

Integrating a Hamamatsu FDSS 7000 with onboard 1536 TipCharger Pin Tool System into the TOX 21 Robotic Workcell at NIH/NCATS

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Abstract

The Toxicology in the 21st Century (Tox21) Program is a federal collaboration among NIH's NCATS and the National Toxicology Program at the National Institute of Environmental Health Sciences; the Environmental Protection Agency; and the Food and Drug Administration. Tox21 researchers aim to develop better toxicity assessment methods to quickly and efficiently test whether certain chemical compounds have the potential to disrupt processes in the human body that may lead to negative health effects.

To achieve the goals of the project, a new approach to high throughput processing of assays run on a Hamamatsu FDSS 7000 was required. Pin washing can be extremely challenging. Originally, the FDSS started with three wash stations and a touch stage. Later a vacuum station was added so liquid residue on the pins could be dried. In that configuration, complete washing and vacuuming took three, sometime four minutes. With the 1536 TipCharger cleaning time was reduced and the entire process is done inside of FDSS.

For this project to succeed, the integration of multiple new technologies that had never been integrated together before was required.

Functional screening is commonly run with low capacity automation hardware or manually. Integrating an FDSS with a Kalypsys robot alone was major challenge. It has never been attempted before. Many seeming small but important engineering projects made outsized contributions. The two handoff positions to the FDSS are a custom design with clear access to the vertical sides of the microplate while it is precisely held at the corners. Drop-off and pick-up force on the holder was reduced to near zero to eliminate vibration and improve long term reliability of the mechanism. Software integration was supported by Wako Automation who developed a software bridge to link the scheduler to the FDSS.

The Tox21 Program requires long automation runs, higher throughput speeds and maximum assay sensitivity. The internal upgrades for the FDSS included dual tracks, custom engineered handoffs, an upgraded high resolution camera and integration of IonField Systems 1536 TipCharger for Pin Tools to replace the tip blot station. The combination of new components and better scheduling of the work cell results in increased daily throughput, increased sensitivity, reduced random assay noise and dramatically reduced pin tool carryover with the cleaning process taking half the time of standard FDSS pin cleaning.

The principal challenge integrating the Hamamatsu 7700EX to the TOX 21 high throughput screening system is one of plate grip position. The TOX 21 uses the proven and very reliable Wako/Kalypsys/Aspect gripper. The FDSS when operated as a standalone system receives its plates from integrated, proprietary stackers, which lower them vertically from directly above the instrument's extensible plate nests.

To integrate these two approaches, intermediate handoff lifters were designed and fabricated to facilitate loading. These consist of a handoff nest of SBS standard plate footprint with clearance cutouts to clear the gripper jaws, and plate stop/guides on all four sides allowing about .5mm freedom. Their normal resting position is "down", which is below the level of the FDSS nest. Additionally, optical sensors are provided to verify the presence of the microtiter plate in the up-position handoff nest, and that the FDSS nest is extended, thus ready to receive the plate.

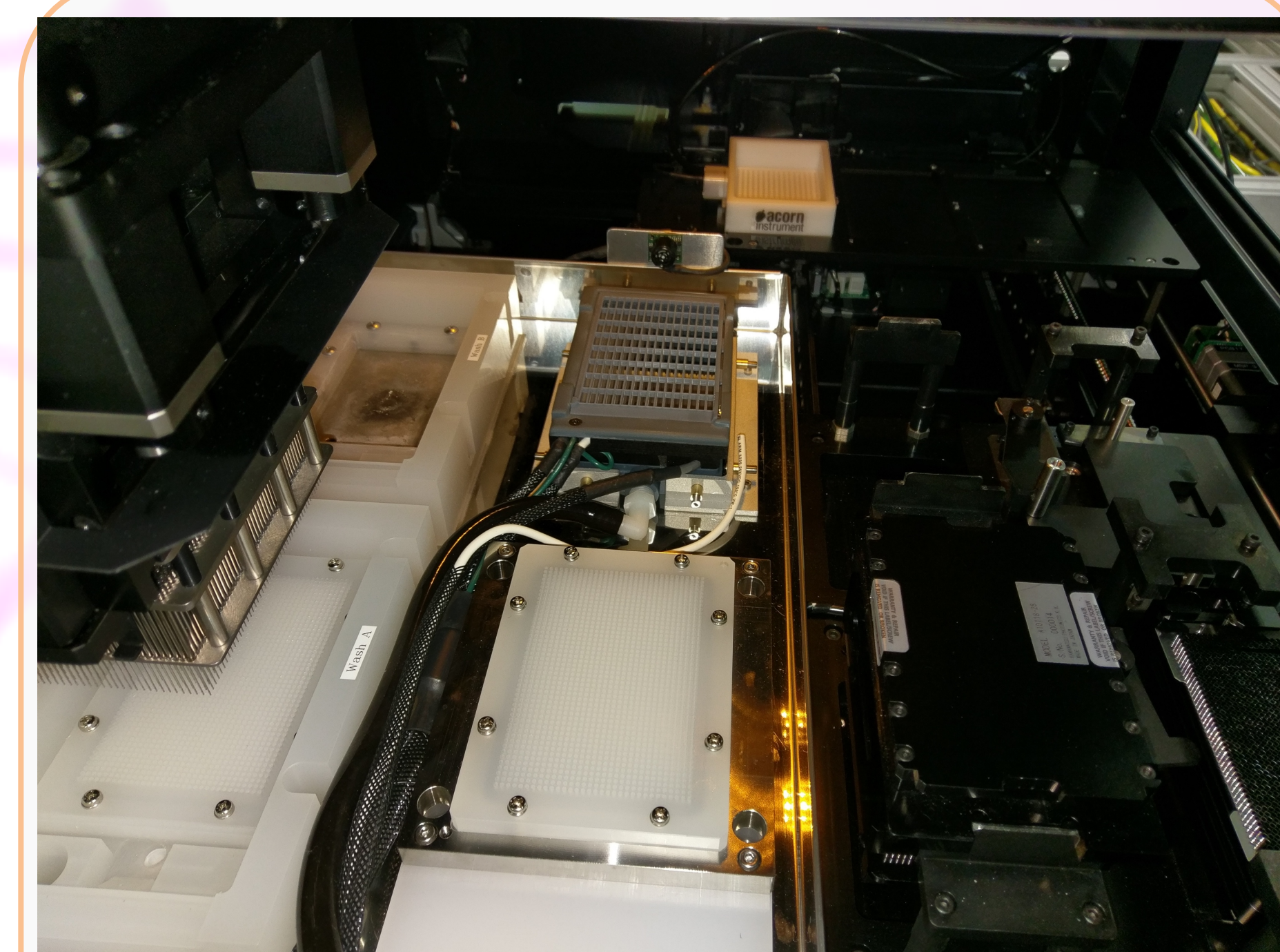


The TOX 21 gripper places the plate in the handoff nest, the plate present status is verified, and the plate is lowered into the handoff nest. The plate is "caught" by the FDSS nest which then retracts, loading the plate into the instrument.

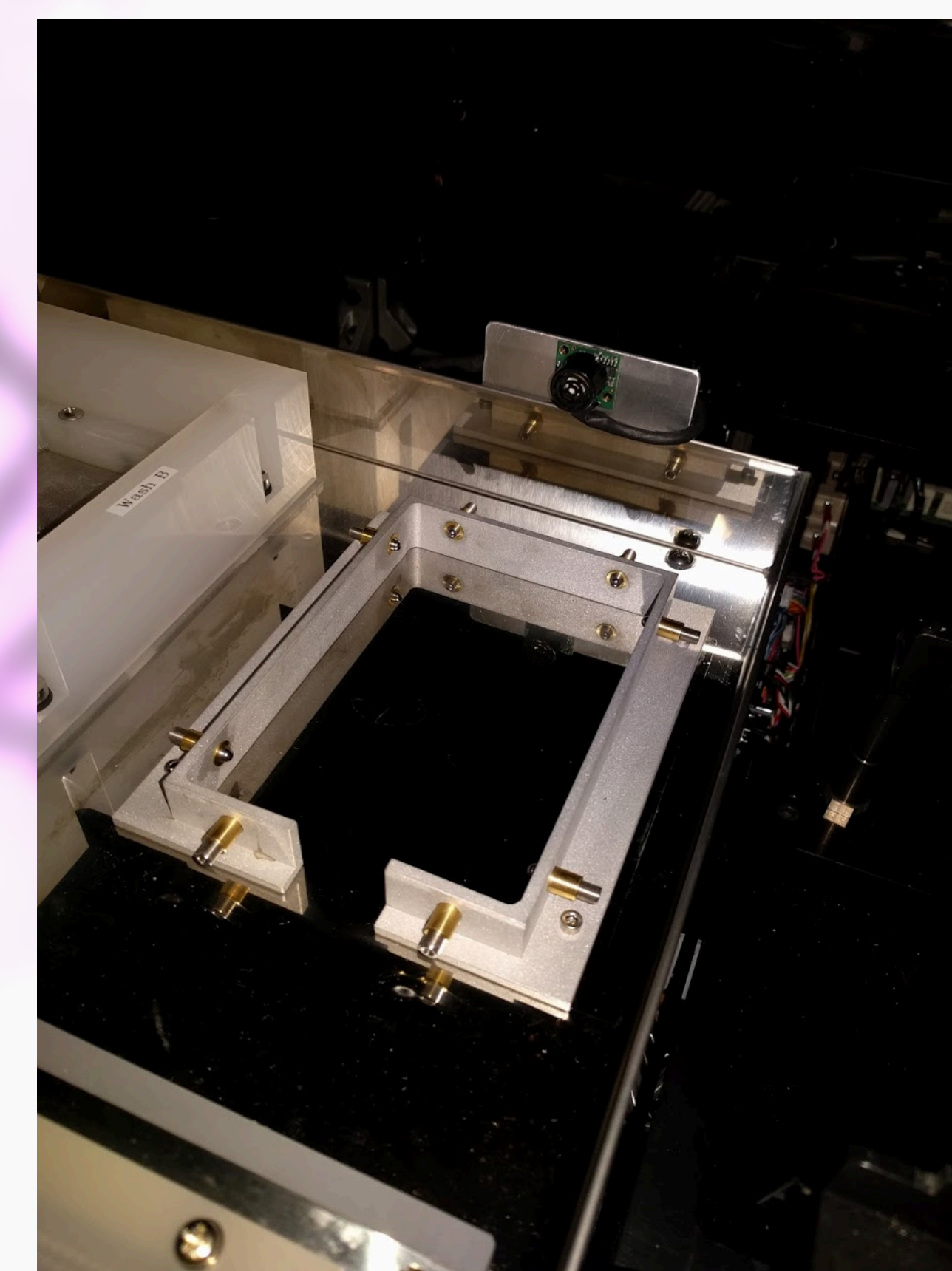


IonField redesigned the cover with large, rectangular openings which tremendously eases position teaching. A custom base was also designed to lower the Z height by 17 mm.

The final modification was an Acorn Auto-fill reagent bath/well for use with protocols requiring bulk reagents.



Integration of the IonField Tip Charger presented the greatest challenge as the FDSS wasn't designed with any empty bays in its tip/pin tool wash area. The pin tool blotter station was deemed the best location. Initial trial revealed that a mount with a very fine positional resolution would be necessary, and the X-Y gantry robot too low to clear the Tip Charger when in the pin tool pickup position.



A kinematic mounting base with multiple 100 threads per inch adjustment screws facilitates rotational alignment of the Tip Charger with the X-Y axis of the gantry robot.

Conclusions

This project took almost a year to identify all the needed upgrades, formulate specifications, work with multiple vendors to get proposals and in the end get several of the vendors to work together.

Perhaps the most important factor making this project successful was to reach an understanding that each vendor has their own way of describing the engineering of their products. Multiple problems needed to have vendors on conference calls exchanging information; and some problems resisted solution until vendors were physically in the same room working with one another.