



Case Study

HERMES 24/7 customized for fully autonomous mRNA and Protein Trafficking in Yeast models



Figure 1 - The Hermes 24/7 system at the Gerst lab, Weizmann Institute. The system is integrated to a *Freedom Evo* liquid handler by Tecan.

IDEA Bio-Medical developed the new [HERMES 24/7](#) fully autonomous imaging platform to address the unmet need of the laboratory of [Professor Jeffrey Gerst](#) at The Weizmann Institute of Science in Israel. The customer inspired **Hermes 24/7** establishes a new standard for simplicity and compactness in completely automated, image-based experimentation.

Introduction

Prof. Gerst is a Principal Investigator with over 24 years of experience in the Dept. of Molecular Genetics at The Weizmann Institute. His lab studies the role of mRNA and protein trafficking in cellular processes such as organelle biogenesis, polarized growth, and

morphogenesis in yeast and mammalian cell model systems.

Protein localization within the cell is a key determinant for the establishment of sub-cellular domains and functional organelles, which create environments enabling proper protein function. Though research into the molecular mechanisms determining protein localization are ongoing, it is established that protein mislocalization can dramatically

affect cell viability. The Gerst lab investigates both mRNA and protein trafficking within single cells using fluorescence microscopy to precisely quantify the separation between intracellular structures and determine if they colocalize.

Several aspects of the colocalization experiment performed by the Gerst lab make it technically challenging. Nonetheless, Prof. Gerst sought an automated solution for large-scale screening of their colocalization experiment in yeast for a new laboratory facility. In particular he required:

- Flexible interface with existing equipment
- Small footprint
- As few suppliers involved as possible
- High magnification of at least 60x
- Brightfield & Fluorescence images
- Z-stack acquisition
- Image deconvolution
- Automated image analysis

IDEA Bio-Medical's in-house expertise in areas of precision machine design, manufacture and software development enabled the creation of the **Hermes 24/7** fully automated setup, which includes sample-manipulator and high content imaging system as a tailor-made solution satisfying the demanding requirements set forth by the Gerst lab.

Customer Challenge

Yeast cell growth occurs in high cell count suspension cultures. Such conditions make cell segmentation during image analysis exceptionally difficult. For this purpose, applying high content screenings for yeast

studies is beneficial since dilute, low cell count samples can be used together with rapid acquisition of many fields of view from the each well to cover broad areas and numerous cells. In this way large datasets with multiple treatment replicates can be obtained with samples optimized to enhance the fidelity of single-cell identification.

The Gerst lab's yeast-based colocalization assay visualizes mRNA labeled either using single-molecule FISH probes (Cy3, Cy5 or TAMARA) or fluorescent reporters (GFP, RFP, mCherry), along with secondary fluorescent markers that target intracellular structures (e.g. mitochondria, endoplasmic reticulum, etc.). Each mRNA label produces small foci 50-200nm in diameter, thus requiring high quality and high-resolution images for reliable analysis. The distance between intracellular mRNA and organellar reporters is measured and reported on a cell-by-cell basis to generate a full distribution of spacings for each condition.

Prof. Gerst required this multi-color imaging experiment to be made fully automated and performed in 96 or 384 well plates. Making such a workflow automated posed several challenges regarding sample manipulation, image acquisition and image analysis.

"I wanted a high content imaging system that was reliable at high magnifications for screening the relative localization between mRNA and organelles in yeast. My main goal while searching for a suitable supplier was minimizing the number of external suppliers I would have to interact with and address. In this aspect, IDEA Bio-Medical offered me an integrative solution that included the image acquisition and analysis, together with interfacing of the microscope to existing systems I already had. Such a comprehensive solution from a single company significantly simplified the whole process. This was a huge advantage."

~Professor Jeffrey Gerst Ph.D.

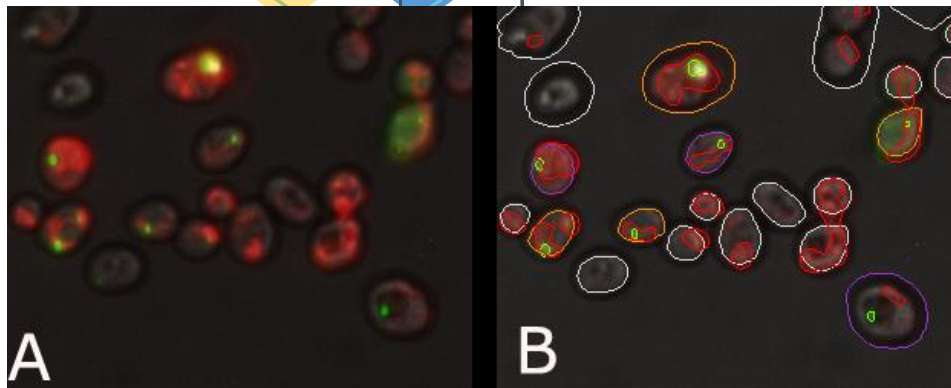


Figure 2 - Yeast Colocalization assay as analyzed in the new, tailor-made Athena application. A: Overlay image of Yeast cells with RNA (green) and Mitochondria (red) labeling. **B:** Analyzed image of yeast cells (white outline), mitochondria (red outline), mRNA complex (green outline) and colocalized events (cells marked using orange outline) are shown.

The Gerst lab required that the plates be prepared by their existing [Tecan FREEDOM Evo®](#) automated liquid handler. Moreover, the automation solution was required to be small, occupying a minimal floor area, and to be mobile such that the *Freedom Evo* could also be available for interfacing with other lab equipment. According to Professor Gerst: *"The existing options when I began trying to automate the workflow required that I work with intermediate third parties that put machines together, but did not themselves make them. In my experience, having multiple parties involved complicates communication and makes collaborative design less efficient. So, I wanted to get everything from one source."*

Solution

IDEA Bio-Medical tailor-made a complete solution for Prof. Gerst's requirements, taking advantage of our experienced in-house software development teams and expertise in precise motion systems development and manufacturing.

At Idea Bio-Medical, our versatile team of professional engineers, scientists and software developers is dedicated to meeting the unique needs of our customers. Our business model endows us with the flexibility to create novel solutions when existing solutions do not

fit a project's needs and requirements. Our team collaborates closely with customers to

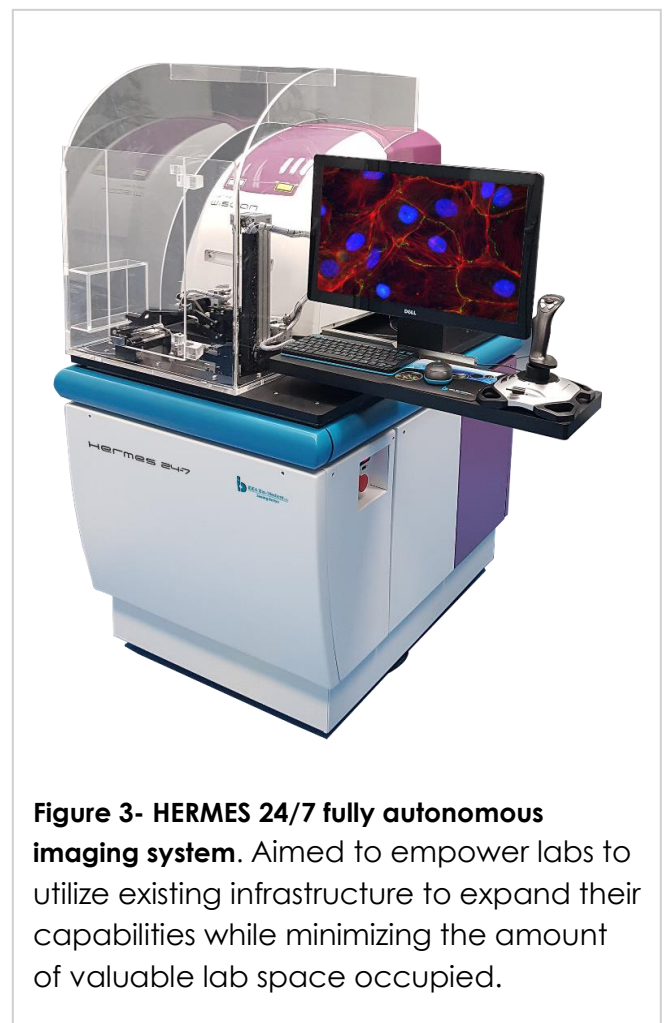


Figure 3- HERMES 24/7 fully autonomous imaging system. Aimed to empower labs to utilize existing infrastructure to expand their capabilities while minimizing the amount of valuable lab space occupied.

fully understand their specific workflow needs and provide effective, custom solutions.

In designing our new **Hermes 24/7** automated system, we aimed to empower labs beyond the Gerst lab to utilize existing infrastructure to expand their capabilities while minimizing the amount of valuable lab space occupied.

To this end, we interfaced with the lab's Tecan Freedom Evo liquid handling unit. The new **HERMES 24/7** system integrates a manipulator arm manufactured by IDEA Bio-Medical with our [Hermes](#) high content imaging system, all placed on a dedicated mobile cart with **footprint of just 1.3m²** to fit into even the most crowded lab space. The **Hermes 24/7** also includes the [Athena](#) application-based analysis software, which performs automated analysis of the images acquired on the Hermes system.

During development, IDEA Bio-Medical's software team collaborated closely with Tecan's local representatives ([Neotec](#)) to

design the complete API interface for the two systems to work together seamlessly. The *Freedom Evo* liquid handler directly communicates with the **Hermes 24/7**, such that all workflow is done autonomously: plate loading, image acquisition, image analysis and production of presentation-ready results. This solution greatly simplifies the entire workflow because it requires only a single integration step between the **Hermes 24/7** and the *Freedom Evo* in moving from experimental design to final results.

We at IDEA Bio-Medical simultaneously designed the imaging and analysis platform required for the colocalization assay that the Gerst lab intended to perform. The process begins with acquisition of the requisite **high-quality and high-resolution images** enabling extraction of the nanometric distance between two fluorescent foci within a single yeast cell. Furthermore, **image acquisition required Z-stacks** to gather 3D data in brightfield and multiple colors, since yeast are roughly spherical and most organelles move

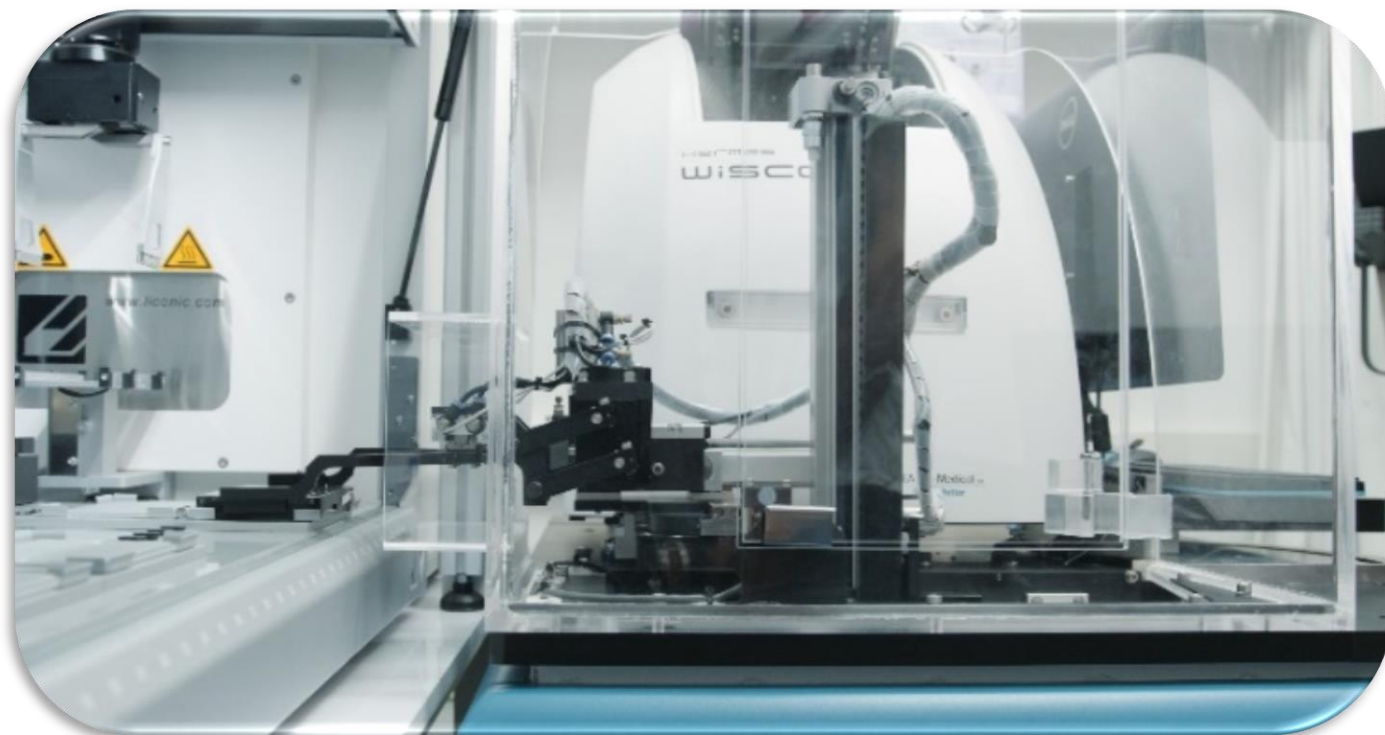


Figure 4 - Plate loading. Hermes 24/7 includes an integrated manipulator arm to load and unload plates for imaging.

in three dimensions within the cells. The Hermes microscope's capability to image rapidly and reliably with its 60X/0.9NA objective ensures that all images are in sharp focus and not blurred due to sample movement during acquisition.

For image analysis, we at IDEA Bio-Medical developed a new, multiplexed application following the Gerst lab design specifications. This new application is also now part of the *Athena* applications portfolio. Analysis includes **image deconvolution** and maximum intensity projection image generation for every field of view. Because it was requested that yeast cells be identified and segmented using bright field illumination, we developed new image analysis algorithms especially designed to identify the yeast cells and locate fluorescent foci within them.

The Yeast Colocalization application now allows the Gerst lab and all WiScan Hermes users a precision measurement of spacing between small, intracellular complexes and organelles within single cells, which utilizes label-free cell detection.

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