

Platform Integration For High-Throughput Functional Screening Applications

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ABSTRACT

Screening throughput is a common bottleneck in many research areas, including functional genomics, drug discovery, and directed evolution. High-throughput screening techniques can be classified into two main categories: (i) affinity-based screening and (ii) functional screening. The first one relies on binding assays that provide information about the affinity of a test molecule for a target binding site. Binding assays are relatively easy to establish, however, they reveal no functional activity. In contrast, functional assays show an effect triggered by the interaction of a ligand at a target binding site.

Screening of large cell or gene libraries based on direct activity rather than binding affinity is now a preferred strategy in many areas of research as functional assays more closely resemble the context where entities of interest are anticipated to act. Droplet sorting is the basis of high-throughput functional biological screening, yet its applicability is limited due to the technical complexity of integrating high-performance droplet analysis and manipulation systems. As a solution, the Droplet Genomics Styx platform enables custom droplet sorting workflows, which are necessary for the development of early-stage or complex biological therapeutics or industrially important biocatalysts.

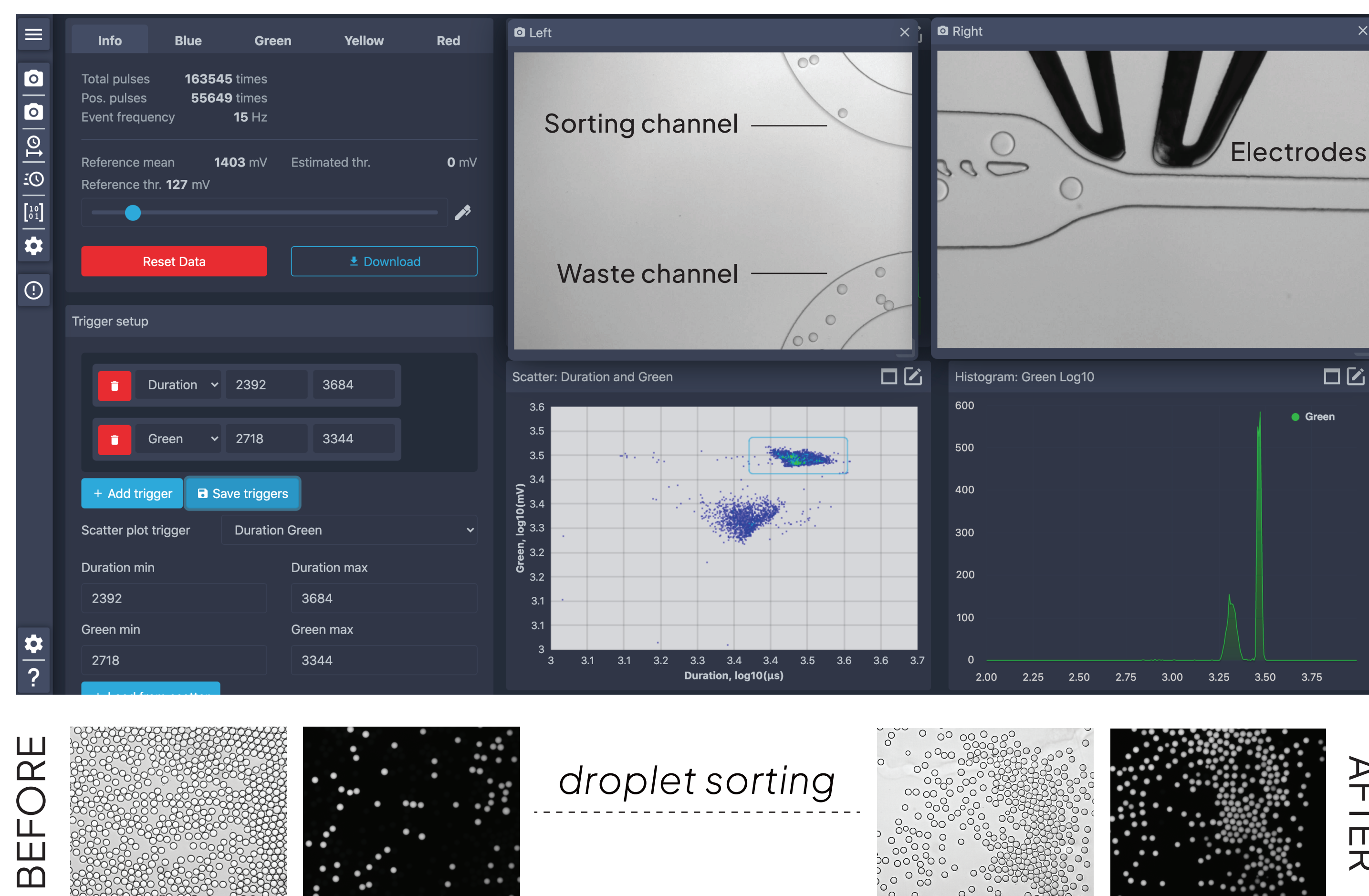


Figure 1. An overview of the droplet sorting process with the Styx system.

DROPLET SORTING

If the outcome of a high-throughput screening assay can be linked to the change of the optical signal, the primary choice of droplet selection method is **fluorescence-activated droplet sorting (FADS)**. FADS is the most mature on-chip droplet selection technique with the following advantages:

- ✓ sensitive detection;
- ✓ allows to sort a broad range of droplet volumes (fL-nL);
- ✓ sorting rates might be as high as tens of kHz, which is comparable to the speed of fluorescence-activated cell sorting (FACS);
- ✓ the high-speed camera allows visualizing each droplet sorting event.

Droplet Genomics Styx system eliminates the technical complexity of FADS setup while retaining maximum design flexibility to enable any high-throughput functional screening campaign.

APPLICATIONS

- **ANTIBODY DISCOVERY.** FADS screening allows performing phenotypic analysis of **individual** mAbs-secreting cells in the presence of coencapsulated reporters.
- **SMALL MOLECULE DRUG DISCOVERY.** Compartmentalization of DNA-encoded library (DEL) into microfluidic droplets retains the **chemotype-genotype connection**.
- **FUNCTIONAL METAGENOMICS.** Functional metagenomic screens using droplet microfluidics has proved to be instrumental for efficient **identification of rare genes and activities** that could have not been previously predicted by sequence homology.
- **PROTEIN ENGINEERING.** Droplet microfluidics paves the way to design **complex functional screening assays**. Any fluorogenic substrate responsive to target protein activity will allow sorting positive hits from the population.



PRESSURE PUMPS

Type: piezo-electric
Independent channels: 4
Pressure range: up to 35 kPa

FLUORESCENCE

Lasers: up to 4 (405/488/561/633)
Laser power: 0-20 mW
Detection channels: 4 independent
Detection sensitivity: 100 μ s-100 ms
duration light pulses, lower limit of
photon flux at 1 photon/ μ s at 25°C
Measurement throughput: >1 kHz

ARTIFICIAL INTELLIGENCE

GPU: 512-core NVIDIA Volta, 32 TOPs
CPU: 8-core NVIDIA Carmel Arm®v8.2
64-bit CPU 8 MB L2+4MB L3
Memory: 32 GB 256-bit LPDDR4x 136.5
GB/s
Chip and droplet analysis rate: <2.0 s
Droplet size precision: \pm 5 μ m

MICROSCOPY

Optical magnification: 0.7 μ m/px (area 1),
1.5 μ m/px (area 2)
Illumination source: 0-0.25W LED 760
nm monochromatic
Illumination type: infrared
Chip dimensions: 25 x 75 mm
Stage: motorized 3 direction stage

HIGH-SPEED CAMERAS

Resolution: 1440 x 1080
Exposure time: 45 μ s - 2 ms
Recording framerate: 10-5000 frames/s

HIGH-VOLTAGE PULSE GENERATOR

Pulse amplitude range: 100-1000 Vpp
Duty cycle: up to 50%
Frequency tuning: automatic
Pulse duration: 100 μ s-100 ms
Pulse synchronization delay: 100 μ s -10
ms with 10 μ s jitter



LEARN MORE

[DROPLETGENOMICS.COM](https://dropletgenomics.com)

