

Meeting the Increasing Demand for Next-generation Spatially Resolved, Single-cell Transcriptomics

Summary

A biotech customer with a breadboard instrument tasked Gener8 with developing a fully integrated, image-based benchtop instrument for single-cell gene expression profiling. The technology enables medical researchers to efficiently interrogate biology on a systems scale.

Methods Employed

Gener8 converted the customer's existing, complex fluidics into an easily usable consumable that reduced the size and improved reliability. This was accomplished by replacing the reagent fluidic tubing with a rotary valve capable of selecting reagents from multiple different reservoirs. This was bonded to the custom-designed consumable cartridge body. To accomplish this, we had to have tight tolerances on the cartridge and the valve. The over molded port adapter was designed to interface with the instrument so as to pull fluid from the rotary valve. In turn, the rotary valve interfaced with a stepper motor on the instrument to control which cavity on the base cartridge to fill from. The valve rotates to select the required reagent. In designing and developing the cartridge, appropriate materials were selected that were inexpensive, rigid and biocompatible with the onboard reagents.

For the instrument, we designed a custom epifluorescence microscope based on an oil immersion lens. Using an immersion objective offered a higher numerical aperture, providing enhanced resolution and decreased aberrations

At A Glance

Customer

Biotech company

Product

Single-cell Spatial Genomics Platform

Services/ Market

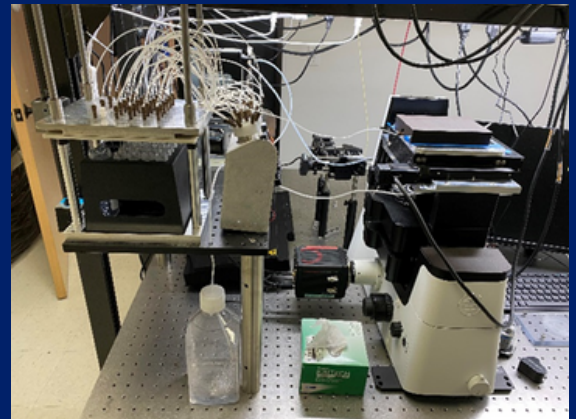
Biotech, life sciences/ translational research

Challenges

The primary challenge was in taking a well-functioning but complex prototype instrument and converting it into a commercial benchtop system. The prototype consisted of 35 reagent connectors, and valves. Another challenge was to make the design compact using generic off-the-shelf components, and to develop a consumable cartridge containing the reagents for running a measurement on the platform.



Original fully functional prototype including high resolution microscope and fluidics system attached to a flow cell holding the sample under test.



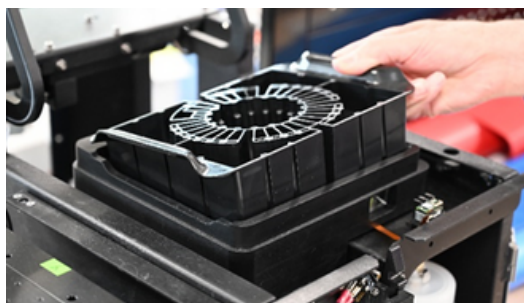


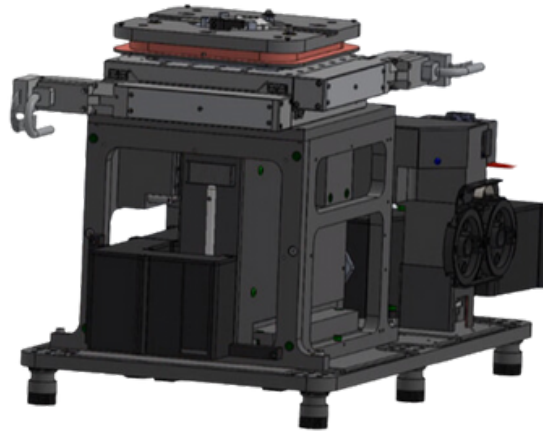
Detail of the valve system which was replaced by a simple single valve in the Gener8 developed disposable

Solution

Gener8 met the customer's requirements in designing and developing a simple, easy to use, compact instrument that combined high resolution imaging for single-cell and spatial genomics analysis. We used off-the-shelf optics components to keep development time and effort low. We were also able to reduce cost and improve stability by using custom mechanics, geared specifically to the instrument's application. Only essential parts of the required microscope functions were implemented to reduce cost and size. By minimizing the overall size of the instrument, Gener8 eliminated the need for an optical table. This was achieved by generating very stable connections of the most sensitive optical components and placing vibration isolators in strategic places.

During assembly of the cartridge, the chambers in the carousel portion of the consumable were filled with the required reagents and then heat sealed. The channels connecting each chamber were covered with a thin film and were sealed using laser welding. The reagents, originally onboard the early prototype instrument, were transferred to a biocompatible consumable which helped reduce the size of the instrument and improved maintenance and serviceability.





CAD of the Gener8 custom epi fluorescence microscope including convenient to use holder for flow cell, high precision x-y stage for scanning the sample, IR autofocus, and vibration control.

Expertise Employed

- Fluidics design and testing
- Optics design and development
- Thermal simulation and testing
- High-volume consumable development
- Electronics design
- Embedded firmware engineering
- Design for manufacturability
- Project Management