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MxW Tips and Tricks: Activity Scan Assay

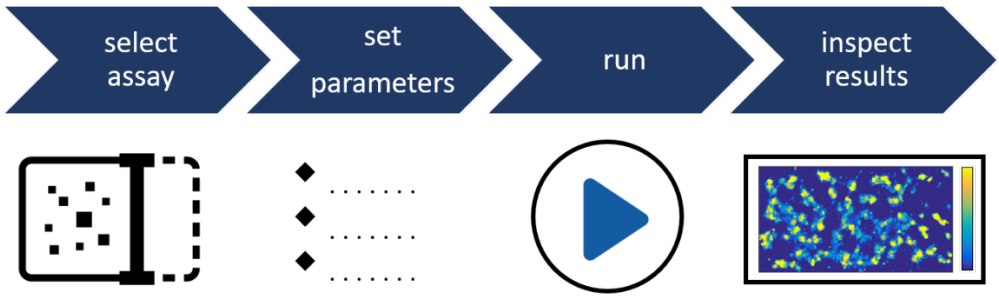
Summary

The first issue of our new blog series "MxW Tips and Tricks" presents how to use the **Activity Scan Assay** to acquire a **whole-sample electrical image** using your MaxOne chips. In this article, we

- introduce the new assay workflow in the MaxLab Live software,
- review what to consider when defining the assay parameters,
- discuss which metrics can be extracted based on the Activity Scan Assay,
- illustrate an application of the assay.

Introducing the MaxLab Live Assay Workflow

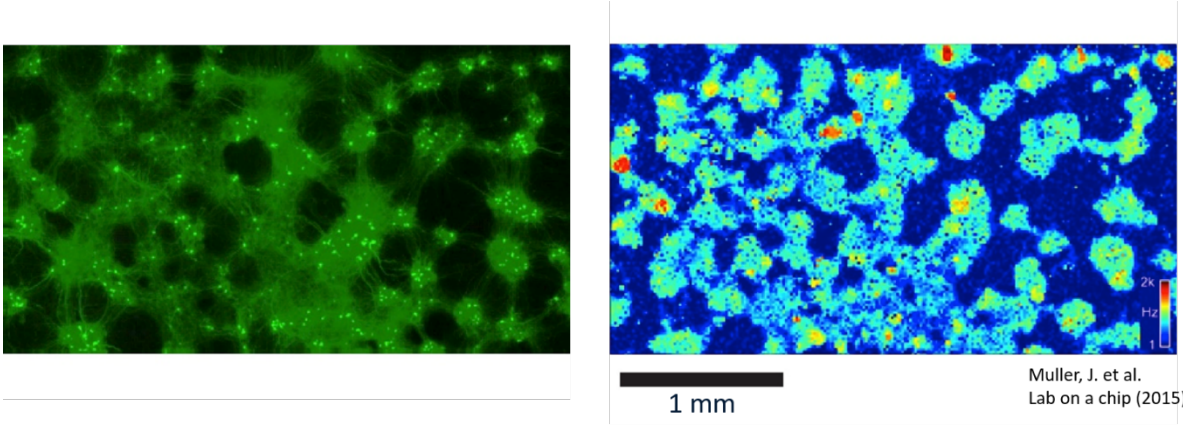
MaxLab Live software features the novel **assay workflow** to plan and execute experiments. These automatized experiments range from simple to fairly complex workflows. The four steps of such a workflow are illustrated in the following chart:



Assay Workflow Steps

Activity Scan Assay

When starting an experiment with cultured neurons, acute slices, retina, or organoids, the first step is assessing whether the neurons are electrically active (i.e. firing action potentials, or spikes) and identifying their position on the array. This information will reveal important details about viability and developmental status of the cells. The **Activity Scan Assay** provides a quick and automated framework to obtain this information and is typically the first step in every MaxOne experiment. The assay sequentially records configurations of electrodes and thereby "scans" the entire array for spikes, which are then visualized as electrical image (or *activity map*; see Figure below).



Left: Optical Immunofluorescence Image *Right:* MaxOne Electrical Image

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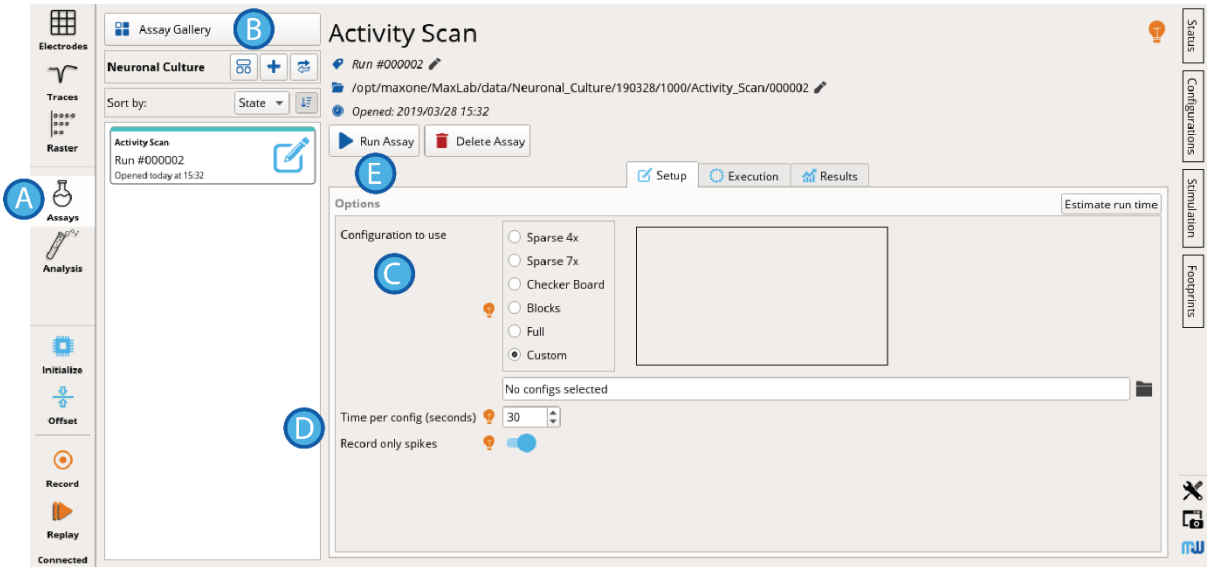
MaxOne-technology-based activity scans have been used to assess the spontaneous activity from primary skeletal muscle cells (Lewandowska et al., 2018), to follow the neuronal development over several DIV of organotypic slice cultures (Gong et al., 2016) and dissociated cortical cultures (Yada et al., 2016) and to target neurons for patch-clamping based on their firing activity (Jäckel et al., 2017). In some cases, the activity maps were combined or compared with optical images, such as for dissociated cortical cultures (Müller et al., 2015, see Figure above) or acute brain slices (Frey et al., 2009 / Dragas et al., 2017 / Bakkum et al., 2018 / Obien et al., 2019).

Running the Assay

To run the assay, execute the following steps

- Click on the **Assays** button on the right side of the software window (A).
- Open the **Assay Gallery** (B) to see the available assays.
- Select **Activity Scan** to create the assay.
- In the Setup window, define which **set of configurations** (C) to use.
- Set the recording time per configuration and the recording mode: either saving the full data or only detected spikes events (D).
- Press the **Run Assay** button (E) to start the scan.



Select Assay and Set Parameters

Setting the right parameters

When setting the experimental parameters, namely the **configurations to use** and the **recording time per configuration**, the tradeoff between experiment duration and spatial coverage must be considered. The assay provides five predefined sets of configurations and a custom option:

- **Sparse 4x** - Provides a quick assessment of the electrical activity sampling 12.5% of the electrodes.
- **Sparse 7x** - Every second electrode in x- and y-direction is selected.
- **Checkerboard** - This scan covers 98% of the array area with every other electrode.
- **Blocks**- Scanning every electrode in the center area.
- **Full** - This scan provides the highest possible resolution, including every electrode.
- **Custom** – Customizable configurations.

For example, if the recording time per configuration is 30 seconds, a **Sparse 7x scan**, which includes seven sequential configurations, will last approximately 5 minutes and will provide a good overview of the cellular location and viability. The results of a **Full scan**, on the other hand, will require 20 minutes and provide a highly detailed activity image, more data for your statistical analysis and a better basis for identifying isolated neuronal units.

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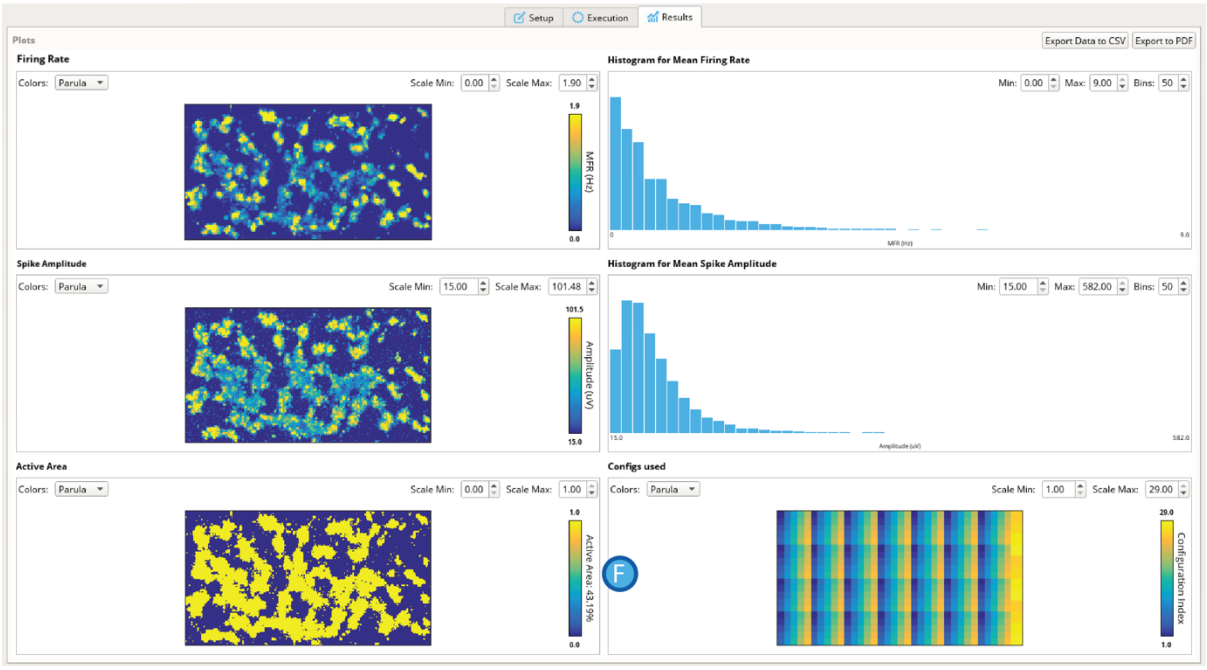
Importantly, the recording time per configuration must be long enough to capture the dynamics of the neuronal activity. If a preparation exhibits strong bursting activity with inter-burst-intervals of several seconds, the recording duration should be large enough to include enough bursts in each configuration in order to obtain reliable firing rate values. For preparations with fast, regular spiking activity, 20 – 30 seconds per configuration is often good enough to acquire proper firing rate distributions.

Inspecting the Results

Once the scan is finished, the Results window will automatically appear:



Assay Results

The central outputs of this assay are

- Firing rate [Hz] per electrode
  number of detected spikes / recording time
- Spike amplitude [µV] per electrode
  90th percentile of the negative amplitude of detected spikes
- Active area
  electrodes with firing rate > 0.1 Hz AND spike amplitude > 20 µV

Both the firing rate and the spike amplitude values are displayed as an activity map (left) and as a histogram (right). The activity map representation is very useful to optically assess the activity, to visually compare between different preparations or to follow the development of a neuronal culture over multiple days.

The output Active Area measures on how many electrodes APs appear and is a suitable metric to detect the growth development of a neuronal culture. The Active Area electrodes are visualized as yellow pixels in the binary map (bottom left), and the percent area covered is displayed next to the color bar (F).

All the results can be exported as CSV files, which can be analyzed further in other data analysis software.

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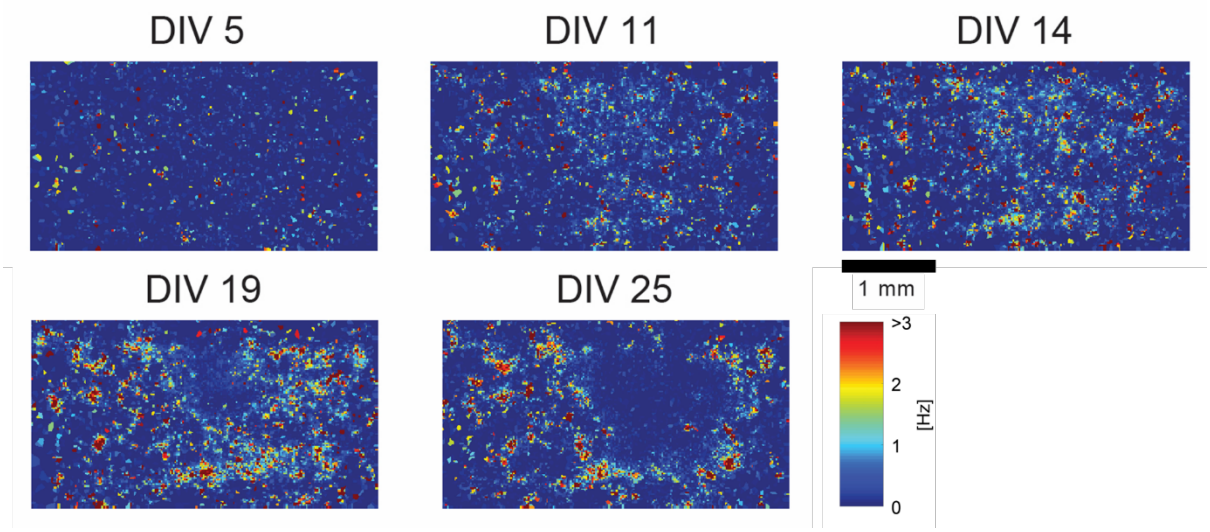
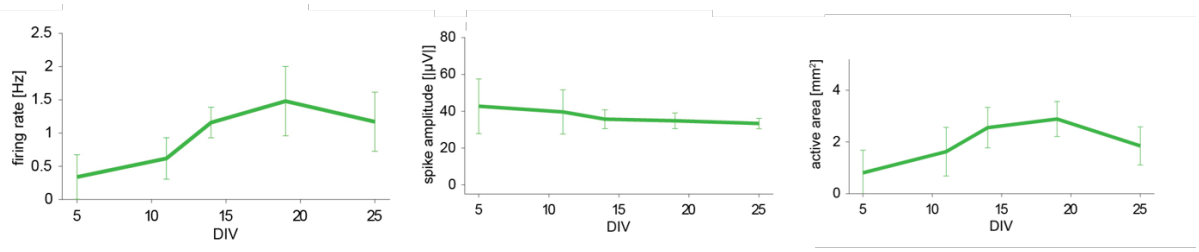
Application example: Observing neuronal development over days and weeks

The following example shows how the development of a neuronal culture can be studied over weeks by measuring the activity maps over multiple days. The visual maps reflect with great detail the positioning, as well as the activity of the neurons on MaxOne:



Activity map for multiple days in vitro (DIV)

Finally, the extracted metrics are used to quantify the neuronal development. While the firing activity and the active area increased during the development, the spike amplitudes slightly decreased:



Extracted metrics over multiple days

Conclusion

The Activity Scan Assay gives a detailed activity overview and is typically executed at the beginning of an experiment. Furthermore, the metrics can be used to quantify the neuronal parameters. Using the newest version of the software, the Activity Scan Assay can be configured for your experiment and can run easily with just a few clicks.

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