GeneChip Fluidics Station 450 design improvements

The fluidic operations performed on the Applied Biosystems™ GeneChip™ cartridges are crucial to the delivery of high-quality results. An essential component of the Applied Biosystems™ GeneChip™ Scanner, the Applied Biosystems™ GeneChip™ Fluidics Station 450, incorporates new features and important design improvements to enhance the operation and performance of the GeneChip assay (Table 1).

This product bulletin outlines important attributes of these design improvements and their impacts on operation and performance of the GeneChip Fluidics Station 450.

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Table 1. Features of the GeneChip Fluidics Station 450.

Design improvements	Benefits
Three position sampling with individual vial detection	• Flexible loading and operation to meet script and user requirements • No increase in liquid volume required
Unattended operation ("walk-away freedom")	• No interruptions to the operator during the run—simply "load and go" • Labor savings
Modular design	• Existing GeneChip Fluidics Station 400 customers gain access to the new functionality and robust design of the GeneChip Fluidics Station 450 • Protects the customer's existing investment in GeneChip instrumentation • Fluidics processing capability can grow with GeneChip array usage
Improved cartridge loading through redesigned door mechanism	• Easier cartridge loading • Secure fluidic connections • Reduced potential for leaks
Improved vial loading through redesigned vial loading mechanism	• Reduced likelihood that the operator will contact the needle • Less chance of sample contamination • Repeatable vial detection through non-contact sensors
New sample detection sensor	• Robust performance • Elimination of fluid errors caused by sample carryover
Leak path isolation	• Critical fluidic components are protected from potential damage • Should leaks occur, a single channel enables rapid identification and resolution by the user
Improved user diagnostics	• User can quickly identify and correct faults without the need for a service call

Three position sampling with individual vial detection

Based on the fluidic script initiated, the GeneChip Fluidics Station 450 will automatically prompt the user for one, two, or three vials containing stain and antibody needed for proper script operation. Vial positions are labeled for intuitive operation and error elimination.

The operator loads all of the vials at the beginning of the run and then lowers a handle that moves all three of the sample needles in tandem. A precision-ground, stainless steel pivot mechanism provides repeatable needle motion, while a ball bearing catch provides smooth needle engagement. The sample probes are spring loaded and retract to eliminate accidental contact with the operator. Likewise, when the lever is down and the vial is absent, a feature in the vial holder protects the operator from accidental contact with the sample needle (Figure 1).

Non-contact optical switches provide reliable performance, as there are no moving parts to wear out. A software "debounce" feature eliminates false detection caused by vibration or user motion. The leaf spring used in the cantilever arm provides a repeatable force to bottom the needle on the vial and eliminates the potential for fatigue failure from repeated flexing. The leaf spring controls the location of sample needles without the use of sliding parts, which can bind. Mechanical stops prevent over-travel of the leaf spring, making possible the repeatable location of the sample needles into the vials without requiring any operator contact with the sample probes.

Unattended operation

The fluidic scripts for the GeneChip Fluidics Station 450 are denoted by the "450" suffix. They maintain the same timing of sequences as the previous version, but enable unattended operation by detecting the three vials and controlling the sequence by which liquid is removed from the vials. Walk-away capability frees the operator to perform other tasks and responsibilities that can improve the workflow of GeneChip array analysis and other laboratory operations.

In many situations, unattended operation will result in faster completion of fluidic functions, as potential delays waiting for an operator to replace a vial are completely eliminated. Many sites have dedicated operators for the washing and staining procedure. Unattended operation can significantly reduce direct labor costs by saving three to four hours per day, as indicated in the example in Figure 2.

GeneChip Fluidics Station 450 throughput per day

A fully dedicated operator working a day shift can perform 16 arrays per day of an assay that has an ~90-minute wash and stain protocol (e.g., the Applied Biosystems™ CytoScan™ HD Array Kit) with one GeneChip Fluidics Station 450. This translates to 4 CytoScan wash and stain batches of 4 chips per batch per day. Shorter wash and stain times would increase throughput.

Additionally, a single Applied Biosystems™ GeneChip™ Scanner 3000 TG System can be expanded to 8 total GeneChip Fluidics Station 450 arrays (128 CytoScan arrays per day). However, at that high of a volume, additional scanners may be needed. An individual CytoScan array takes about 30 minutes to scan, totaling a throughput of 48 arrays per scanner per day. Other array formats can increase throughput. Contact your technical sales specialist for more information.

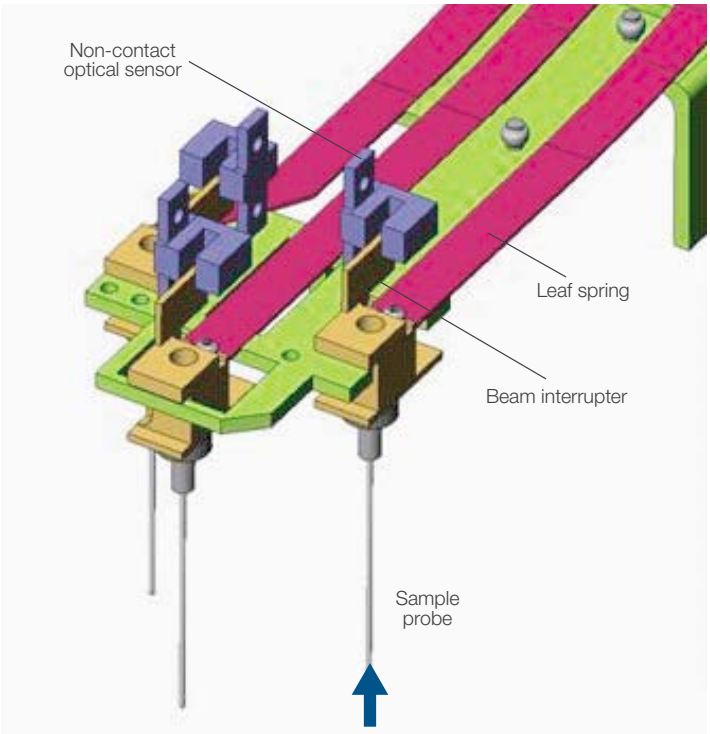

Figure 1. When the operator presses the vial lever down, the sample probes will contact the bottom of any vials that are present. This bottoming action lifts the cantilever arm and causes the beam interrupter to block the optical beam. The interrupted beam of the optical switch indicates to the GeneChip Fluidics Station 450 that the vial is present. The GeneChip Fluidics Station 450 compares the state of each switch against what is expected in the script and will continue to the next step only when the expected vials are detected.

Cost savings

GeneChip Fluidics Station 450 labor savings:

- 1.25 direct labor hours saved per fluidics station run
- 3 fluidics station runs per day at 4 arrays per run
- 4 days per week of fluidics station use → 15 hours direct labor hours saved per week or 780 hours per year

Figure 2. Possible annual labor cost savings with the GeneChip Fluidics Station 450.

Modular design

The front panel is divided into sections attached to each module on the GeneChip Fluidics Station 450. Module replacement by the user is much easier, and this modularity provides new product offerings to GeneChip system customers (Figure 3A).

Self-aligning pins in the base, coupled with the use of a single mounting screw, have simplified the time and effort required to replace a module. External testing has validated the ability for customers to quickly and properly replace modules, providing additional service options and the assurance of higher system uptime, as spares can be kept on site (Figure 3B).

Improved mechanical and fluidic interfaces with the GeneChip cartridge

A number of design modifications have been implemented to improve the interaction between the GeneChip Fluidics Station 450 and the GeneChip cartridge (Figure 4).

Cartridge orientation

Keyed features on the GeneChip Fluidics Station 450 door and GeneChip cartridges ensure proper orientation and eliminate the risk of damage to both the cartridge and the instrument during loading.

Linear door motion and cartridge engagement

The GeneChip Fluidics Station 450 door and mechanism move in a straight-line manner to align the cartridge with the instrument's heater block and fluid probes. The motion is accomplished by a locking cam mechanism attached to an ergonomically designed handle. Non-contact optical sensors confirm that the GeneChip cartridge or wash block is properly engaged.

Elevated guide rails and precision bushings

The rails upon which the door mechanism slides have been repositioned above the GeneChip cartridge septa. This location eliminates the potential for corrosion from contact with salt solution. Precision bushings have been selected for their low friction, zero-maintenance characteristics, and repeatable motion. These preventative measures ensure years of smooth sliding action for the cartridge loading mechanism.

Reduced actuation force

Handle motion is smooth and consistent due to an optimized cam design and repositioning of the cartridge door handle. The force to open and close the door has been reduced, yet still provides proper engagement.

Closing spring

As the operator releases the door lever, predefined forces provided by the mechanism's spring ensure proper engagement of critical features of the GeneChip Fluidics Station 450 to the GeneChip cartridge and the wash block. The engagement force has been optimized by extensive testing of springs with different stiffnesses.

Alignment pins

As the door closes, the cartridge is engaged by tightly toleranced pins that key precisely located features on the cartridge. The pins make initial contact with the cartridge, ensuring proper positioning prior to the fluid probes piercing the septa of the GeneChip cartridge. This eliminates potential damage to the fluid probes or cartridge caused by misalignment. The alignment pins also protect the fluid probes, should the cartridge not be inserted fully.

A

Fluidics Station model	Benefits of modularity
GeneChip Fluidics Station 450	Consists of a new four-module product
GeneChip Fluidics Station 450 upgrade	Customers using the older version can upgrade their existing base station to gain "walk-away capability" and design improvements

B

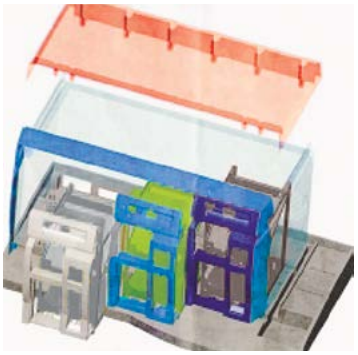

Figure 3. Modules can be individually replaced in the GeneChip Fluidics Station 450.

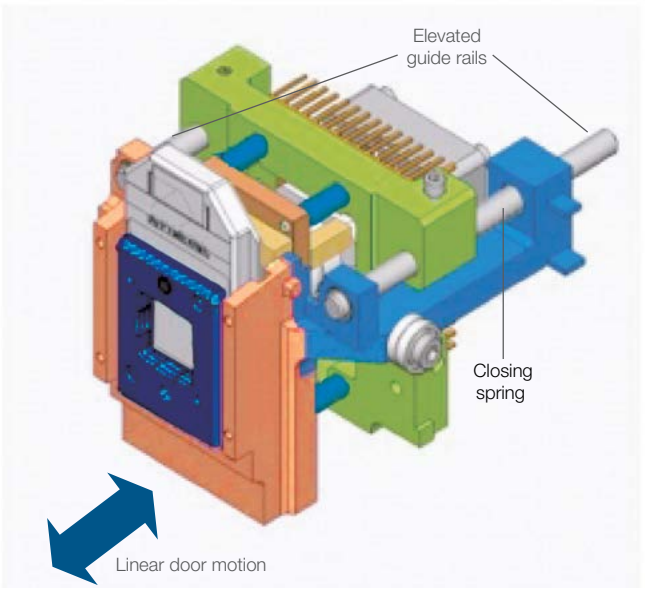

Figure 4. Design modifications improve interaction between the GeneChip Fluidics Station 450 and the GeneChip cartridge.

Controlled depth of penetration of fluid probes

Redesign of the sensor block ensures fixed depth penetration of the fluid probes into the GeneChip cartridge. High-tolerance alignment features have been added to the fluid probes to fix their location in the mounting assembly. These features eliminate the potential for the probes to rotate or shift position, and ensure repeatable fluidic connection between the instrument and the cartridge.

Improved fluid probe design

A new process has been developed to fabricate the side port of the probes. The port location is controlled, reducing the possibility of leakage. The diameters of the port and flow path have been enlarged, and the surface finish on the inside diameter has been modified to eliminate flow disturbances that can create foaming.

Simplified maintenance procedure

The replacement of maintenance parts by service personnel is facilitated by easy, on-site disassembly. Important maintenance parts can be changed without requiring removal of the module or the faceplate.

New fluidic detection sensor

Real-time liquid detection is useful in ensuring that fluidic operations on GeneChip arrays are being completed properly and with the minimum amount of buffer and stain. Additionally, it can identify problems caused by improper or missing reagents.

The presence or absence of fluids is detected by electronic circuitry that measures the conductivity of the liquid present between the fluid probes that contact the GeneChip cartridge. Voltage is applied in very short duration pulses, avoiding the concern of sample degradation due to a voltage potential. Each measured conductivity value is compared against established threshold values in the individual script to determine if the proper liquid is present. If the threshold value is not reached, liquid is either not present or there may be an operator-induced problem in mixing or installing the solutions. Detection of these different situations is important to ensure the quality of GeneChip array analysis.

In the GeneChip Fluidics Station 450, a specially designed circuit board creates an electrical circuit with the fluid probes that pierce the septa of the cartridge. Mounted on the backside of the heater block, these electronics are protected from potential damage that may be caused by leaks.

The conductivity is measured between the fluid probes, thus sensing the conductivity of the liquid in the cartridge. This method has many advantages over prior sensor designs. First, the conductivity probes are much farther apart, minimizing false positives caused by liquid draining down the walls of the sensor block utilized in the older version. Second, the conductivity probes are larger, minimizing false negatives caused by the surface of the probe becoming non-conductive from protein buildup. Every time the cartridge is removed, the probes are wiped clean by the septa on the cartridge. Furthermore, the conductivity path is renewed with every cartridge replacement, eliminating the chance of solids buildup in the conductivity path. Trapped solids can lead to false-negative or false-positive liquid detection, depending upon their conductivity.

Leak path isolation

The module's integral bezel has been designed to accommodate a "drip tray" to divert any leaks away from internal components. Fluids are directed down the front of the pump door and into a "gutter" along the front of the base of the GeneChip Fluidics Station 450. This path provides for easy visual detection and corrective action by the operator.

Improved user diagnostics

The GeneChip Fluidics Station 450 now generates comprehensive diagnostic messages to assist the operator in troubleshooting activities. These messages are displayed on the system's LCD (Figure 5).

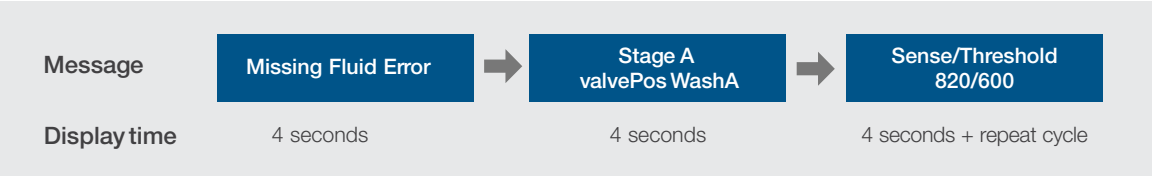

Figure 5. Diagnostic messages are displayed on the system's LCD.

This sequence is continuously repeated on the display until corrective action is taken. In the example in Figure 5, the additional information enables the operator to consider which reagent may be the cause of the problem. If the same problem is present across multiple modules at the same time, it could flag a mix-up in the placement of Wash A and B, or an improperly mixed reagent resulting in the unexpected conductivity. These messages also support more effective dialogue with Thermo Fisher Scientific technical support.

New troubleshooting information that accompanies the GeneChip Fluidics Station 450 directs the operator to take appropriate action (Table 2).

Summary

Significant design modifications have been implemented on the GeneChip Fluidics Station 450 to provide new capabilities and robust performance to users of the GeneChip system. These modifications improve the critical mechanical and fluidic interfaces between the GeneChip Fluidics Station 450 and the GeneChip array. They are expected to assist researchers in producing high-quality genomic information in a more cost-effective manner.

Table 2. GeneChip Fluidics Station 450 troubleshooting quick reference card.

Reported error	User action
Error While Filling	**Cause: system detects improper conditions while filling.** Note where in protocol error occurred. **Identify and correct potential causes.** • Missing or insufficient stain or antibody in vial? • Wash or DI water empty? Air bubbles in line? • Leaks? **Identify if chip is filled.** • If important to recover fluid in chip, then run Recovery script, followed by Resume function. • If not important to recover fluid in chip, run Resume function.
Missing Fluid Error	**Cause: system detects improper conditions.** Note where in protocol error occurred. **Identify and correct potential causes.** • Missing or insufficient stain or antibody in vial? • Wash or DI water empty? Air bubbles in line? • Leaks? **Identify if chip is filled.** • If important to recover fluid in chip, then run Recovery script, followed by Resume function. • If not important to recover fluid in chip, run Resume function.
Invalid Command	**Cause: communications error detected.** Note where in protocol error occurred. **Identify if chip is filled. If important to recover fluid in chip, then run Recovery script.** • Attempt to rerun script if sample loss can be tolerated. If problem persists, contact Thermo Fisher Scientific for service. • If sample loss cannot be tolerated, do not attempt to rerun script. Contact Thermo Fisher Scientific for service.
Improper Script	**Cause: user is attempting to run a GeneChip Fluidics Station 400 script on a GeneChip Fluidics Station 450.** Download proper GeneChip Fluidics Station 450 script and continue.
Sensor Timeout	**Cause: user has waited too long to perform the requested action.** Run Resume function to continue.
Temperature Timeout	**Cause: temperature has not reached required level in expected time.** If ambient temperature is within operating specifications (15–30°C), contact Thermo Fisher Scientific for service.
Valve Motion Error	Run Home script and run desired script again. If problem persists, contact Thermo Fisher Scientific for service.
Valve Not Homed	Run Home script and run desired script again. If problem persists, contact Thermo Fisher Scientific for service.
Valve Out of Position	Run Home script and run desired script again. If problem persists, contact Thermo Fisher Scientific for service.