



# Development of a semi-automated magnetic bead purification platform for milligram-scale protein production

Contributors:

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## 1 Introduction to magnetic bead protein purifications and the MagWash® system

The growing demand for purified proteins at various scales to support research, diagnostics, and therapeutics highlights the need for efficient and scalable purification workflows. Magnetic bead-based purification has gained widespread interest due to key advantages it offers over traditional methods, such as ease of liquid handling, scalability, and versatility. Efforts have been increasingly focused on integrating magnetic bead-based purification into automated and semi-automated systems to streamline laboratory workflows and enhance efficiency.

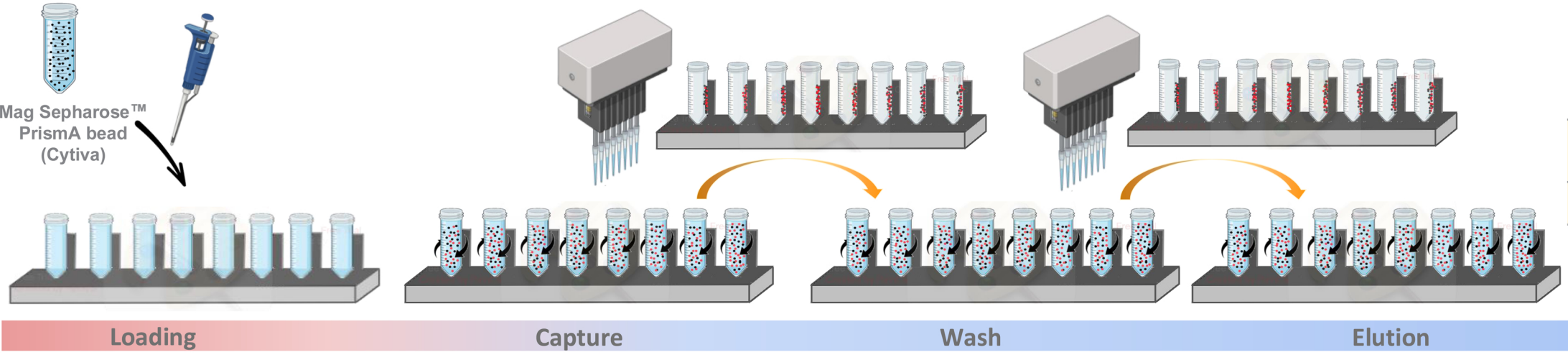
In this study, we introduce a semi-automated magnetic bead purification platform that integrates the MagWash® module, designed by V&P Scientific, with a Tecan liquid handler. This innovative platform is optimized to simplify the purification process for milligram-scale material generation. By leveraging advanced automation tools, the system minimizes manual intervention while ensuring consistent, high-quality protein yields. With the capability to process multiple samples in parallel, it provides a scalable and reproducible solution for high-demand protein purification applications.



**MagWash® Module for 8 Positions**

The MagWash system employs a pulsed radial flow methodology<sup>1</sup> to gently and uniformly mix magnetic beads with supernatants. When the flow is halted, the magnetic beads adhere to the magnetic rods positioned along one side of the module, enabling efficient liquid transfer while maintaining bead integrity.

## 2 Overview of the semi-automated purification workflow with MagWash®



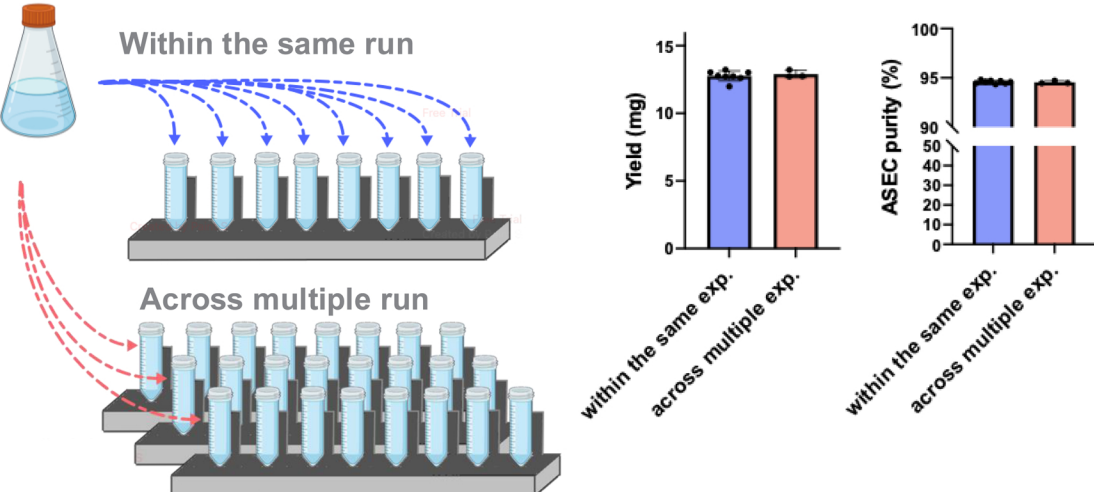
**Time required to process 8 samples in parallel**

|         | Total processing time (min) | Total hands-on time (min) |
|---------|-----------------------------|---------------------------|
| MagWash | 45                          | 5                         |
| Manual  | 30                          | 30                        |

The MagWash system is integrated with the Tecan liquid handler, which manages both the On/Off spinning commands and the liquid transfer steps. The only manual step in the process is loading the magnetic bead mixture into the tubes containing the HCCF (harvested cell culture fluid).

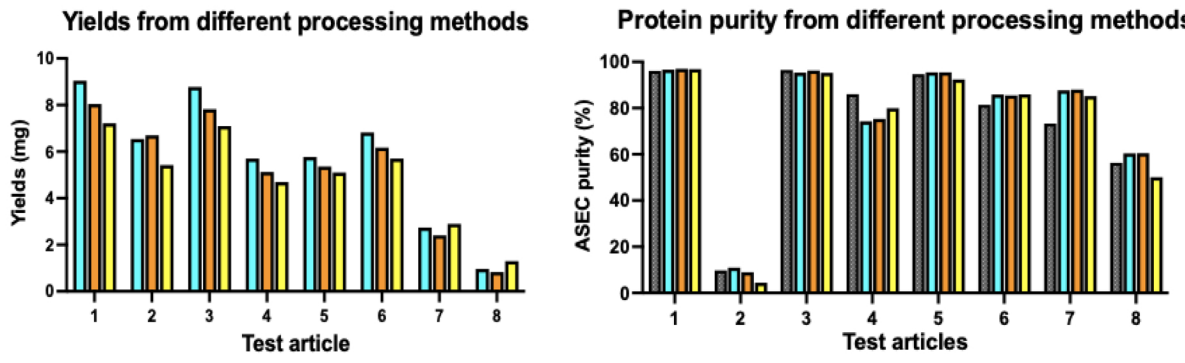
## 3 Evaluation of the MagWash® system

### I. Reproducibility



The experiment's results indicated that purifications are consistent among all 8 positions and demonstrate reproducibility across multiple purification runs.

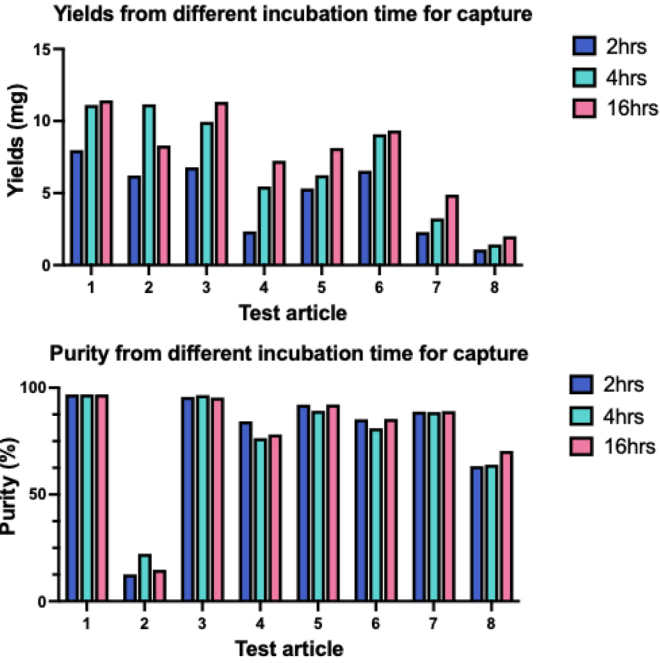
### II. Comparison between MagWash® process and manual processes across multiple proteins modalities



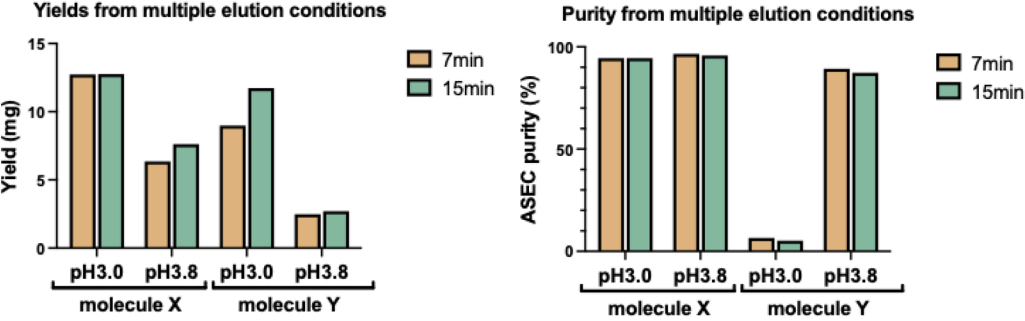
8 proteins of different modalities were purified using three different processes and compared with AKTA purification. The consistent yields and purities observed across these molecules highlight the effectiveness of the MagWash system, not only for purification but also for achieving uniform mixing of magnetic beads during the capture step. This streamlines the workflow and removes the need for manual handling during the purification process.

## 4 Optimization of the MagWash® purification process

### A. Impact of capture time on yields and purity



### B. Impact of Elution pH and time on yields and purity

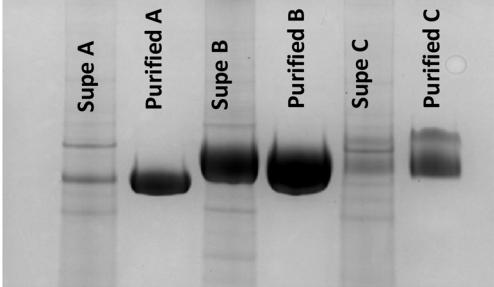


A. Capture steps of 2h, 4h, and overnight were evaluated, showing recovery plateaued between 4 hours and overnight. Purity was unaffected by the capture duration, allowing flexibility in incubation time to suit process needs.

B. Multiple elution conditions were evaluated. A higher elution pH proved critical for certain proteins to achieve high purity, although it often resulted in significantly reduced yields.

## 5 Other application and future work

- Extend the workflow to other type of magnetic bead-based purifications
  - The system is versatile for different types of magnetic bead purifications, e.g. IMAC purifications for 6his-tagged proteins.
- Further improvements towards a fully automated purification workflow
  - The SpinVessel module without the magnetic piece can be further integrated for magnetic bead dispensing to make the entire process fully automated.
  - The MagWash® system is modular, allowing additional modules to be easily integrated in multiples of 8, to increase throughput.



Protein A, B, and C were all 6his-tag proteins purified on MagWash® using Ni-charged beads (Genscript).



## Summary

The novel semi-automated purification workflow employs the MagWash® module integrated into the Tecan Fluent liquid handler. This integration seamlessly streamlines the purification process by significantly reducing hands-on time. Using this workflow, we can generate milligram quantities of material with equivalent, if not superior, product quality. The system also offers potential for further enhancement, including full automation and the addition of extra modules to increase throughput.