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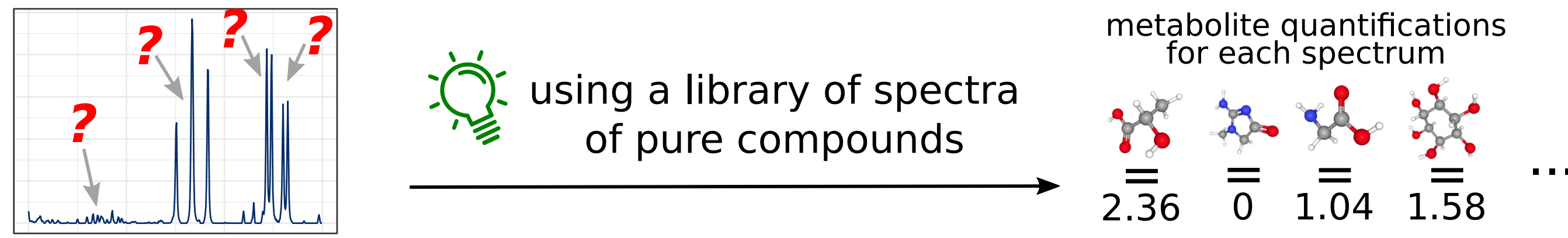


# Joint automatic metabolite identification and quantification of a set of $^1\text{H}$ NMR spectra

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## From NMR spectra to metabolite quantifications

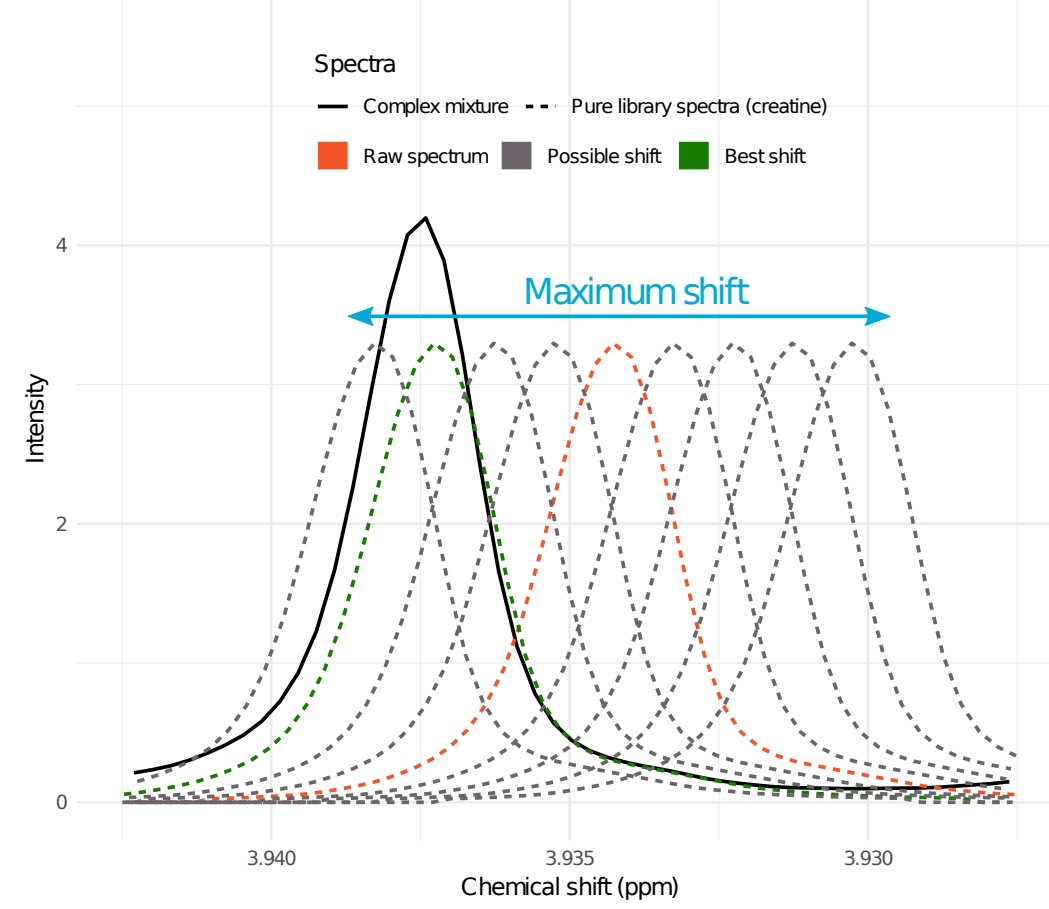


## Main features

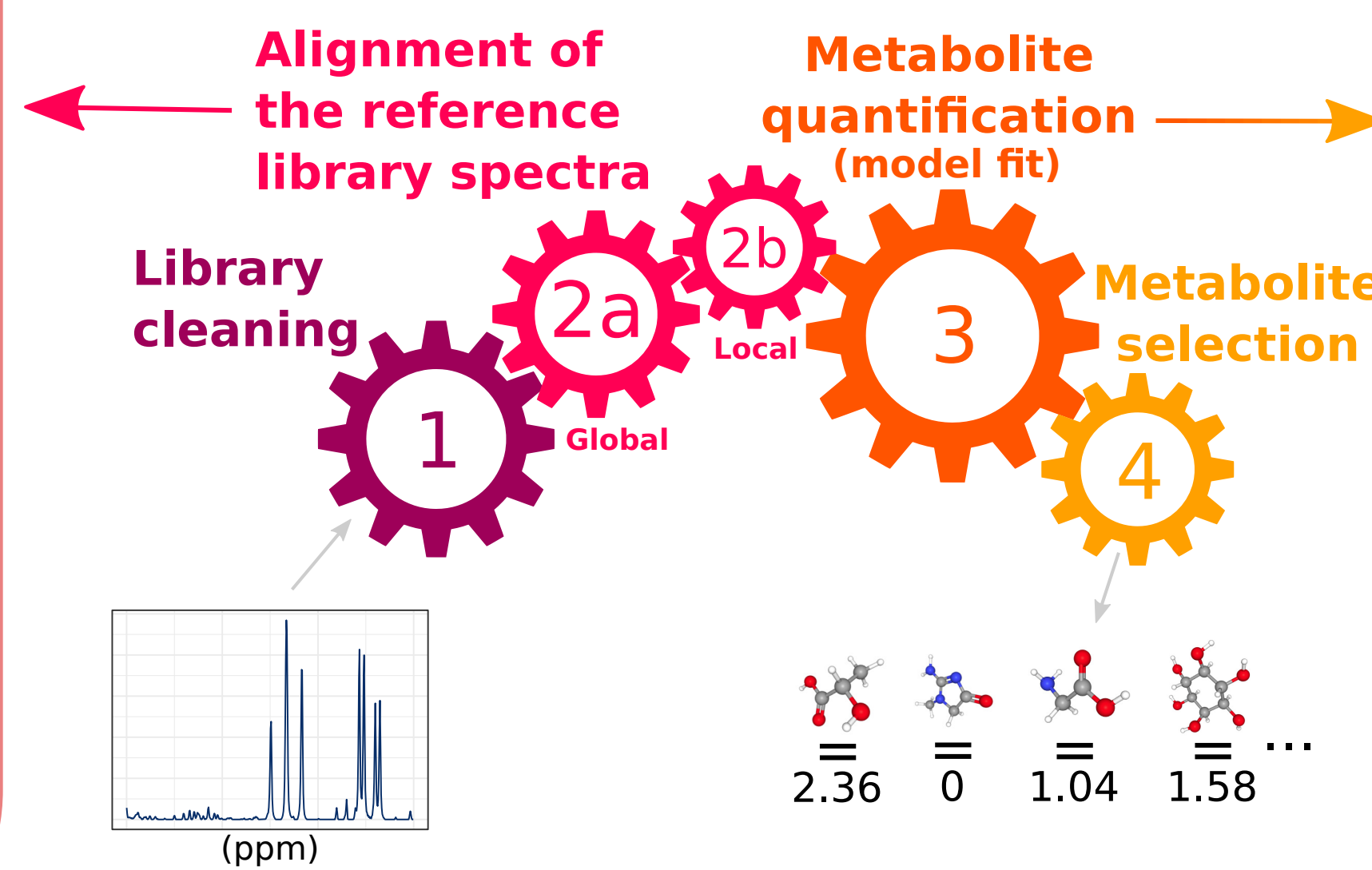
- Joint alignment of pure library spectra by using all complex mixtures together
- Joint quantification and identification of metabolites using multi-response model with a group-Lasso penalty

## Independent vs. joint alignment and quantification

**ASICS v1 [1]**  
**Independent**  
Optimization of the FFT cross-correlation [2] between all possible shifted pure spectra and complex mixture with a common **maximum shift** for all pure spectra



### Quantification workflow



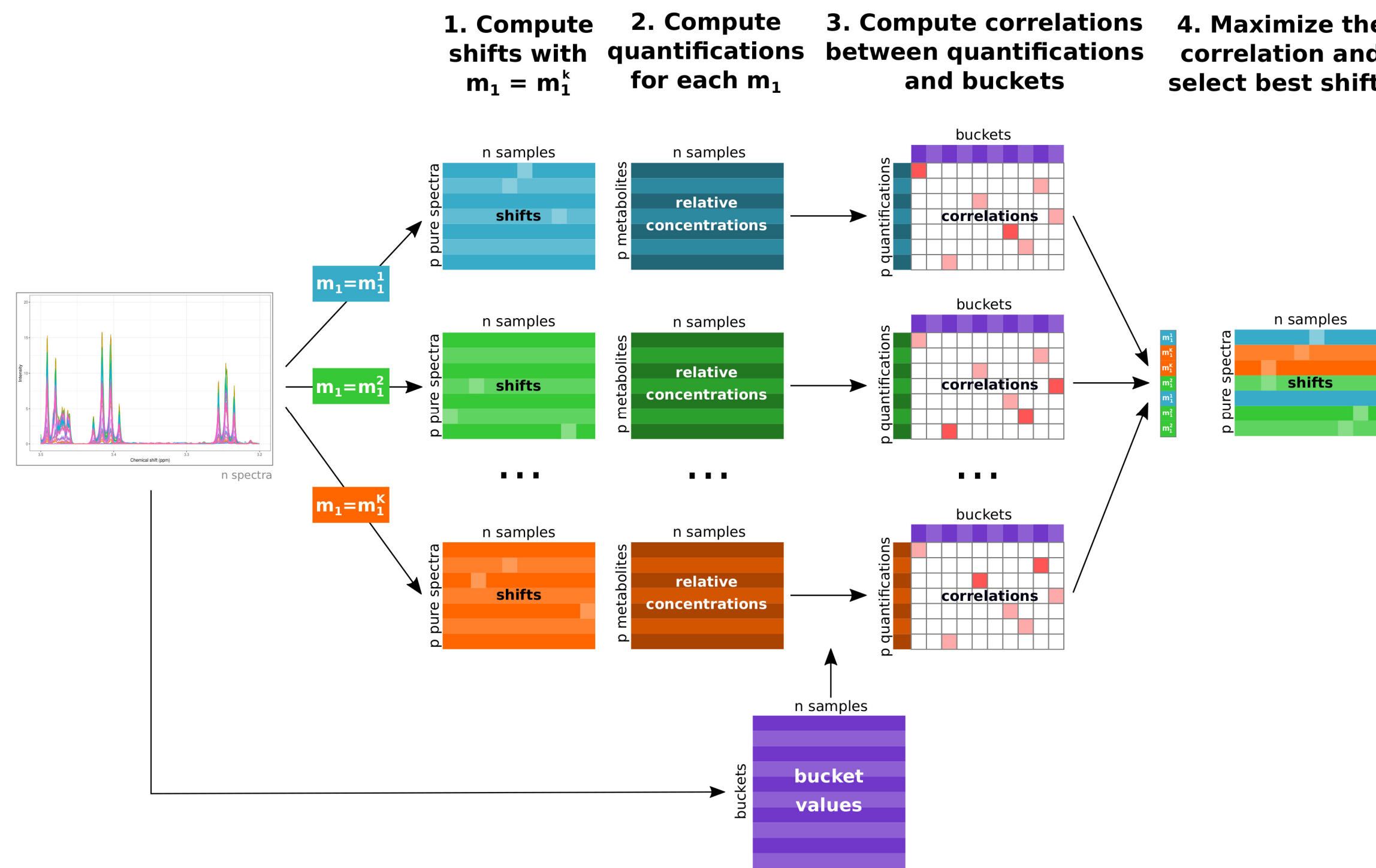
**ASICS v1 [1]**  
**Independent**  
Estimation of metabolite quantifications using linear combination of pure spectra followed by metabolite selection procedure based on FWER [3]

$$f(t) = \sum_{j=1}^p \beta_j g_j(t) + \epsilon(t) \quad \text{with } \beta_j \geq 0$$

Complex mixture    Pure spectra

Metabolite quantifications

**Joint**  
Optimization of the **maximum shift** for each pure spectrum using all complex mixtures



**Joint**  
Joint quantification of metabolites using a multi-response model [4] with a group-Lasso penalty [5]

$$\arg \min_{\beta \in \mathbb{R}^{p \times n}} \left\{ \frac{1}{2} \|F - rG\beta^T\|_F^2 + \lambda \sum_{j=1}^p \|\beta_j\|_2 \right\}, \quad \text{st } \beta_{ji} \geq 0$$

All complex mixtures    Pure spectra

Metabolite quantifications of all complex mixtures    Group-Lasso penalty

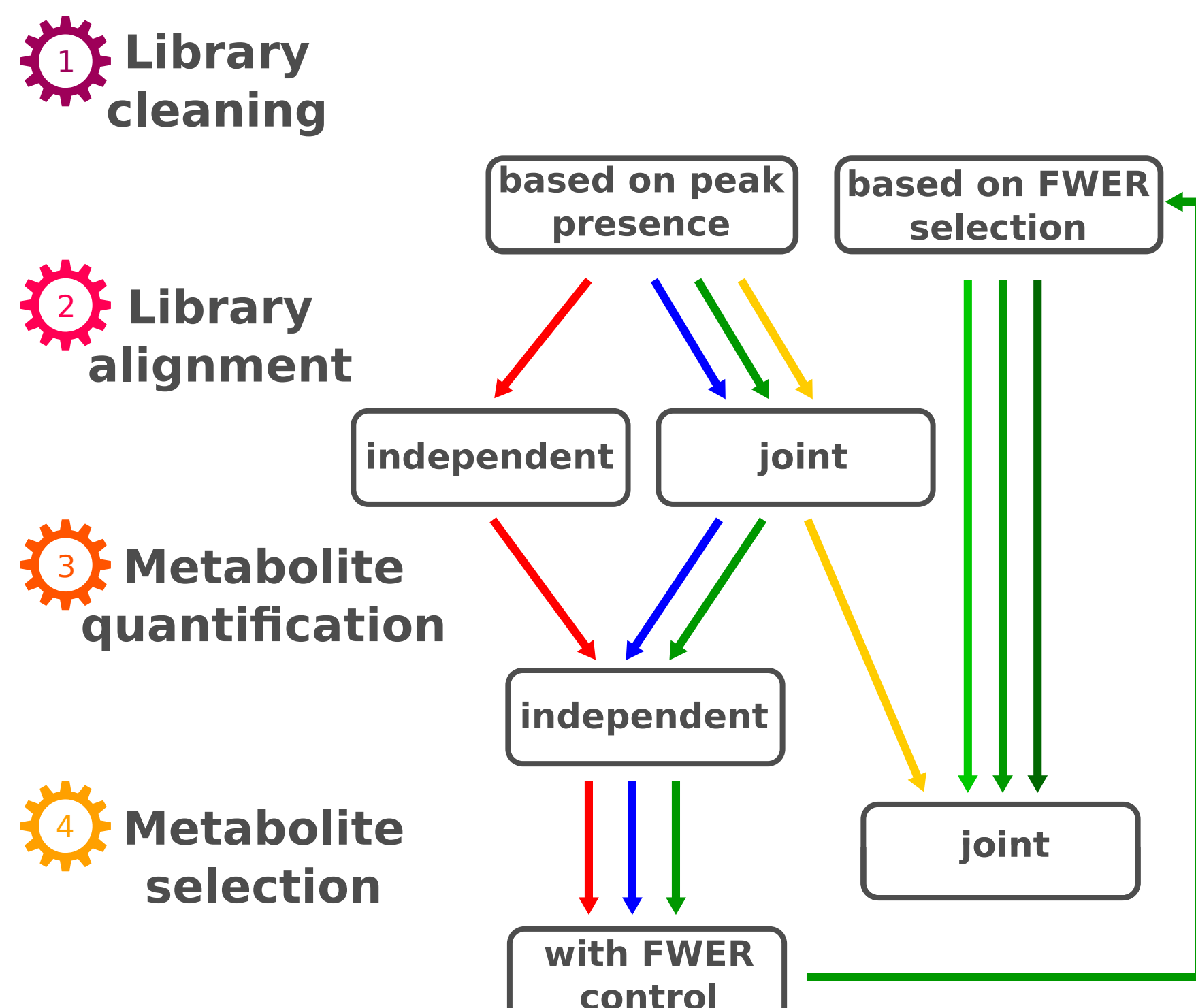
- [1] Lefort, G. et al. (2019). ASICS: an R package for a whole analysis workflow of 1D  $^1\text{H}$  NMR spectra. *Bioinformatics*, **35**, 4356–4363.
- [2] Wong, J. et al. (2005). Application of fast Fourier transform cross-correlation for the alignment of large chromatographic and spectral datasets. *Analytical Chemistry*, **77**, 5655–5661.
- [3] Tardivel, P. et al. (2017). Représentation parcimonieuse et procédures de tests multiples : application à la métabolomique. *PhD thesis*, Université Toulouse 3 Paul Sabatier.
- [4] Friedman, J. H. et al. (2010). Regularization paths for generalized linear models via coordinate descent. *Journal of Statistical Software*, **33**.
- [5] Yuan, M. and Lin, Y. (2006). Model selection and estimation in regression with grouped variables. *Journal of the Royal Statistical Society*, **68**, 49–67.

## Evaluation of the new algorithm

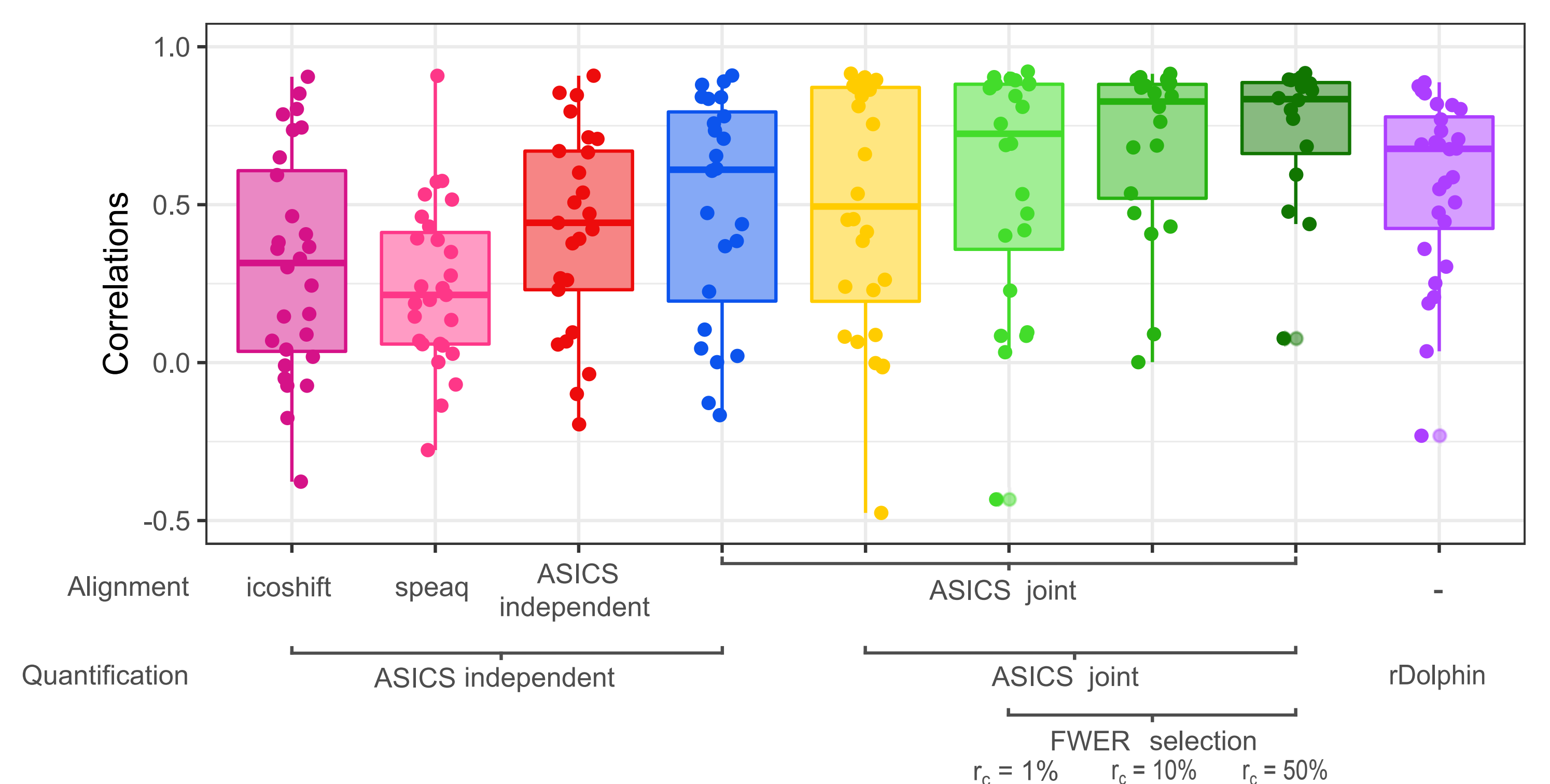
**Data** 97 samples of newborn piglet plasma on which NMR spectra and amino acid UPLC dosages were obtained

**Other tested methods** icoshift [1] and speaq [2] for alignment and rDolphin [3] for quantification

**ASICS** Different scenarios tested with ASICS are represented in the figure below



## Quantification/UPLC dosage correlations



**Figure 1.** Correlations between metabolite quantifications from NMR spectra and UPLC dosages obtained on same samples shown that **ASICS joint alignment** is better than other alignments and **ASICS joint quantification** is better than other methods if it was used with a FWER procedure for metabolite selection ( $r_c \geq 10\%$ ).

## Conclusions

- Better results with joined alignment and quantifications
- Available in R **ASICS** (<https://bioconductor.org/packages/ASICS/>)

## Acknowledgements



- [1] Savorani, F. et al. (2010). icoshift: a versatile tool for the rapid alignment of 1D NMR spectra. *Journal of Magnetic Resonance*, **202**, 190–202.
- [2] Beirnaert, C. et al. (2018). speaq 2.0: a complete workflow for high-throughput 1D NMR spectra processing and quantification. *PLoS Computational Biology*, **14**, e1006018.
- [3] Canueto, D. et al. (2018). rDolphin: a GUI R package for proficient automatic profiling of 1D  $^1\text{H}$ -NMR spectra of study datasets. *Metabolomics*, **14**, 24.