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CAST Chemometrics and Advanced Separations Team

AUTOMATION AND CHALLENGES IN ONE- AND -DIMENSIONAL LIQUID CHROMATOGRAPHY METHOD DEVELOPMENT: WHAT IS OPTIMAL?

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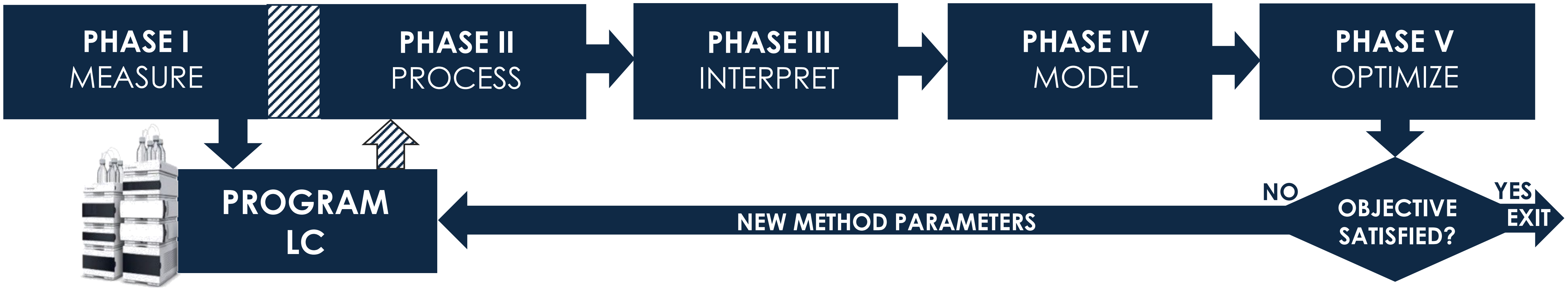
Monday, February 3rd, Luik

The Multidimensional Chromatography (MDC) Workshop

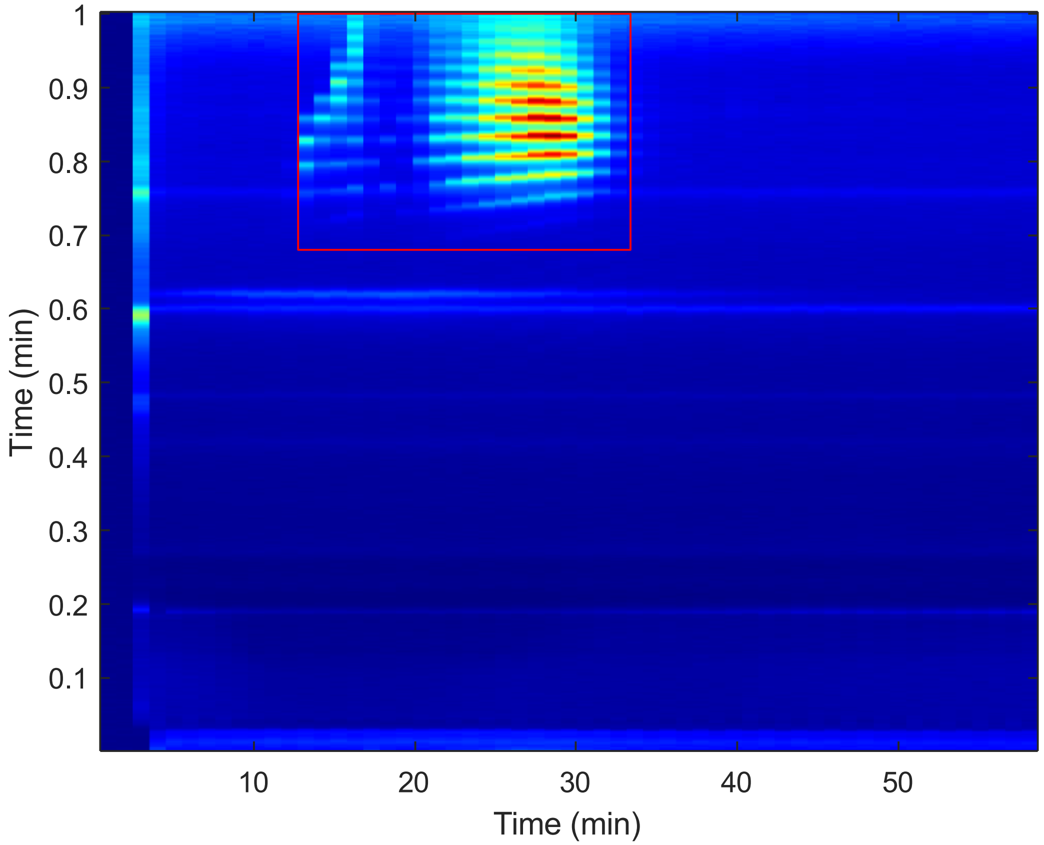
Automation of liquid chromatography

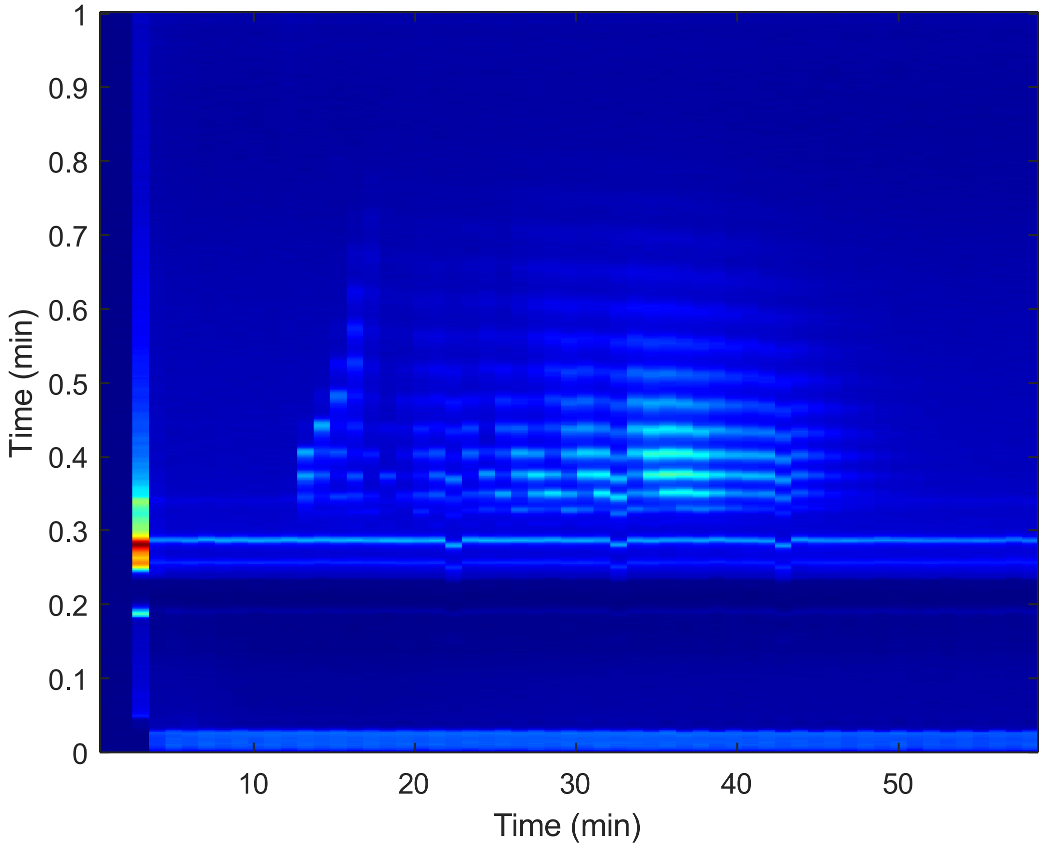
UPSTAIRS project: Unleashing the Potential of Separation Technology to Achieve Innovation in Research and Society

- Automated method development workflows
- Peak tracking and describing chromatography
- Alternative strategies for selectivity screening



Automated gradient optimization

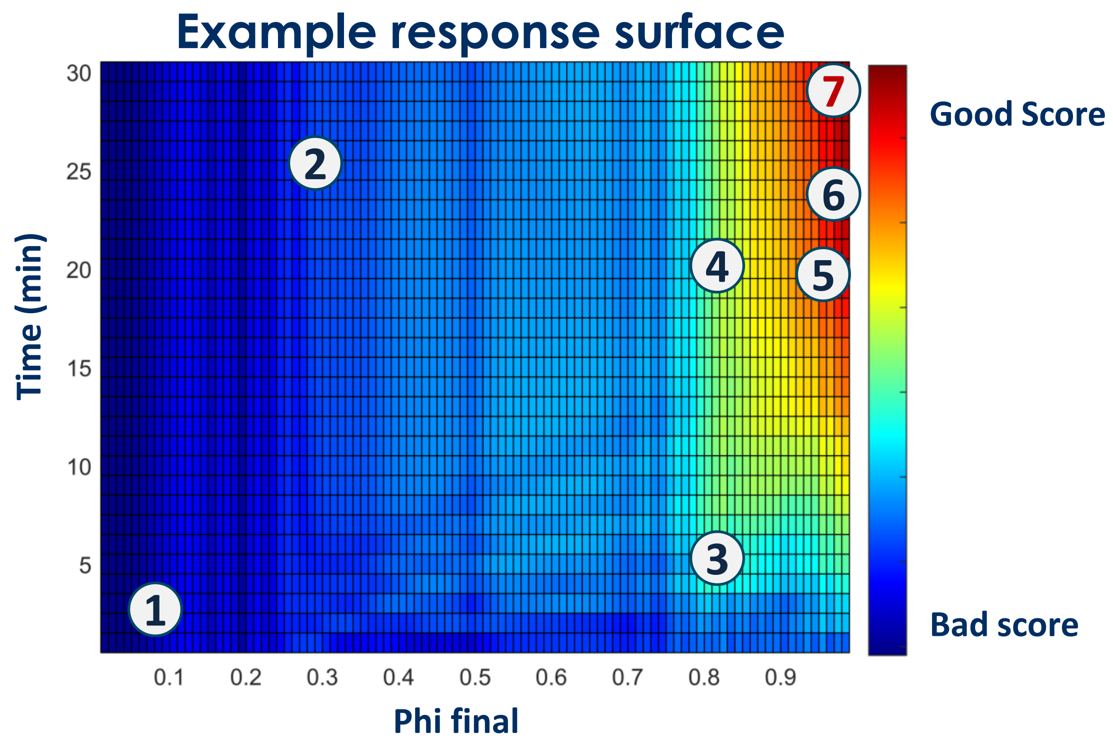




Tijmen Bos, Dwight Stoll, Bob Pirok, *in preparation*

What is an optimization algorithm

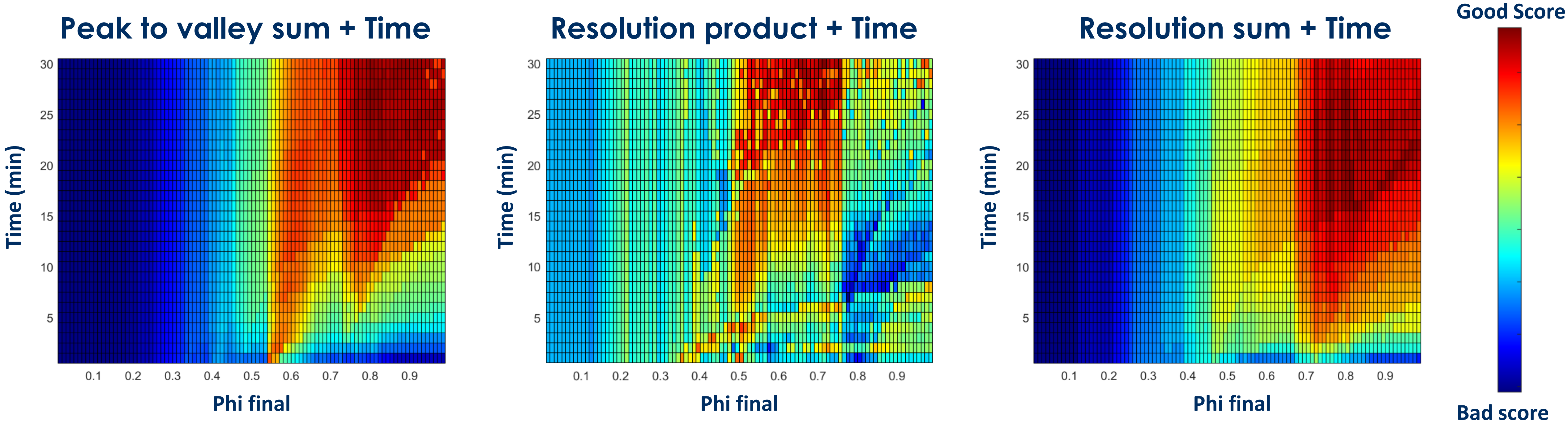
Optimization algorithms: Mathematical procedures used to find optimal solutions to complex problems. They do this by minimizing or maximizing some type of function.



Performance influence by:

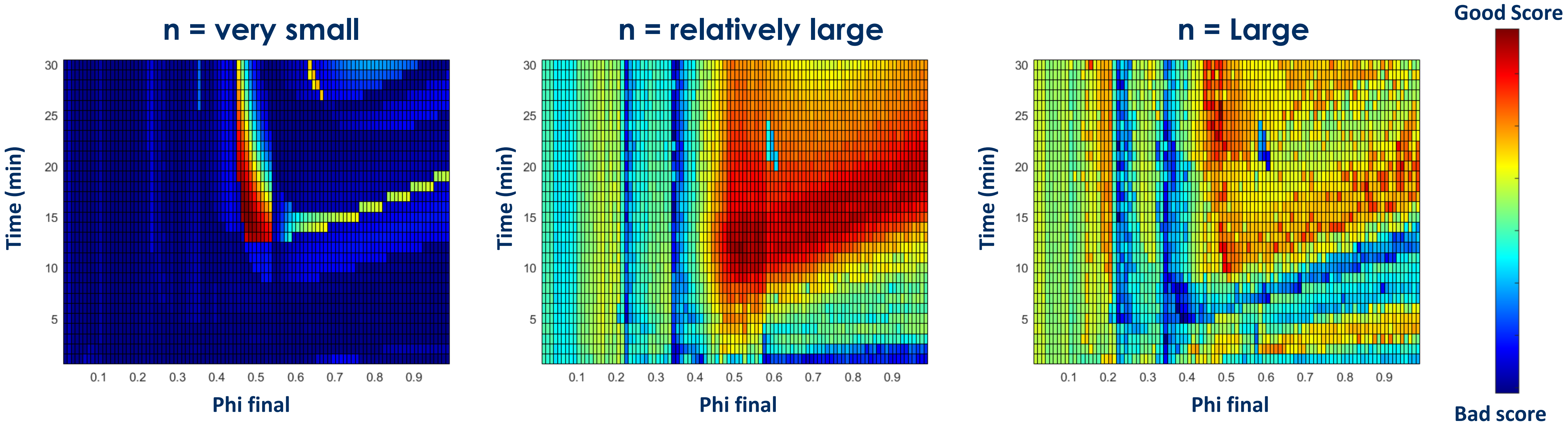
- **Optimization algorithm**
- **The starting point**
- **Complexity influences the result**

Same Sample, Different scoring functions



- The complexity is also influenced by the type of scoring
- The optimal method parameter may vary for each scoring function (CRF)

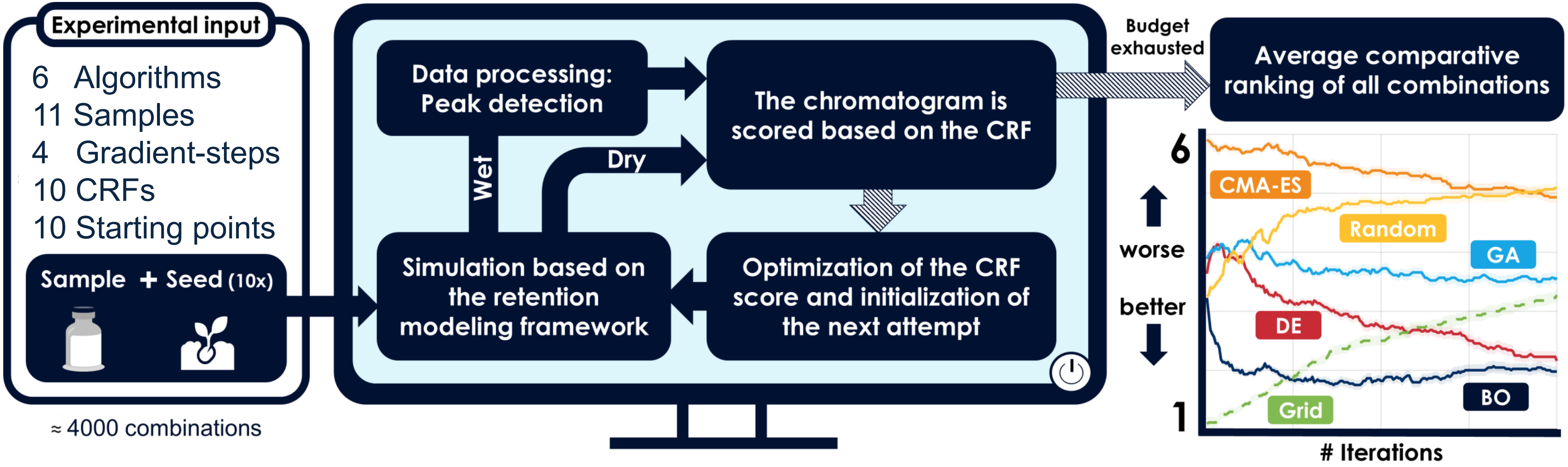
The scoring function (Chromatographic response function)



Influenced by:

- The number of compounds in the sample
- The type of sample

Schematic Workflow



Algorithms:

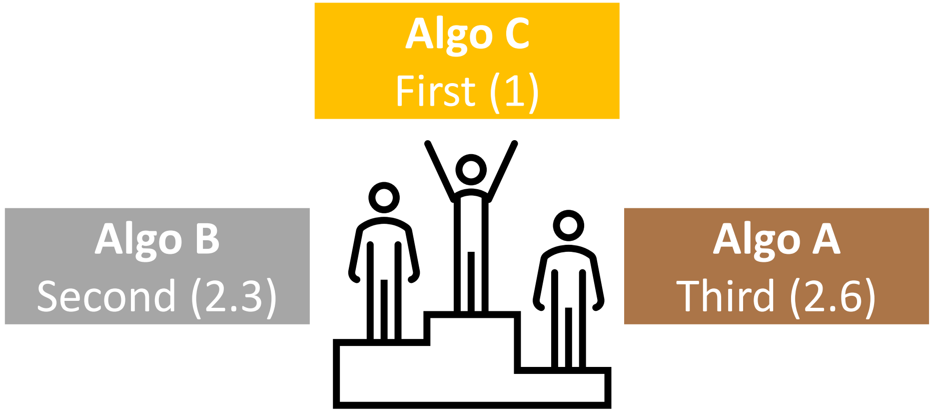
Bayesian optimization (BO)	Genetic algorithm (GA)	Differential evolution (DE)
Grid Search (Grid)	Random search (Random)	Covariance matrix assisted evolutionary strategy (CMA-ES)

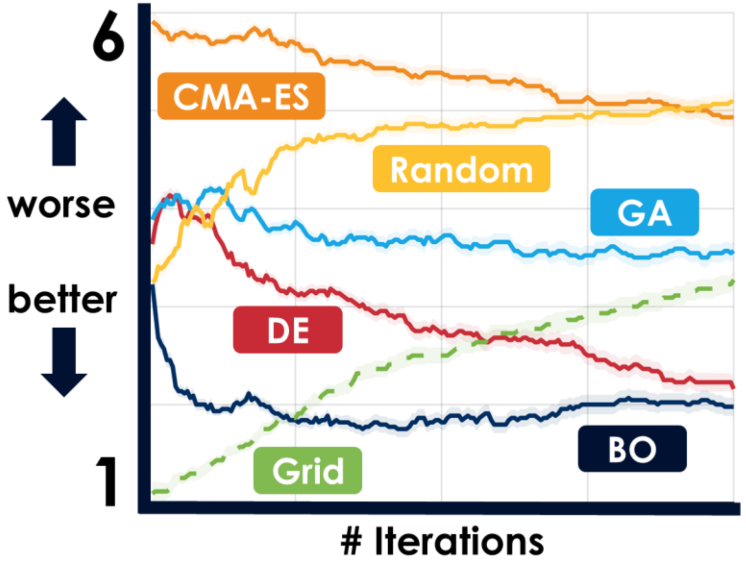
Visualization of the comparison

The benefit of the comparative ranking

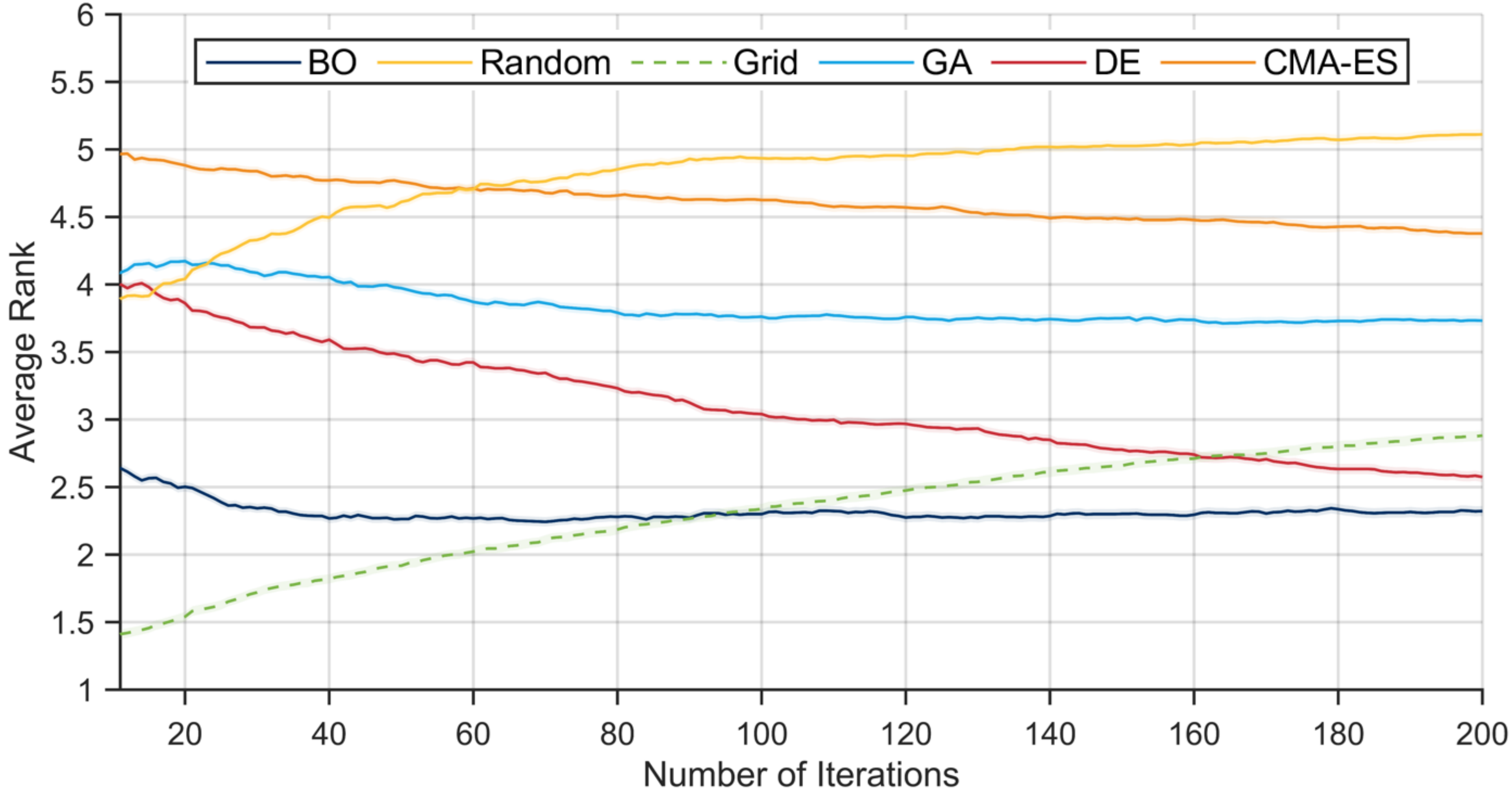
- It is easily interpretable which algorithm, on average, outperforms the other algorithms
- We do not need to know the quality of the score

Sample	X	Y	Z
Algorithm A:	3	2	3
Algorithm B:	2	3	2
Algorithm C:	1	1	1





AutoLC method development



Bayesian Optimization is well suited optimization with limited itterations

Van Henten, Boelrijk, Kattenberg, Bos, Ensing, Forré, Pirok, **2025**, Journal of chromatography A, 1742, 465626

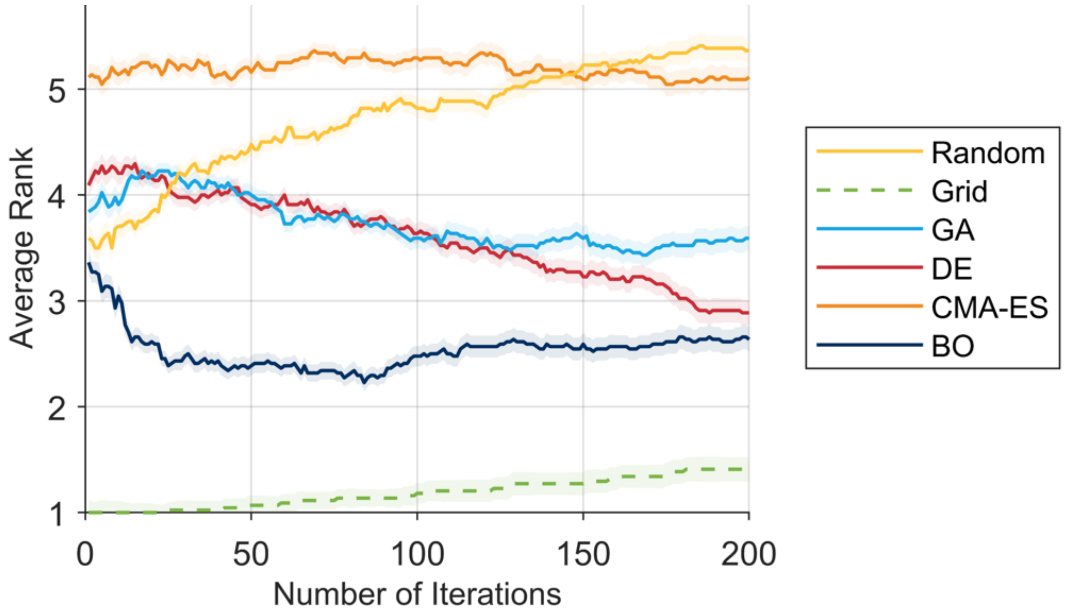
Challenge: defining a good CRF

The success or failure of the optimization process critically depends on the CRF

So, this means taking into account:
- the complexity of the CRF
  - Especially if n = high
- Composite Response Functions (combined CRFs)
- Arbitrary weighing and transformation

Product of resolution + Time penalty:

$$CRF = \prod_{i=1}^{n_{\mathrm{obs}-1}} \frac{R_{s,i}}{R_{s,\mathrm{req}}} \cdot \mathbf{1}(t_{R,i} < t_{\max})$$



Take-home message:

1. For automated gradient optimization workflows:
   - BO highly efficient for optimizing method with limited number of parameters

2. Keep the CRF simple and develop in tandem with optimization algorithms

COST REDUCTION

BETTER INFORMATION

IMPROVED SUSTAINABILITY

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