



# Remote Control and Unsupervised Feedback Microscopy with the Acquirer IM

High-content screening is routinely employed to automatically acquire multi-dimensional image datasets at fixed positions within wells of microtiter plates. While this is sufficient for many applications, it imposes rather inflexible screening workflows as imaging positions are pre-defined by users, often regardless of specimen location or sample characteristics. This can lead to acquisition of unnecessary datasets, omission of features of interest, and could hinder more complex assays that would depend on real-time analysis of image data. Bruker's Acquirer Imaging Machine (IM) overcomes these challenges and enables unsupervised feedback microscopy and automated decision-making for complex high-content screening experiments.

## Smart Imaging

Smart imaging describes methods for the semi-automated or automated recognition and analysis of structures of interest within samples, including the subsequent data acquisition from these regions. The analysis and decision-making are usually performed by external software packages that interface with the microscope's software and hardware to remote control devices and modify imaging workflows depending on sample characteristics.

Smart imaging can massively improve higher magnification assays, as the limited field of view of higher magnification objectives often leads to omission of structures of interest at pre-defined imaging positions. Regions of interest (e.g. certain phenotypes) can be detected by external image processing routines and selectively imaged. This also enables tissue-specific imaging in large specimens (e.g. zebrafish), as the tissues or organ of interest can be automatically identified and imaged at high resolution. By restricting acquisition to interesting structures, smart imaging techniques save time, data volumes, and resources in large screening projects. Moreover, it enables complex assays like organ-specific screening in large specimen, which is not feasible by conventional high-content screening methods.

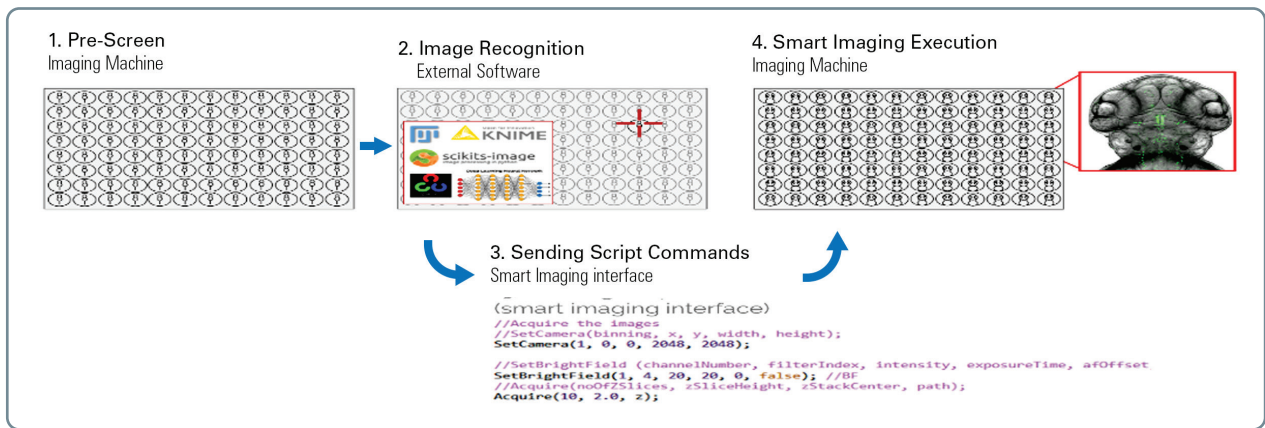


FIGURE 1.

Schematic illustration of smart imaging screening workflows on Acquirer IM: (1) Pre-screen data is captured at a lower resolution to image large field of views. (2) An image recognition step is carried out to detect features of interest such as the position of interesting structures. A vast range of external software can be used to develop customized image analysis tools. (3) The external software sends scripts written in the Acquirer script language to the smart imaging interface which are subsequently transferred to the Acquirer IM controller. (4) Smart imaging scripts are integrated and executed within running screening experiments, e.g. centering and higher-resolution imaging of regions of interest.

## Acquirer IM's Smart Imaging Interface

Acquirer IM offers an easy-to-use smart imaging interface for unsupervised feedback microscopy. Via the Acquirer script language, virtually any external software (e.g. Fiji/ImageJ) that can produce text-based output can be readily interfaced with the screening microscope. This script-based communication between external software and imaging device enables unsupervised feedback microscopy without the necessity of complex hardware communication protocols or dedicated third-party control software.

Acquirer IM also includes an open software interface for developers that provides a built-in script editor for customization of imaging workflows, an easy-to-use file system-based interface to the Acquirer IM, and a TCP/IP interface for more advanced application developments. It also provides intuitive C#-based script language for command and control, the use of scripts for remote control, control imaging workflows, and hierarchical data structures.

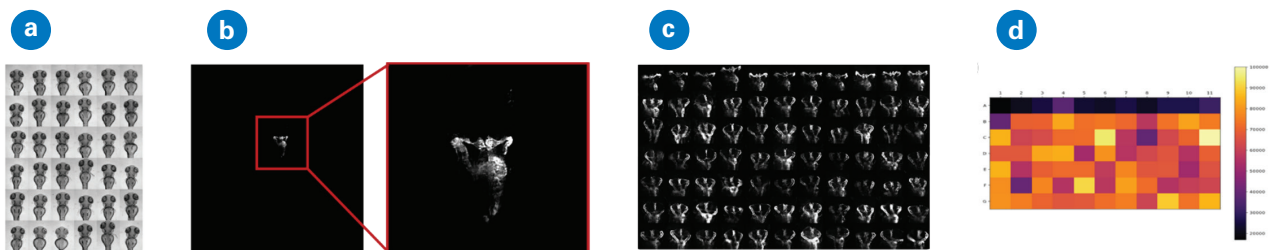


FIGURE 2.

Illustrative example demonstrating the usage of the Acquirer smart imaging workflow for organ- and tissue-specific imaging in zebrafish disease models: (A) Zebrafish embryos are consistently mounted in agarose-coated microtiter plates generated using 3D-printed orientation tools. (B) Kidney regions are detected within low-resolution pre-screen data using a Fiji macro. Smart Imaging scripts are generated by Fiji and transferred and executed via the smart imaging interface of the Acquirer IM leading to higher resolution datasets of pronephric areas. (C) Detailed visualization of kidney regions can be readily obtained for entire 96-well multiwell plates using smart imaging, enabling the scoring of wildtype and disease kidney phenotypes. (D) Smart imaging data allows the subsequent automated quantitative analysis and phenotypic scoring. Figure adapted from Pandey, G., Westhoff, J. H., Schaefer, F., Gehrig, J. (2019). A smart imaging workflow for organ-specific screening in a cystic kidney zebrafish disease model. *International journal of molecular sciences*, 20(6), 1290. <https://doi.org/10.3390/ijms20061290>

## Perform Unsupervised Feedback Microscopy with Ease

Acquifer IM is a system ideally equipped for smart imaging and enabling complex assays. It is adept at the semi-automated recognition and analysis of structures of interest within samples as well as the subsequent data acquisition from these regions. These capabilities have a significant impact on unsupervised feedback microscopy experiments and high-content screenings.

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