APPLICATION NOTE

A seamless integration of the DropGenie platform into the Revvity Fontus and FlexDrop Plus liquid handling ecosystem for high-efficiency cellular delivery.

Authors

Hugo Sinha
Alison Hirukawa, PhD
DropGenie

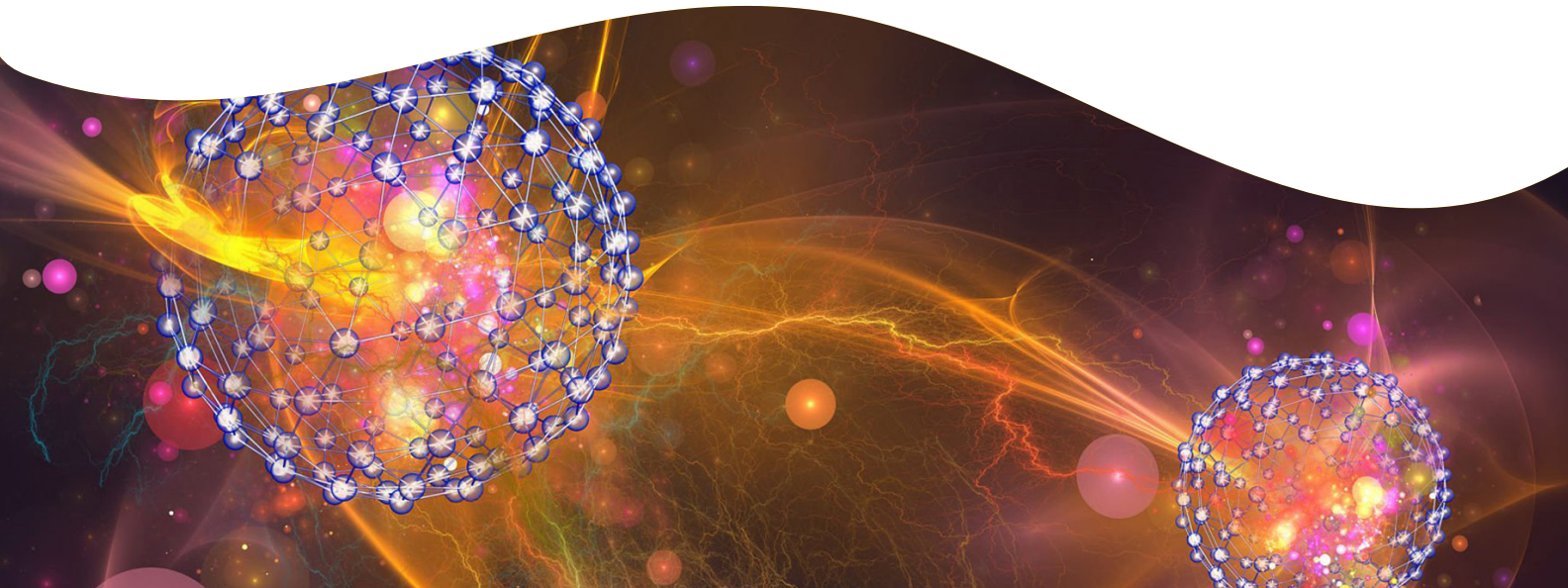
Eric Woodard
Revvity

Introduction

Plug-and-play miniaturized electroporation

Advances in cell and gene therapy, functional genomics, and disease model creation are highly dependent on improvements and standardization of cell engineering, increasing the need for scalable, automation-ready transfection solutions. As drug discovery organizations adopt end-to-end automation for cell engineering workflows, rapid integration of new automation modules into existing liquid handling infrastructure is becoming essential. While nanoliter dispensers and automated workstations enable precise and scalable reagent handling, downstream steps such as cell transfection and electroporation remain difficult to operationalize, particularly when working with new payloads, new cell types, or unfamiliar automation environments. In practice, this frequently results in extended on-site optimization, and delayed access to meaningful biological data, resulting in a reluctance to scale experimental throughput.

Here, we demonstrate the rapid deployment of the DropGenie digital microfluidic electroporation platform within a Revvity automation ecosystem, leveraging the FlexDrop™ Plus nanodispenser for low-volume reagent deposition and the Fontus™ automated workstation for DropGenie cartridge handling and liquid transfer. Across two experiments, the integrated system enabled (i) rapid achievement of high-efficiency GFP mRNA delivery in a new customer automation environment and (ii) fast, multi-parameter electroporation optimization in a challenging neuronal cell line using a single microfluidic cartridge and a total of only 500,000 cells.



Together, these studies highlight how the combination of Revvity automation and the DropGenie platform's microfluidic transfection technology enables speed, robustness, and experimental flexibility, allowing users to move from setup to actionable biological insight within days rather than months.

Real-world deployment in a new Revvity automation environment

The initial deployment of the DropGenie platform was conducted under conditions designed to reflect real-world customer constraints rather than a pre-validated demonstration environment. Five independent variables were introduced simultaneously: a new nanodispenser (Revvity FlexDrop Plus dispenser), a new liquid handling platform (Revvity Fontus workstation), a new cell type, a new payload formulation (first-time spotting of GFP mRNA), and a new laboratory site. Under conventional transfection workflows, each of these factors would typically require isolated validation and iterative tuning, significantly extending deployment timelines.

Despite these challenges, the DropGenie platform's technology was integrated directly into the Revvity automation stack without custom hardware modifications or site-specific engineering. The SBS-compatible DropGenie module and cartridge aligned naturally with the Fontus system's deck layouts and gripper workflows, while the FlexDrop Plus dispenser enabled precise, contact-free nanoliter deposition of mRNA onto defined target locations on the DropGenie cartridge. This integration allowed the team to focus immediately on executing an end-to-end workflow (Figure 1).

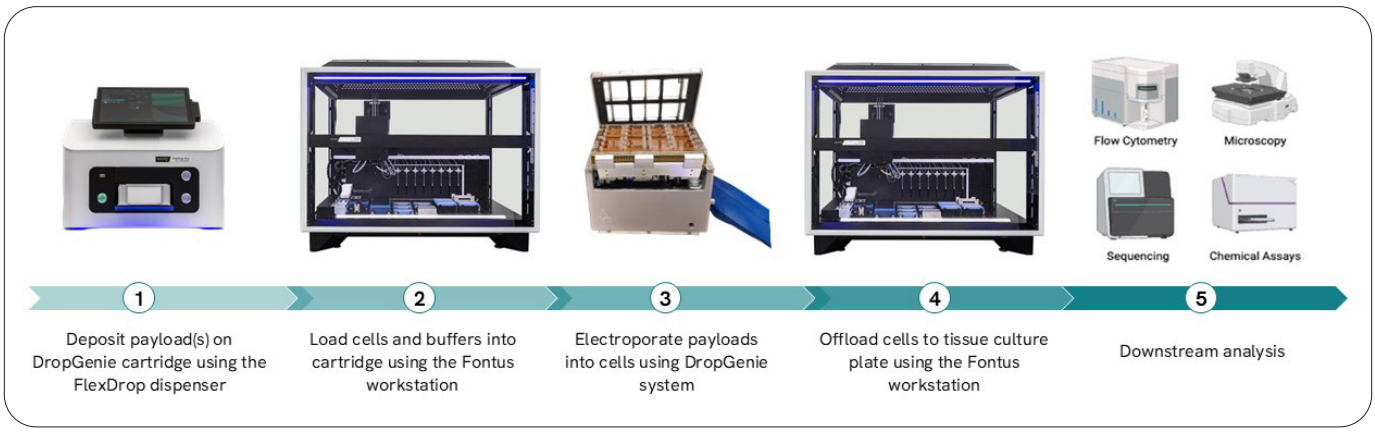


Figure 1: Workflow overview of the DropGenie system integrated into Revvity's instrumentation ecosystem.

Integrated workflow, deposition validation, and rapid multi-parameter screening using FlexDrop Plus and Fontus liquid handlers

In this workflow, GFP mRNA was resuspended in a polymer-based formulation to promote surface adherence and deposited directly onto the DropGenie cartridge using the Revvity FlexDrop Plus nanodispenser, followed by cartridge assembly and reagent handling on the Revvity Fontus workstation by loading suspended cells and the DropGenie electroporation buffers. The assembled cartridge was then processed on the DropGenie instrument, where digital microfluidics enabled controlled droplet manipulation, on-cartridge reagent rehydration, and tri-drop electroporation using user-defined electrical parameters.

Nanoliter-scale droplets were deposited onto predefined target locations on the DropGenie cartridge using the FlexDrop Plus nanodispenser, and reagent deposition fidelity was first validated. Deposition was highly consistent across sites, with droplets landing reproducibly within the intended electrode regions as pointed out in Figure 2a. This precision and low positional drift is crucial in enabling reliable on-cartridge payload rehydration by digital microfluidic droplets without cross-contamination. This step confirmed that the FlexDrop Plus dispenser's deposition was compatible with DropGenie's microfluidic architecture and downstream droplet actuation.

Following deposition validation, the platform was used to perform rapid screening of multiple electroporation conditions within a single consumable. A panel of electrical parameters spanning voltage and pulse-width settings was evaluated to assess delivery performance across conditions (Figure 2b). With its independently tunable electroporation sites, the DropGenie instrument allows the user to control all electrical parameters.

GFP mRNA delivery efficiency across conditions was then assessed by flow cytometry, enabling direct quantitative comparison of electroporation parameters within a single experimental run (Figure 2c). Despite the introduction of multiple unvalidated variables (including a new automation environment, a new payload formulation, and unfamiliar dispensing hardware), greater than 80% GFP-positive cells was achieved within less than five hours of arriving on-site. Together, these results demonstrate how the integrated FlexDrop Plus–Fontus–DropGenie platform workflow supports rapid empirical parameter exploration without requiring multiple cartridges, extended optimization cycles, or hardware reconfiguration.

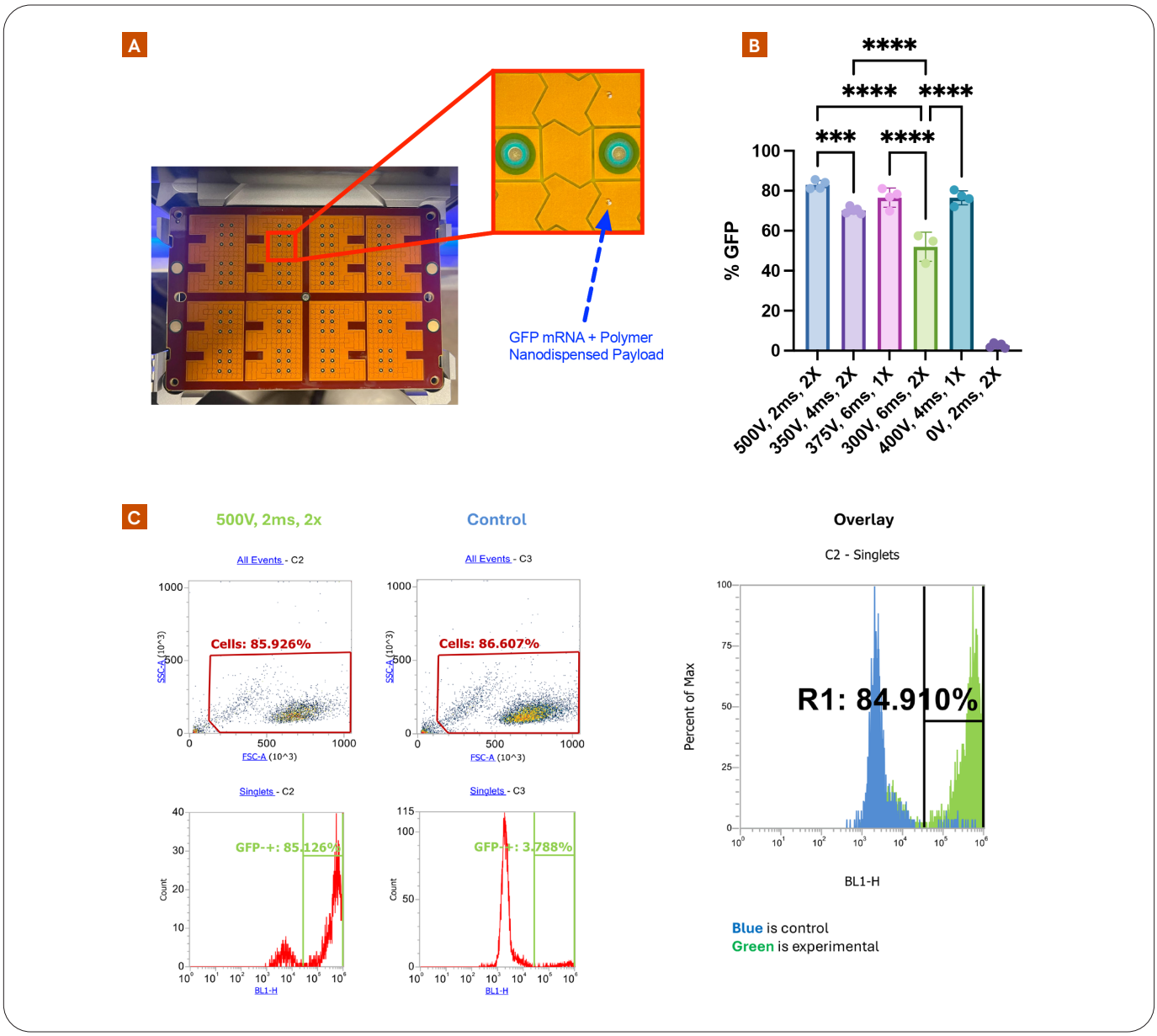


Figure 2: (a) Cartridge post-spotting sitting on the tray of the FlexDrop Plus dispenser with targeted deposition of payload, (b) Bar graph of GFP mRNA delivery efficiency into U937 cells across six electroporation conditions (c) Flow cytometry gating strategy.

Rapid 16-Condition optimization in a challenging neuronal cell line

To further stress-test the platform, GFP mRNA delivery was evaluated in SH-SY5Y cells, a widely used but challenging neuronal cell line known for its sensitivity to transfection conditions. This study was designed to assess both delivery robustness and the speed with which optimal electroporation parameters could be identified using the DropGenie system.

A mere amount of approximately 500,000 cells were used for 48 independent electroporation experiments (5,000-10,000 cells per experiment), with a 16-condition optimization matrix executed on a single DropGenie consumable, spanning four GFP mRNA input volumes (0nL, 20nL, 40nL, 60nL) and four electroporation parameter sets varying voltage and pulse width, all performed in triplicate. Conventional electroporation technologies would require 500,000 cells for each condition, highlighting the dramatic reduction in input cells required and the value of the platform when working with precious primary samples. All reagent depositions were carried out using the Revvity FlexDrop nanodispenser to generate a concentration series directly on the cartridge. The FlexDrop Plus instrument delivered highly reproducible nanoliter-scale reagent spotting, enabling reliable on-cartridge rehydration and consistent delivery across conditions.

Total hands-on workflow time, from cell trypsinization to returning the plate with electroporated samples to the incubator, was approximately 30 to 45 minutes with two operators, including reagent spotting, demonstrating the ability to swiftly perform comprehensive parameter optimization with minimal manual effort (Figure 3).

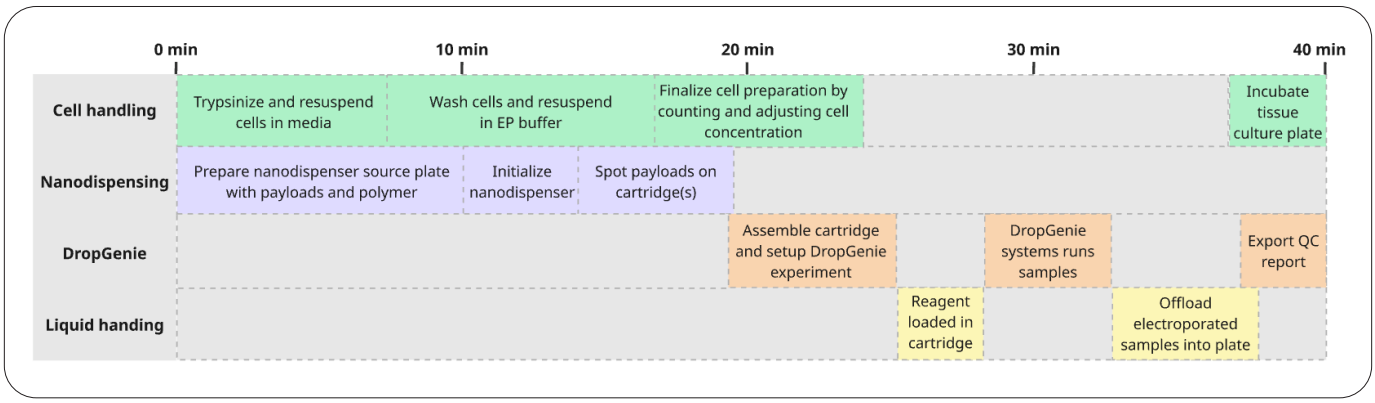


Figure 3: Experimental timeline to electroporate a full cartridge. Each additional cartridge would add approximately 20 min of time.

Cells were imaged 24 hours post-electroporation using an Agilent BioTek Cytation 5 high-content imager, with representative conditions shown in Figure 4. Although imaging artifacts in this experiment limited quantitative analysis (including Phenol Red background, scratches on the plate bottom, fibers in the FBS, along with some bright-field and fluorescence lens misalignment), robust intracellular delivery was clearly observed, with multiple conditions exceeding approximately 90% GFP positivity by visual assessment (Figure 4). These results provided clear guidance for further parameter refinement or even relevant follow-on cell engineering experiments, highlighting how the DropGenie platform enables rapid, empirical decision-making even in challenging biological contexts.

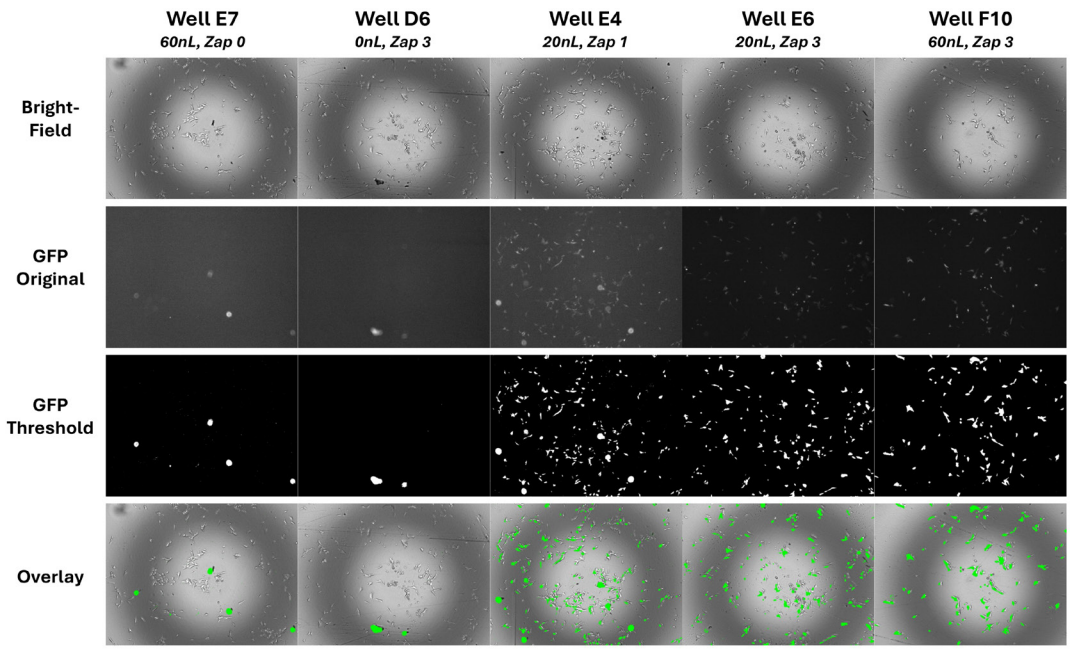


Figure 4: Select images from the 16-condition optimization panel in SH-SY5Y cells. Listed below the Well iD are the conditions, with the volume of deposited GFP mRNA and the electroporation parameters applied (Zap 0 = 2 pulses, 0V, 2ms; Zap 1 = 2 pulses, 450V, 3ms; Zap 2 = 2 pulses, 500V, 2ms (not shown); Zap 3 = 3 pulses, 500V, 3ms). GFP images were segmented using global percentile-based intensity thresholding after Gaussian smoothing (5×5) and large-scale background subtraction (σ = 50), with thresholds set according to relative background noise at the 99.7th percentile for E7/D6 and the 97th percentile for E4/E6/F10; bright-field images were used only for visualization of mask overlays.

Why this matters for automated cell engineering

In practice, laboratories assessing new transfection technologies balance theoretical performance with practical considerations, including the ease and reproducibility of deployment within existing automation infrastructure. The studies presented here demonstrate that DropGenie's platform, when integrated with Revvity's FlexDrop Plus non-contact dispenser and Fontus workstation, minimizes integration risk and significantly shortens the time from setup to biological insight. The combined workflow supports immediate execution of both proof-of-concept delivery experiments and structured, multi-parameter optimization on a single cartridge, eliminating the need for prolonged, iterative method development.

Across both an initial on-site deployment and a stringent neuronal cell optimization study, the integrated FlexDrop Plus–Fontus–DropGenie platform workflow enabled high-efficiency GFP mRNA delivery, rapid empirical parameter exploration, and minimal hands-on time. Together, these results highlight the robustness, flexibility, and deployability of the DropGenie system as a transfection module within modern automated workflows, enabling scientists to move quickly from installation to actionable biological data, even in challenging cell models and unfamiliar automation environments.