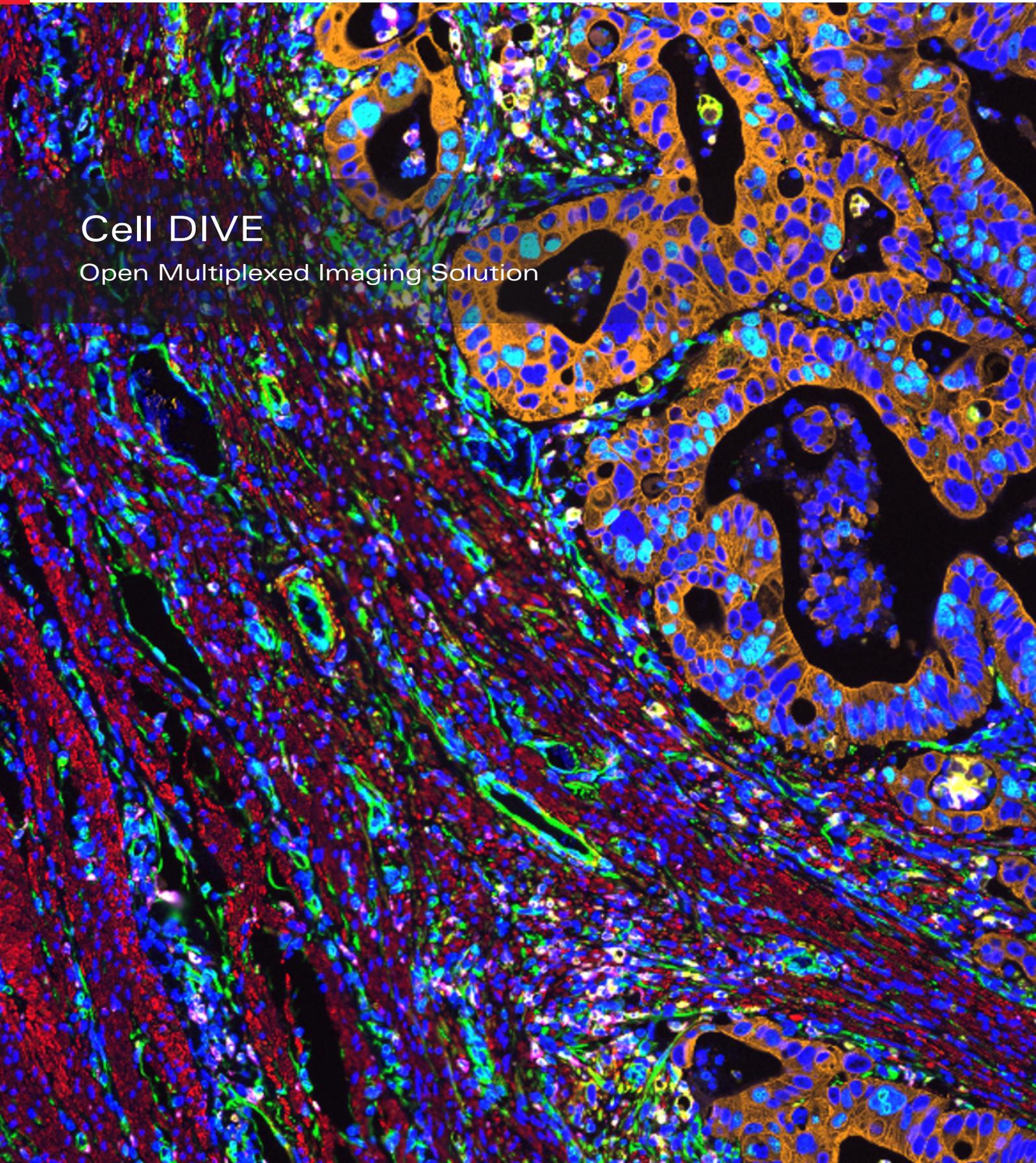


From Eye to Insight

Leica
MICROSYSTEMS

Cell DIVE
Open Multiplexed Imaging Solution



A fluorescence microscopy image of a tissue section. The image shows a complex network of cells and fibers. The cells are stained with various colors: purple, green, red, and yellow. The purple staining highlights the cell nuclei, while the green and red staining indicates the presence of specific proteins or markers. The yellow staining highlights the cell walls or membranes. The overall structure is highly organized, with distinct layers and patterns of cells. The background is dark, making the stained structures stand out prominently.

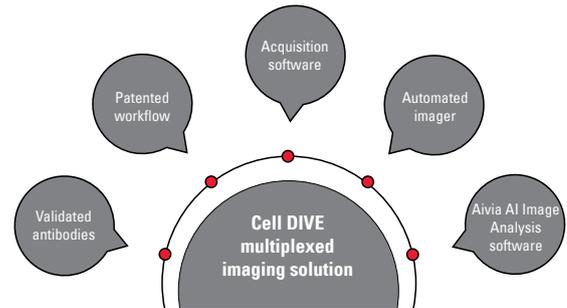
What if...

You could map every cell in a tissue by phenotype, expression profile, and morphology?

Want to choose biomarker panels, antibodies, and automation to suit your specific questions? Cell DIVE is a precise, open multiplexing solution that allows you to follow where the science leads.

An adaptable solution that offers flexibility

- > An adaptable system, Cell DIVE offers the freedom to design your study as you wish, now or in the future
- > With 350+ validated antibodies, you have flexibility to build a panel tailored to your research and be confident in your results
- > Respond to changing research needs in real-time or revisit your study in the future with Cell DIVE's adaptable workflow and tissue-preserving capability



Every component of the Cell DIVE multiplexed imaging solution works together to give you reliable, reproducible results

Multiplexing that's scalable and efficient

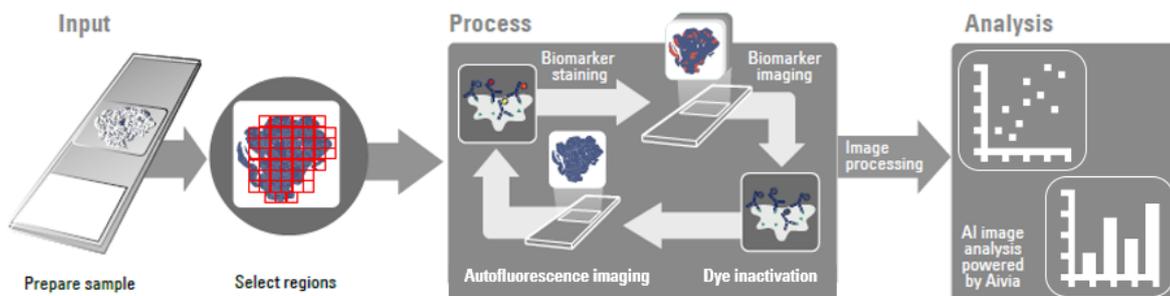
- > Cell DIVE enables easily scalable multiplexing by giving you options for automating workflows to fit your needs
- > Choose the level of automation that is right for your research today and adapt as your needs evolve
- > Develop total confidence in your data and reduce sample-to-sample variation through batch processing of benchwork steps

Data you can trust, backed by a decade of research

- > Cell DIVE helps researchers deepen their understanding of the tissue microenvironment by offering outstanding spatial mapping of single cells within their biological and spatial context
- > Get crystal-clear whole-tissue imaging down to the single-cell level, automatically calibrated and corrected to enable quality analysis downstream
- > The Cell DIVE platform (consisting of hardware, software, and workflow) was developed for scientists by scientists over the course of 10 years, to deliver reproducible results you can rely on

Completely customizable, precise multiplexing

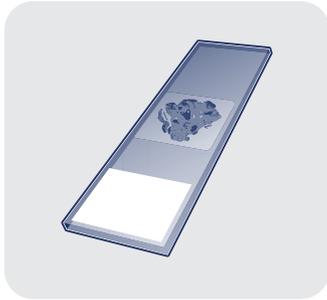
Spatially map 60+ biomarkers from just one tissue section, at the single-cell level



The Cell DIVE process uses integrated software, hardware, and laboratory steps to iteratively stain and destain tissues until up to 60+ biomarkers are imaged and ready for analysis

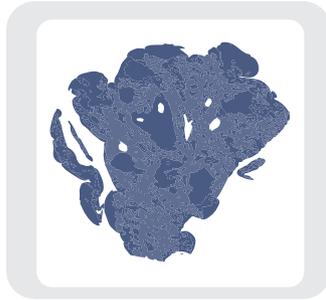
Cell DIVE imaging steps overview

Image processing continues



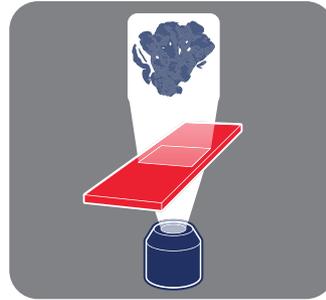
1. Sample preparation

Prepare any FFPE tissue sample or tissue microarray.



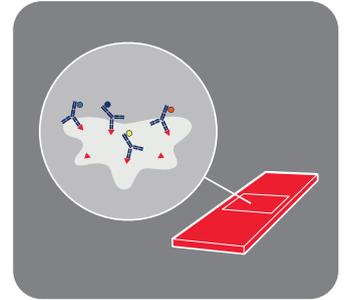
2. Region selection

Select regions of interest (ROI) from a virtual hematoxylin and eosin (H&E) image of the entire sample.



3. Autofluorescence imaging

Capture 20x images for downstream autofluorescence removal to get the clearest biomarker signal possible.

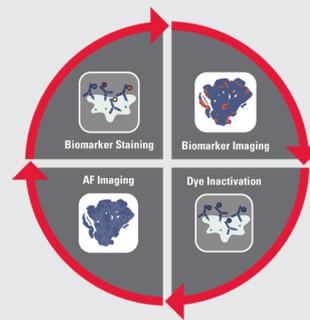


4. Biomarker staining

Stain the tissue sample with DAPI and up to four dye-conjugated antibodies at one time.

Cell DIVE and BioAssemblyBot 200: Scale your research with automation

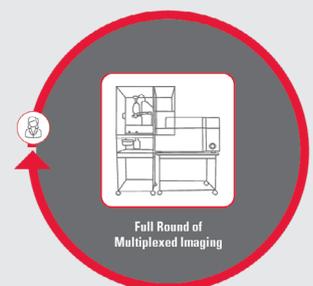
- > Advance your research 24/7 by processing up to 15 slides at a time
- > Reduce tissue damage with the Cell DIVE ClickWell, a coverslip-free slide holder that integrates with Advanced Solutions Life Sciences' BAB 200, a high precision and flexible robotic platform
- > Have confidence in your results by minimizing sample to sample variation



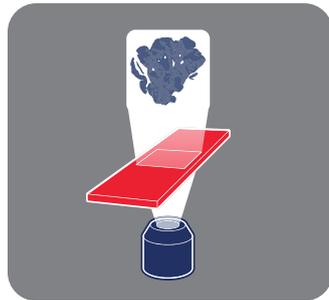
Steps in the Cell DIVE patented iterative staining workflow



BAB 200 automation of iterative staining workflow with one touchpoint per round

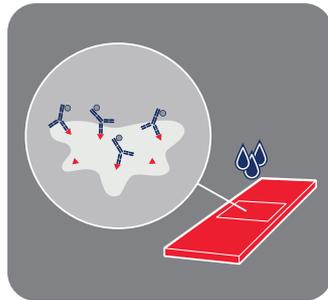


Cell DIVE imaging steps



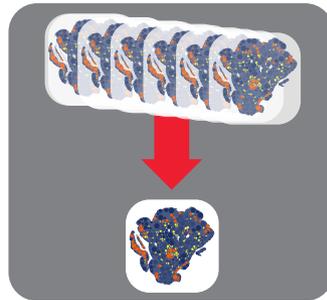
5. Biomarker imaging

Capture the stained biomarker image. Images are automatically processed to perform over 10 independent corrections, including flat-field correction, distortion removal, and intensity calibration.



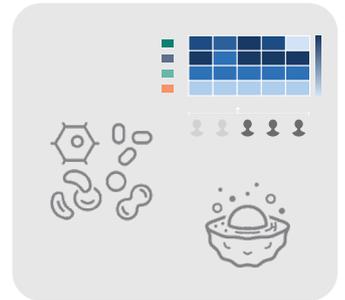
6. Dye inactivation

Use our patented dye-inactivation process to turn off dye molecules without damaging the sample, allowing for additional staining cycles with new biomarkers.



7. Image processing

Conduct true single-cell analysis due to the automated, patented, post-acquisition processing that delivers seamlessly stitched and precisely aligned data.

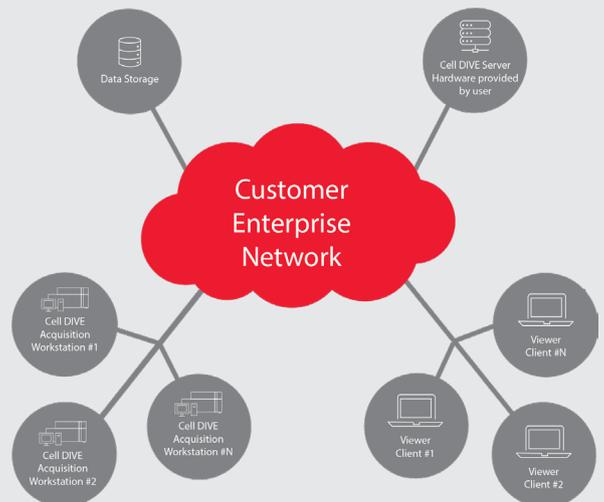


8. Segmentation and analysis powered by Aivia

Segment, extract features, and analyze data to determine abundance and localization of specified biomarkers for comprehensive spatial mapping.

Cell DIVE Connect: Large-scale multiplexing with confidence

- > Maximize throughput by using multiple, networked Cell DIVE imagers to capture data
- > Protocols are shared so you can image any slide on any imager at any time
- > Get sub-cellular registration in final data from images acquired on any Cell DIVE on the network
- > Manage multiple studies easily with the ability to view and modify all slides from any workstation



Cell DIVE Connect allows a user to share a database of slides and metadata between multiple Cell DIVE Imagers and their Acquisition Workstations. A basic diagram of the deployment is shown above.

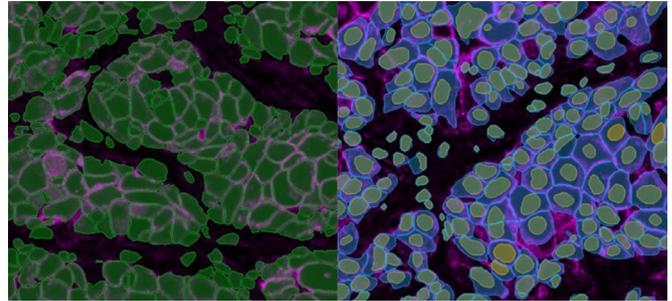
Elevate your research with Aivia AI-based image analysis software

Unveil spatial insights in tissues for a deeper understanding of the microenvironment surrounding their phenotypes

AI access for all

Harness the power of AI without coding or needing to train model

- > Benefit from next-generation, easy-to-use deep learning segmentation and classification tools
- > Open, view, and interact with large, multiplexed 2D images (up to 100 channels, with more than 1 million detected objects)
- > Accurately segment cells with different morphologies in large, multiplexed 2D images with AI
- > Discover the cell phenotypes in your image using AI-powered phenotyping or data-driven unsupervised automatic phenotyping
- > Easily open and interactively explore 2-to-5D microscopy data sets from anywhere using the free Aivia Community software



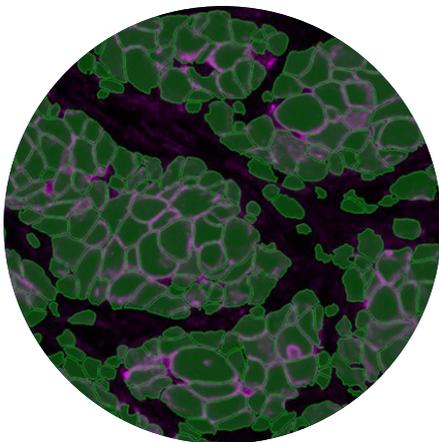
Accurately segment your cells with AI

Two types of generalist algorithms help to accurately detect and partition cells with different morphologies.

Detect using a single (left) or multiple (right) membrane or cytoplasmic markers to segment and partition cells.

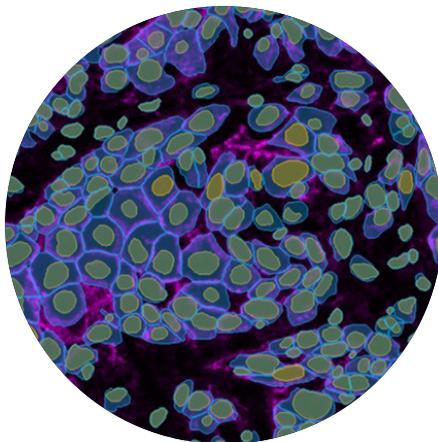
Radically simplified phenotyping

Data-driven automatic phenotyping to discover new phenotypes



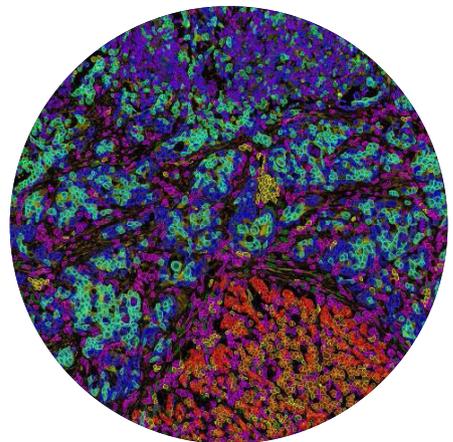
Original Data

Has over a million objects with 30 markers, creating challenges for data interpretation



Automatic Clustering (4 clusters)

Helps to identify structures of interest based on user-selected markers and measurements



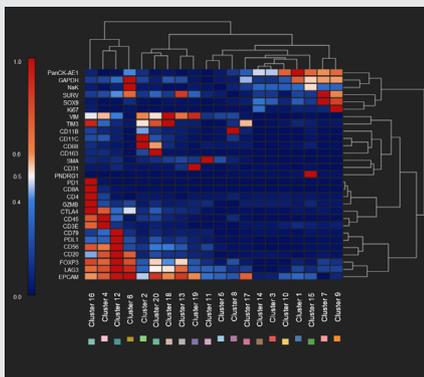
Automatic clustering (10 clusters)

Helps to discover additional phenotypes of interest that may not have been considered with a simple adjustment of parameters

Complete end-to-end workflow to insight generation

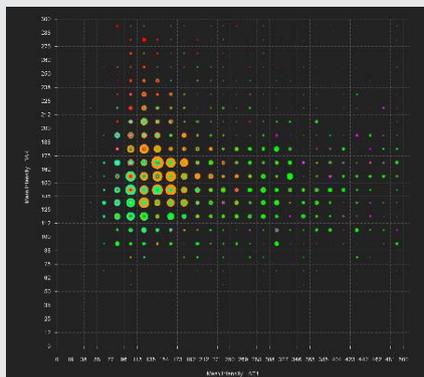
Built-in data visualization tools enable seamless insights and feedback

Aivia unlocks all the value of your data within a single platform. No more having to juggle multiple imaging and analyses systems into your workflow - the Aivia platform offers you a unified user experience. Pictured below are example charts of the insights you can get from large 2D images.



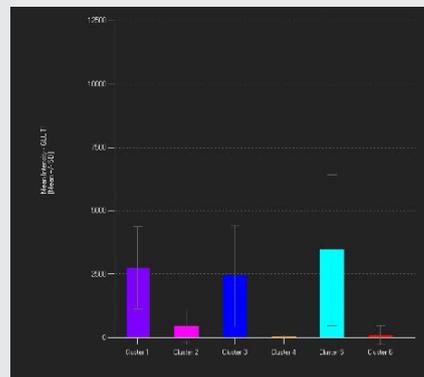
Dendrogram

Interactively viewing the relationship between intensity or morphological measurements and phenotype selection in the image



Binned Scatter Plot

Comparing data distribution of two different measurements for multiple object sets or phenotypes



Summary Chart

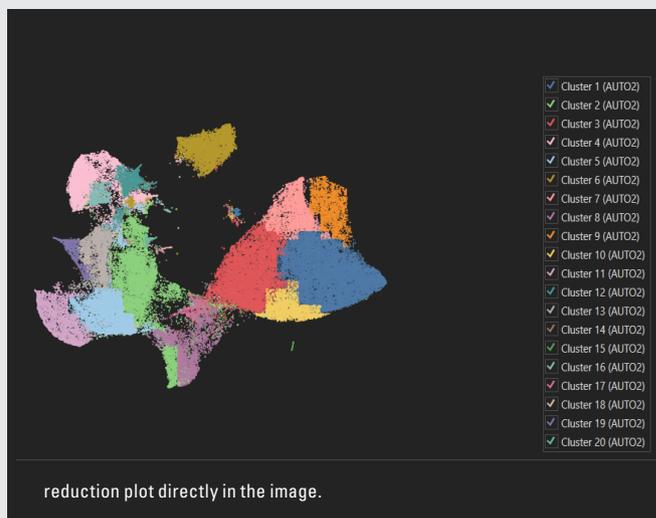
Providing comparison of summary between object groups or phenotypes for any measurements

Rapidly identify patterns in complex data

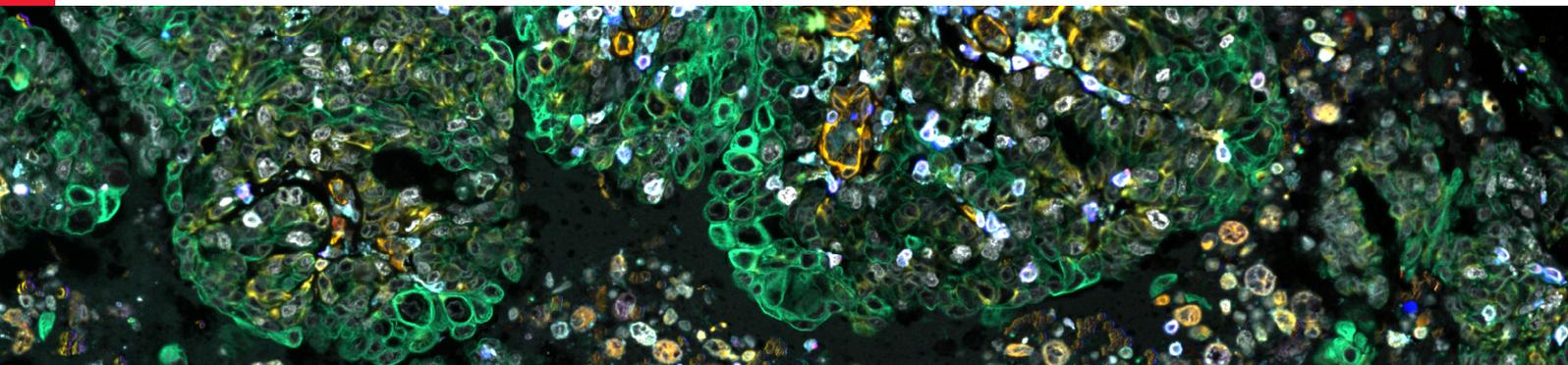
Uncover patterns, simplify analysis, and enhance interpretability with dimensionality reduction

Dimensionality reduction is a mathematical approach to better view and understand data with high number of dimensions by mapping them to a smaller number of dimensions.

Aivia provides users with three distinct ways to perform dimensionality reduction: UMAP, PaCMAP, and t-SNE. Furthermore, Aivia enables users to visualize clusters/phenotypes within the dimensionality reduction plot.



In the example, 29 intensity dimensions have been reduced to 2 with 20 phenotypes generated using the UMAP reduction method displayed in different colors.



Cell DIVE Workflow: Customizable. Precise. Proven.

- > Highly multiplexed imaging without expensive and restrictive commercial panels
- > Tissue-preserving imaging without damaging, stripping or photobleaching
- > Get more information out of a single experiment with an extra-large imaging area
- > Rapid multiplexing at scale with customizable automation
- > Accurate cell detection and automatic clustering with up to 30 markers with Aivia AI image analysis software

CONNECT
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