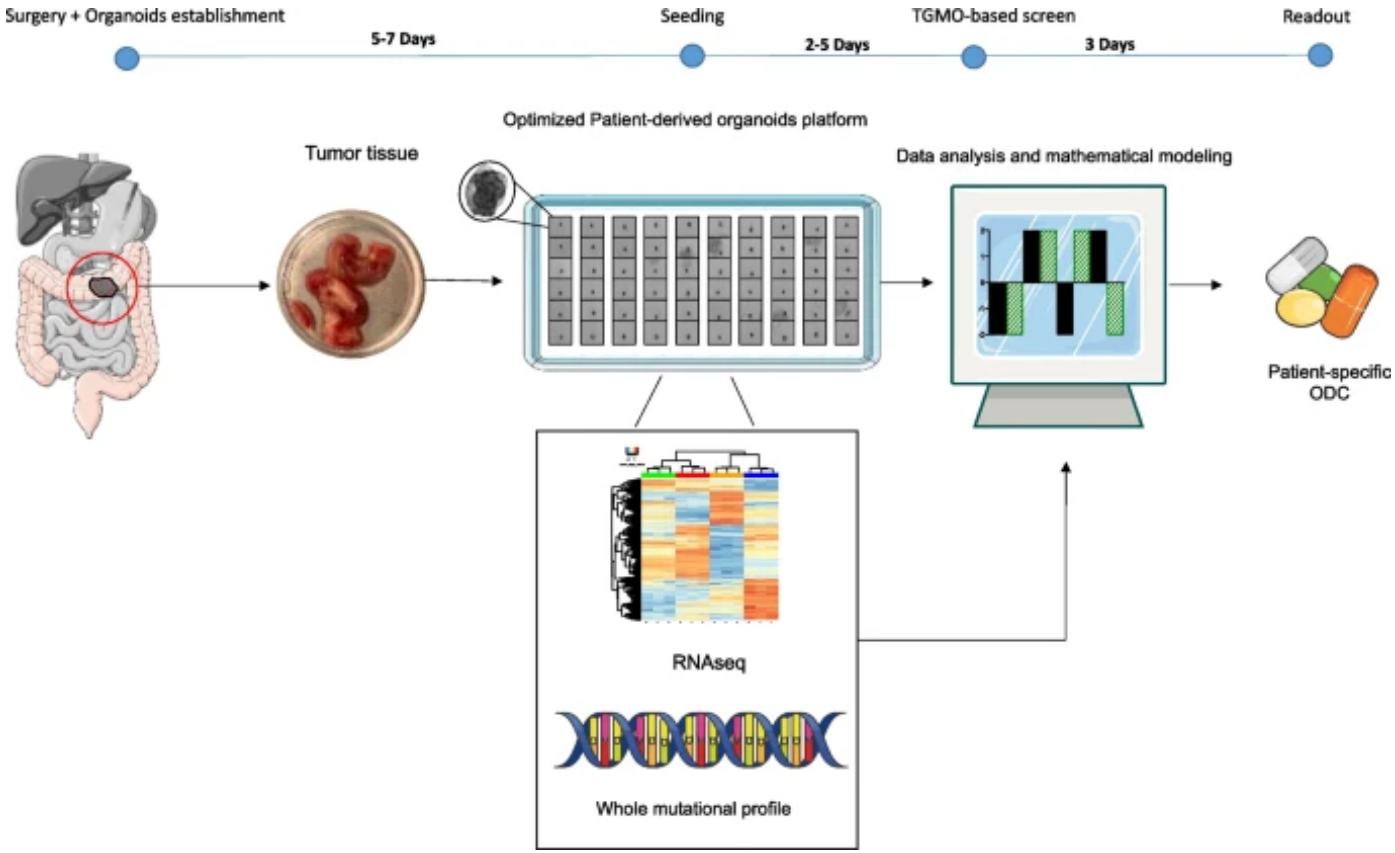
- Hence, it is possible to compute an upper-tail (asymptotic) confidence interval at the $(1-\alpha)$ confidence level:

$$\boldsymbol{z}_j^T \, \hat{\boldsymbol{\theta}} + z_{1-\alpha} \sqrt{\boldsymbol{z}_j^T \hat{\boldsymbol{\Sigma}} \boldsymbol{z}_j}$$

  where $z_{1-\alpha}$ denotes the $(1-\alpha)$-th quantile of the standard normal distribution.
- Consider all treatments satisfying:

$$\boldsymbol{z}_j^T \hat{\boldsymbol{\theta}} < \boldsymbol{z}_{\hat{j}^T} \hat{\boldsymbol{\theta}} + z_{1-\alpha} \sqrt{\boldsymbol{z}_{\hat{j}}^T \hat{\boldsymbol{\Sigma}} \boldsymbol{z}_{\hat{j}}}$$

Example: Colorectal cancer

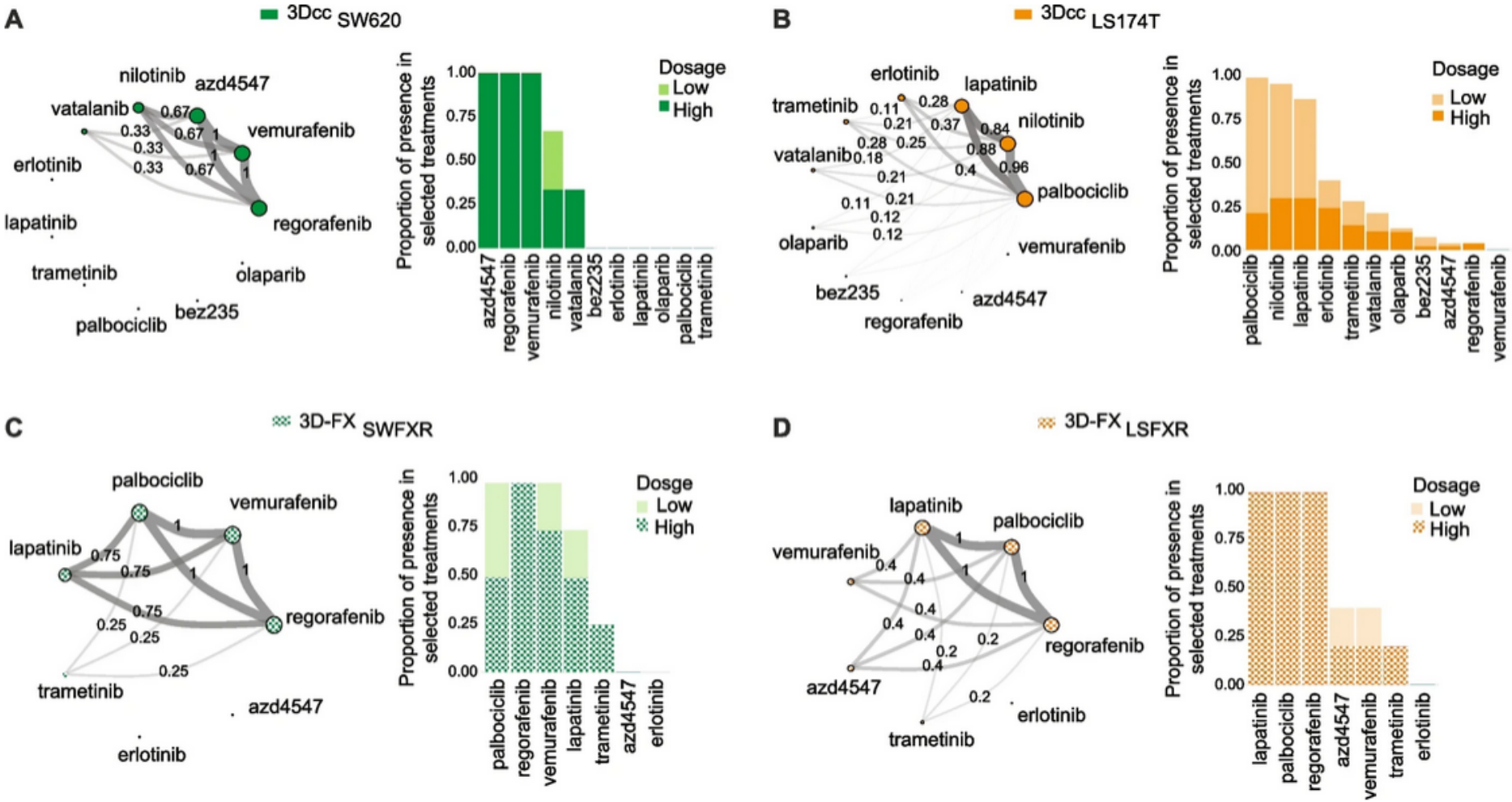


Adapted from Ramzy et al., Platform combining statistical modeling and patient-derived organoids to facilitate personalized treatment of colorectal carcinoma, Journal of Experimental & Clinical Cancer Research, 2023

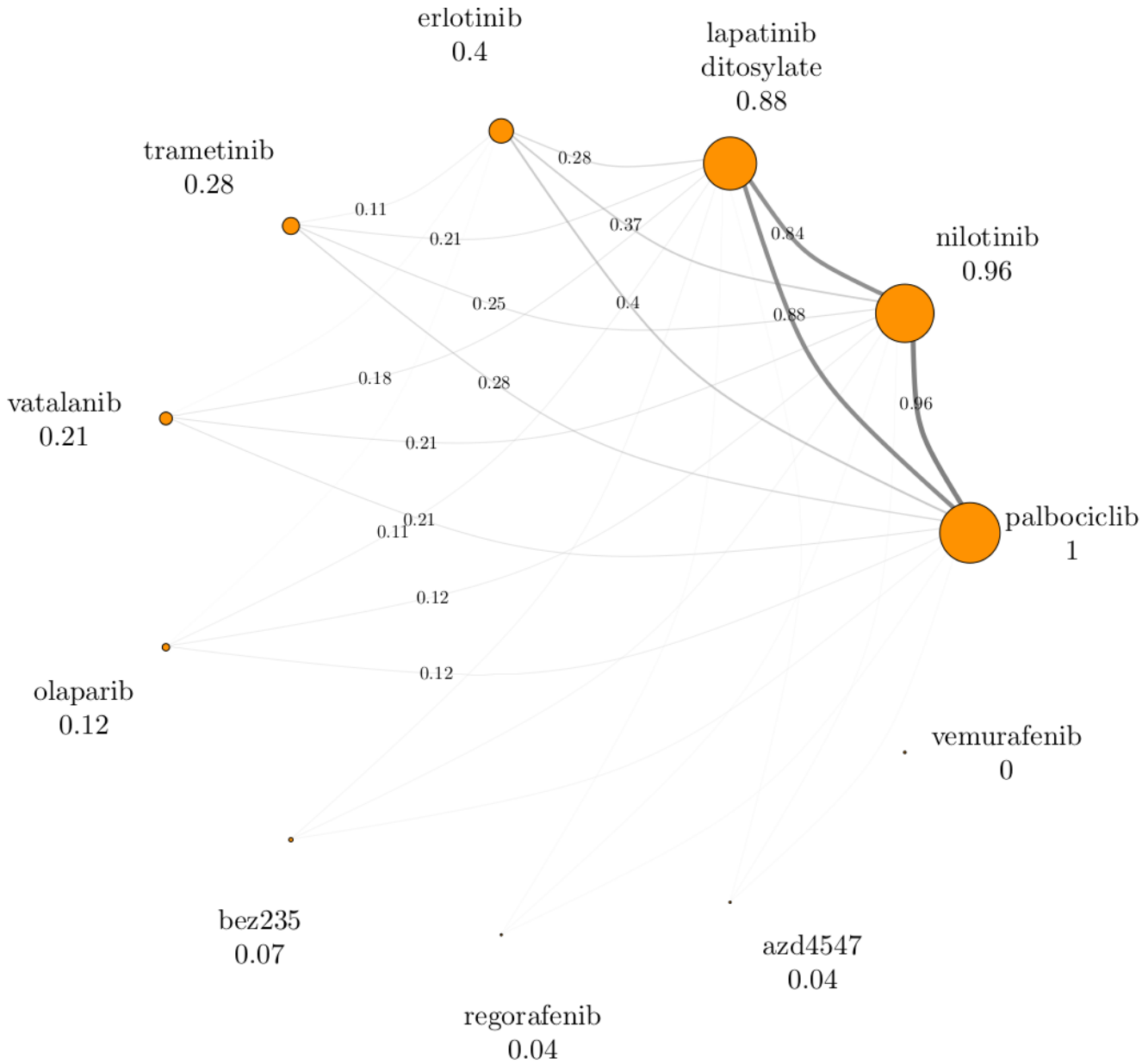
Example: Colorectal cancer

- Colorectal cancer is the third most diagnosed cancer worldwide with newly diagnosed cases exceeding one million per year.
- The effect of a given treatment (i.e., a combination of drugs) is measured by its therapeutic window defined as the difference between healthy cell viability and cancer cell viability.
- We aim to identify treatments with the largest therapeutic windows, i.e., the ones that are highly aggressive toward cancerous cells while having the minimum impact on healthy cells.
- To identify these treatments $\Longrightarrow$ adaptive Lasso approach with weights incorporating domain knowledge.

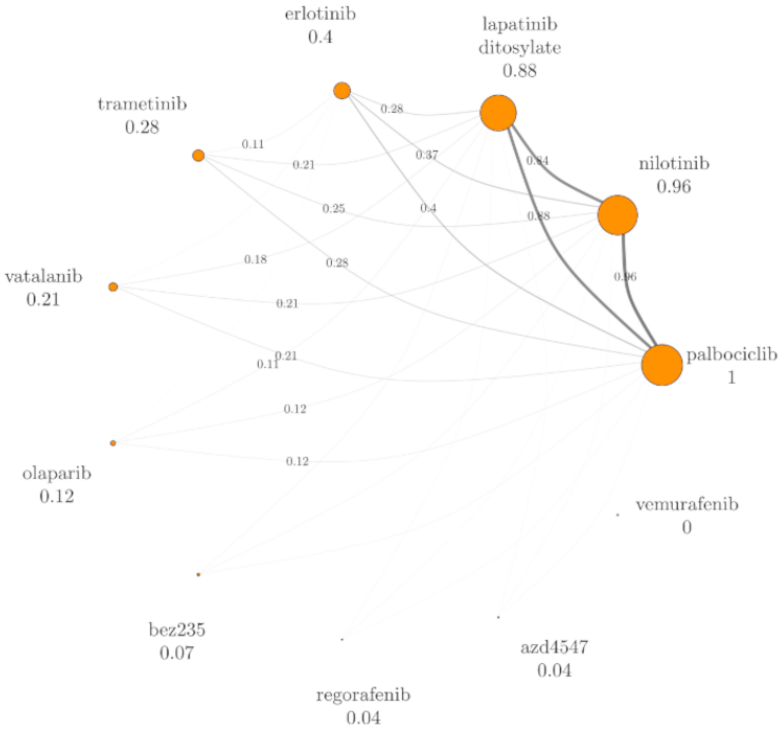
Example: Colorectal cancer

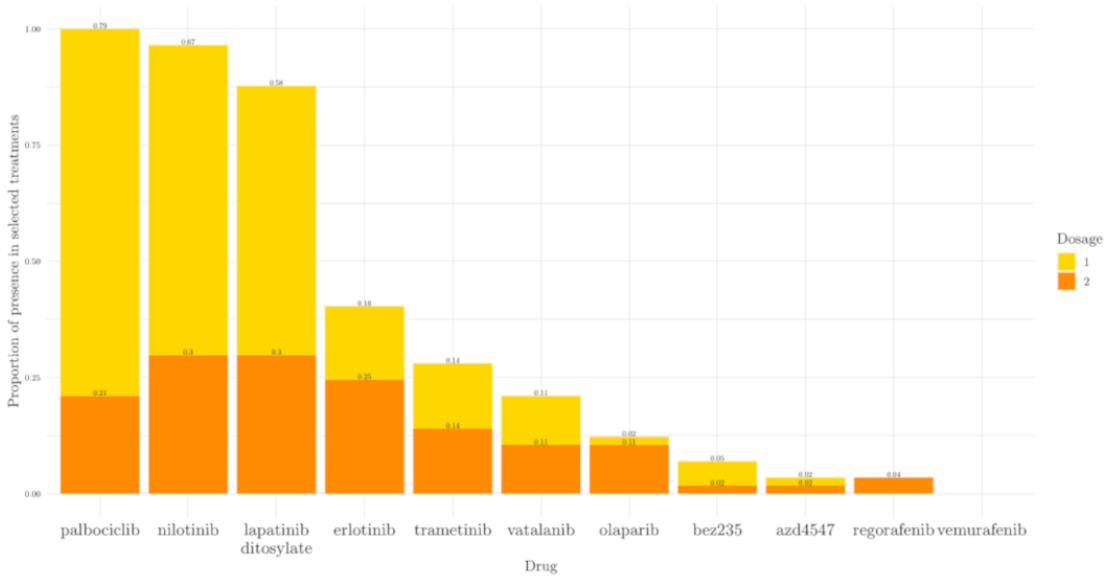


Example: Colorectal cancer



Example: Colorectal cancer





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Data Analytics
for Pharmaceutical Sciences

Chapter 1: A Brief Introduction to R and RMarkdown

Chapter 2: Introduction to Statistical Inference

Chapter 3: Analysis of Variance

`https://intro-data-analytics.netlify.app`

Introduction to Data Science
with R

Chapter 1: Data Structures

Learn to organize data in order to use it more efficiently.

Chapter 2: Control Structures

Understand how control structures dictate the flow of execution of a sequence of operations.

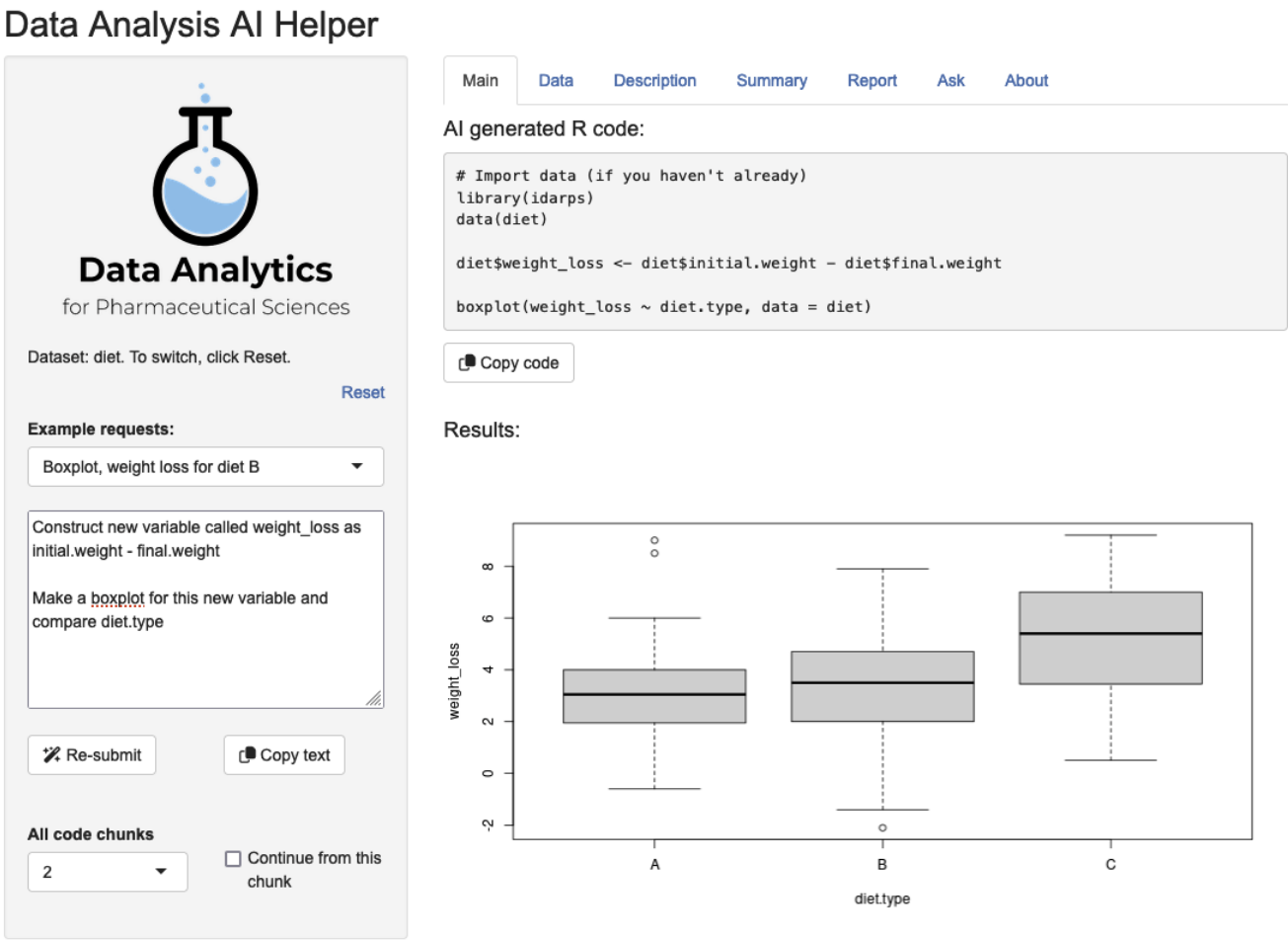
Chapter 3: Functions

Write your own functions.

`https://intro-to-ds.netlify.app/`

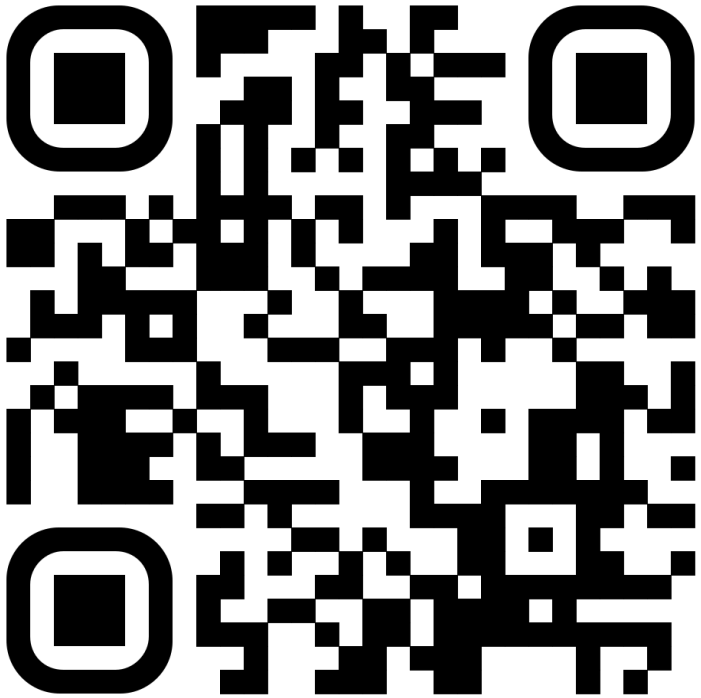
AI helper to simplify coding

In the future, many aspects of data analytics will become more streamlined due to the advances in AI (e.g., natural language processing tools). Building on these new development, we created a web application which allows to generate R code:



https://data-analytics-lab.shinyapps.io/ai-helper-pharma

Thank you very much for your attention!



https://github.com/lionelvoirol/stat_modelling_drug_combination

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