

BACHEM

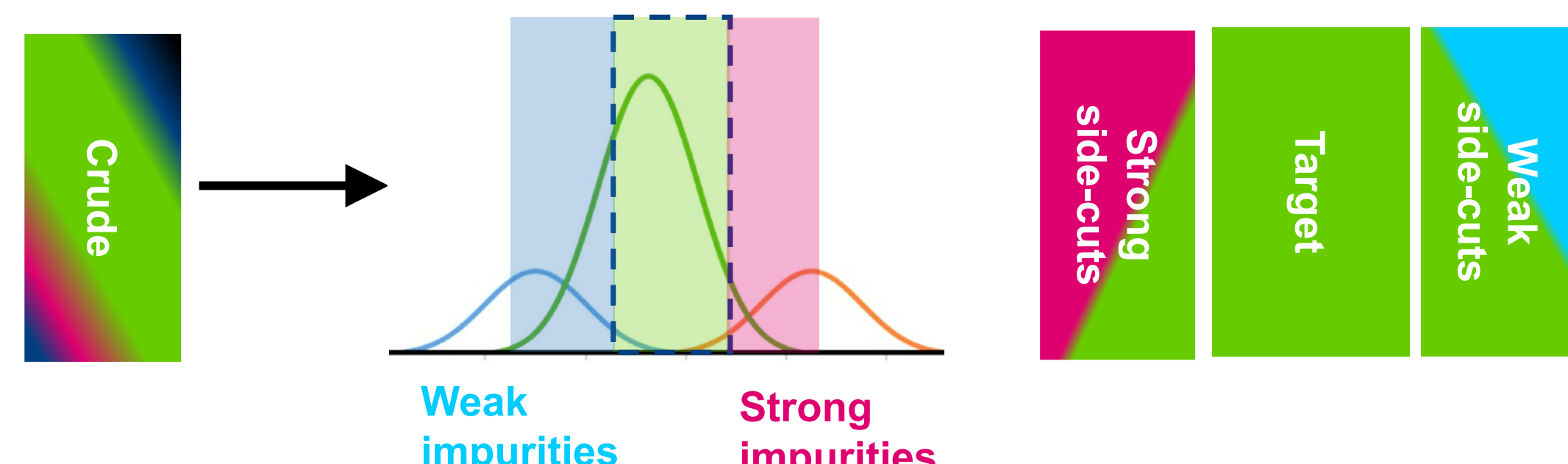
CONTINUOUS CHROMATOGRAPHY OF OLIGONUCLEOTIDES AND PEPTIDES

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For the oligonucleotide as well as the peptide field, a trend to larger batch sizes and higher purity requirements is clearly observable. Combined with a strong focus on sustainability, there is pressure on the industry to significantly optimize the labor and material intense purification stages. In 2017, Bachem identified MCSGP as a potentially disruptive technology that will allow the industry to overcome these challenges. In 2022, Bachem started operating the first two large-scale MCSGP systems in the industry and is ready to tackle the challenges together with our customers.

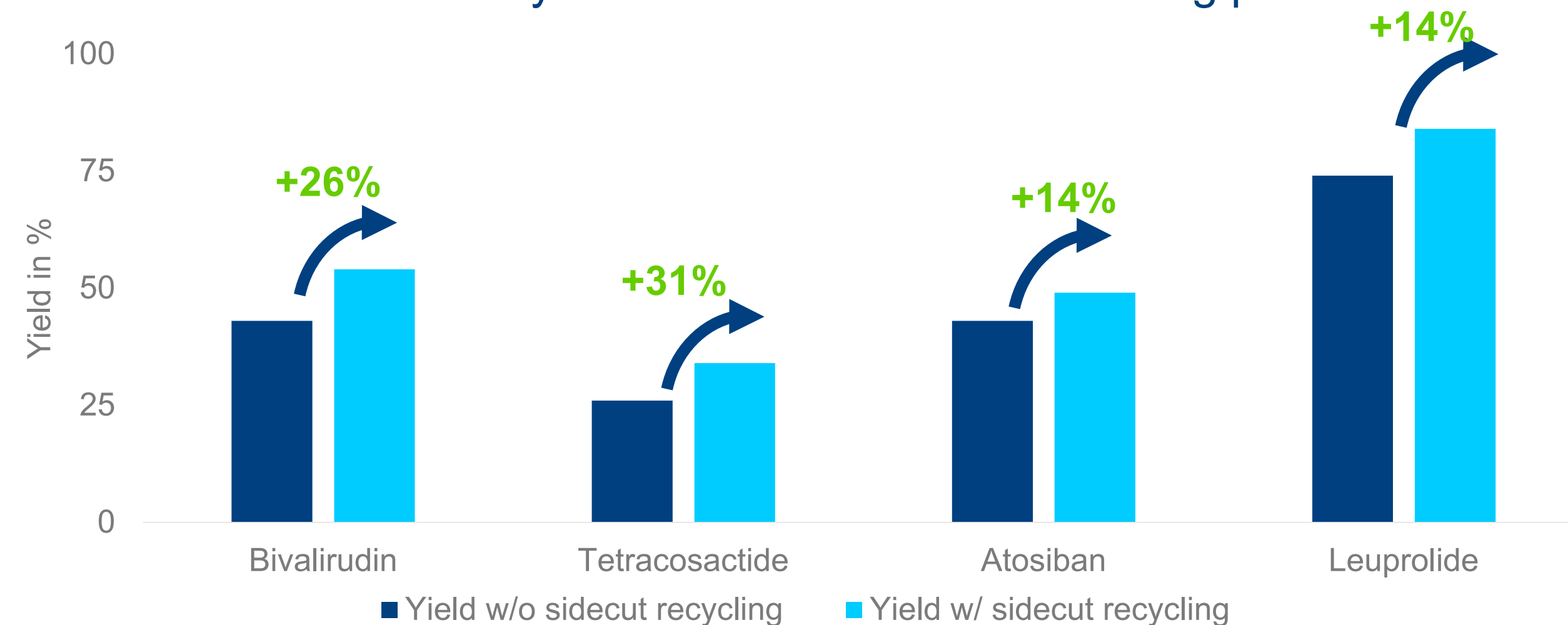
Purification of large molecules - Side cut recycling as the key to yield

- The purification of oligonucleotides and peptides is performed batch wise.
- Application of a displacer gradient allows efficient separation of the target compound from the related substances generated during synthesis and cleavage.



- Material meeting the purity criteria is processed further in the subsequent manufacturing stage.
- Material not meeting the target purity due to the presence of impurities is stored and re-purified using the same chromatographic systems.

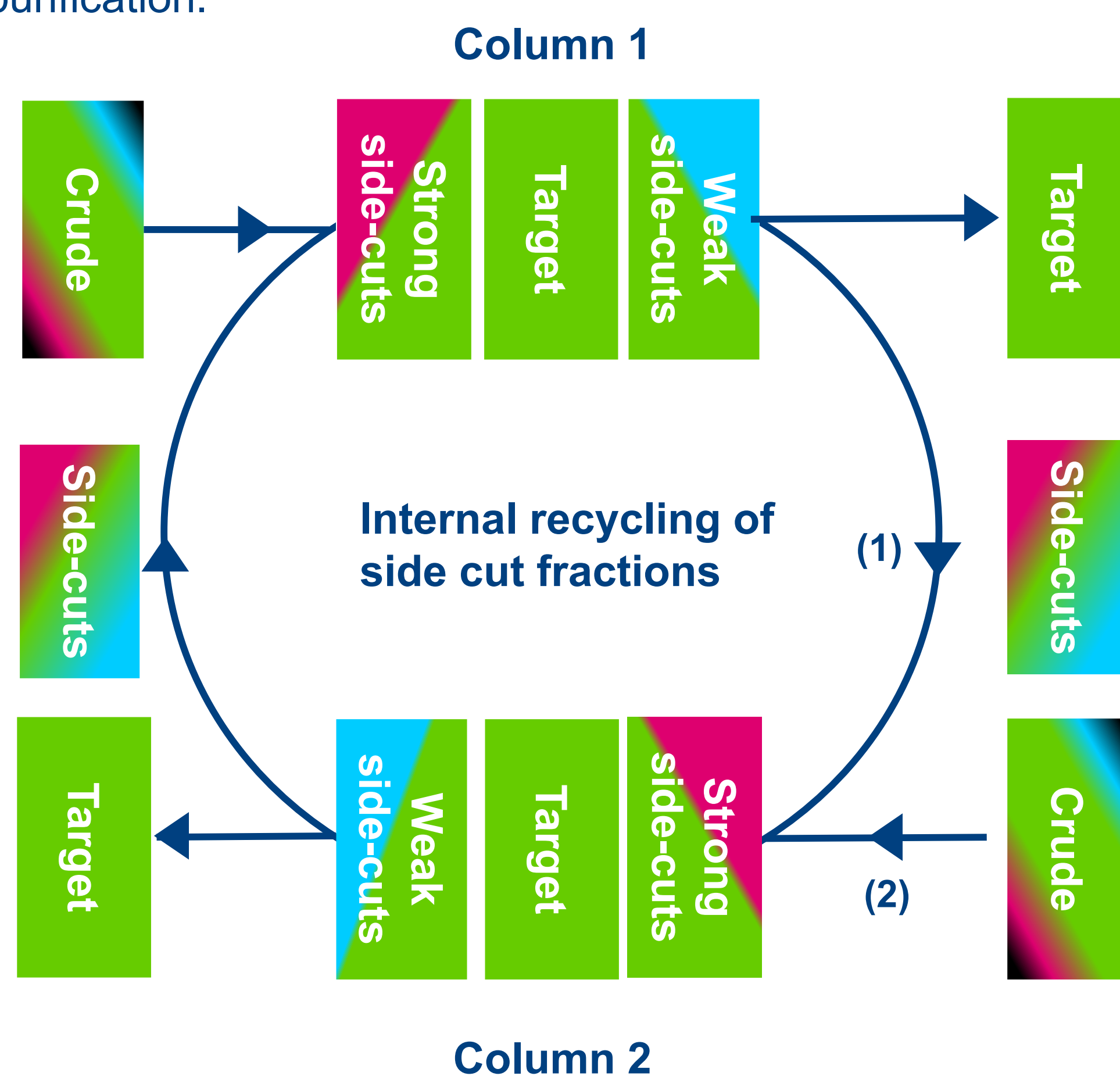
- Side-cut re-purification is standard operating practice in the peptide field and crucial for the overall yield of the overall manufacturing process.



- The re-processing gets complicated on large scales due to the volumes to be handled and the required infrastructure for storage of the side-cut fractions.

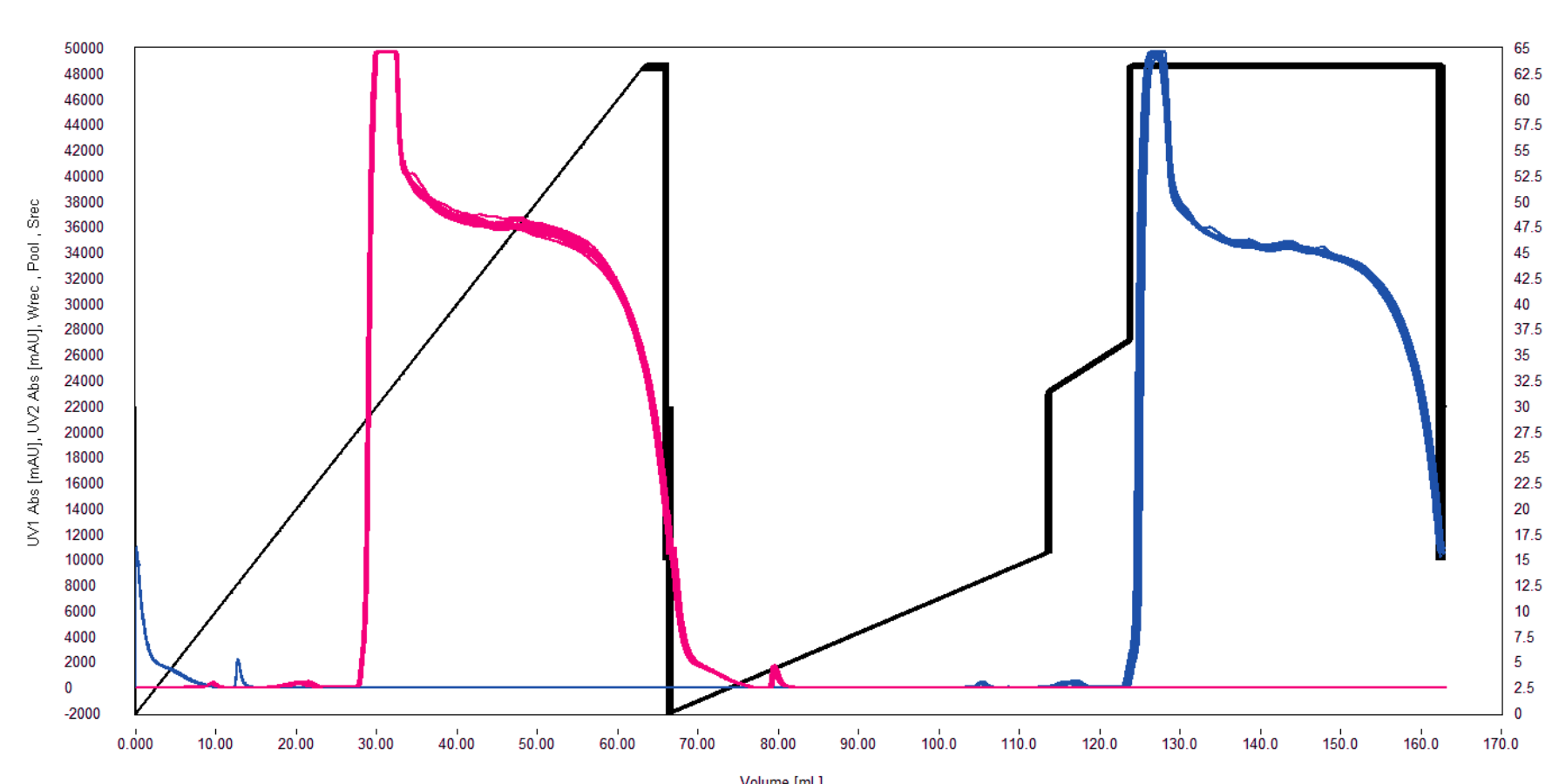
MCSGP –Fully automated recycling of side cuts

- Instead of separately collecting the side-cut fractions for further processing, they are directly used in the next purification (1).
- Addition of crude product to the side-cuts (2) allows an even more efficient re-purification.



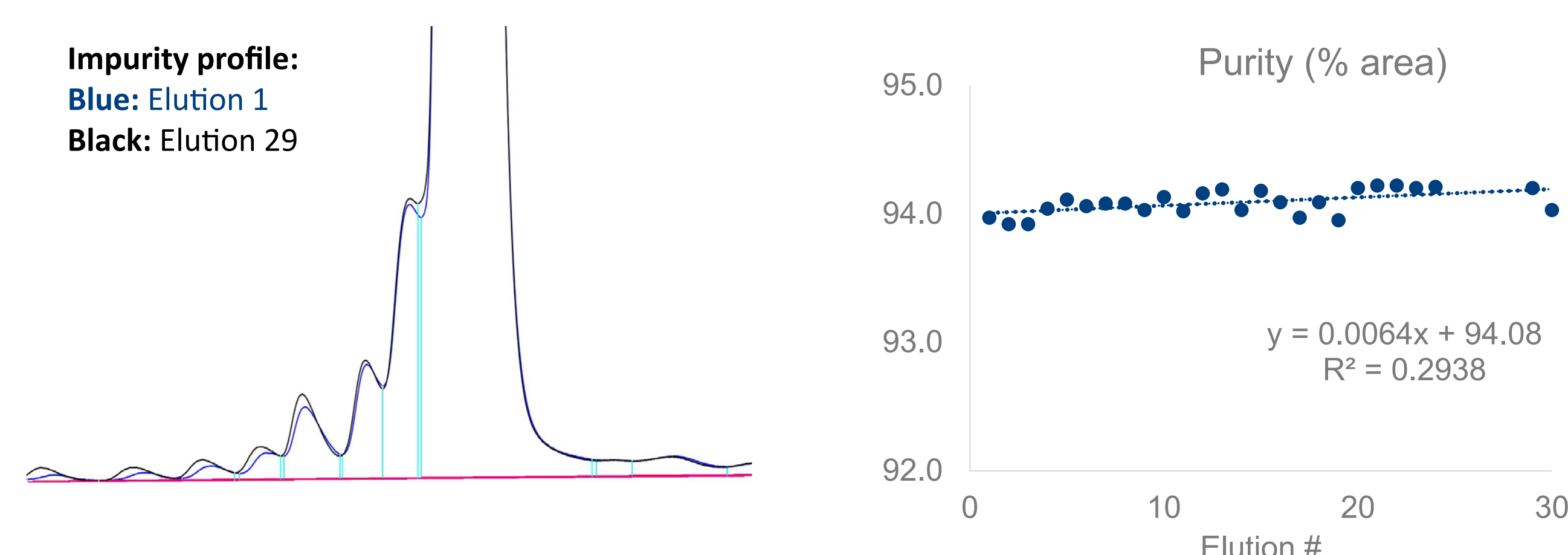
- On every scale, the process is fully automated and no manual operations are necessary.

- After a certain number of repetitions of this process, usually four to six injections, the system will be in equilibrium:



30 elutions of an oligonucleotide in AEX chromatography (15 on each column)

- For each elution, the process will generate product having the same quality:



- The yield will be at least the same as a batch process with optimized side-cuts repurification; with significantly decreased cost of goods.

Development and manufacturing capabilities

- Two Contichrom Cube systems for process development on 1 to 5 cm columns.
- In-house capabilities to pack columns of all sizes
- Capability to manufacture design batches up to 100 g.



Manufacturing capabilities

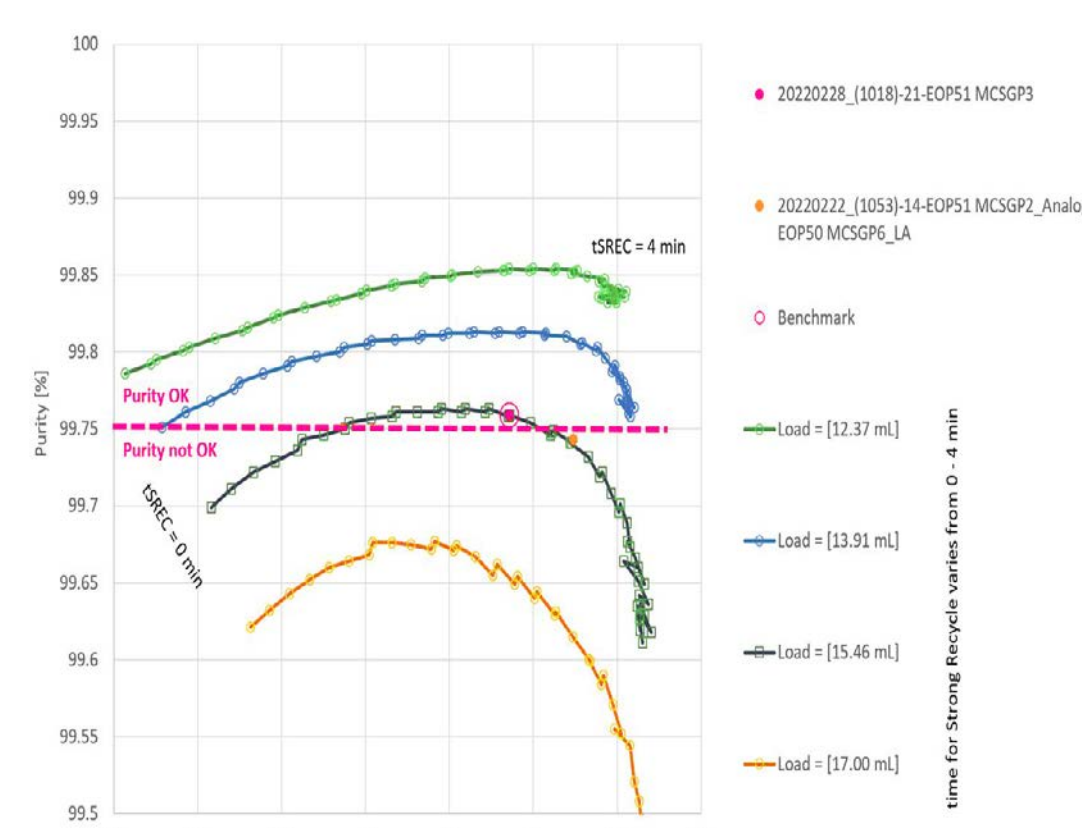
- Two large-scale TWIN systems with 20 and 30 cm columns with a throughput of up to 2 tons of API per year.
- The systems are upgradable to 45 cm columns for even higher outputs.
- Several additional systems with even larger columns in the design stage.



Supported by digital twins

The purification processes can be supported by digital twins to:

- Perform in-silico optimization of throughput and yield.
- Classify process parameters for failure mode and effect analysis.
- Generate deep understanding of the robustness of the process.



Summary

- After thorough evaluation, Bachem came to the conclusion that MCSGP is a disruptive technology for the purification of oligonucleotides and peptides.
- Bachem invested significantly in the technology and installed the worldwide first manufacturing scale systems at its Bubendorf site.
- Developmental capabilities are in place for the transfer products from batch to continuous mode; to tackle the cost of goods and sustainability challenges for large volume drugs.