Table-top Classification and Sorting System for Small Model Organisms

S. F. Graf, D. F. Bösel, I. Kastanis, H. F. Knapp

CSEM's CellFactor platform is used for automated sorting of small model organisms, such as Zebrafish larvae, into multi-well plates for toxicology screens in the pharma and chemical industry. In the newest design, the system is now encased, has a real-time speed measurement implemented and additional sensors/actuators installed. Real-time measurement at frame rates of >60 Hz increases the ejection success while the sensors and actuators reduce user involvement during filling and emptying the system. This allows highly qualified personnel to focus on data interpretation instead of tedious and repetitive work like identification, sorting, and dispensing.

Over the past years, CSEM has developed its CellFactor-technology, which automates the handling of small model organisms to reduce animal testing. The CellFactor technology contains solutions for keeping organisms in a homogenous suspension. To analyze the organisms either fluorescence detection, impedance analysis or imaging in combination with machine learning algorithms for detection and classification can be used. Finally, the analyzed organisms can be sorted into flasks or be dispensed into multi-well plates for further processing. Currently, two applications of the CellFactor technology are being developed. The muTish demonstrator [1] works with small model organisms in the size range of 50 to 800 um while the CellFactor (shown in Figure 1) is optimized for the Zebrafish model with a size range of 500 to 2000 um. The transport mechanism for the Zebrafish larvae is based on viscous drag forces for which the patent recently has been granted [2].

Latest improvements of the CellFactor are the encasing of the sorting and dispensing module into a housing which also contains the mechanics, optics, electronics as well as the buffer and waste bottle (see Figure 1 and Figure 2). Easy access to the bottles and the sample supply port are given and the multi-well plate can now be moved to a suitable position for manual or automated exchange.

Furthermore, bubble detectors and automated pinch valves were integrated to allow the automatic filling and emptying of the system.

The improved imaging system can now additionally be used for real-time measurement of the speed of the passing larvae. More than 60 frames per second (frame size 688 × 164 pixel) are analyzed. A tracker tags each larvae and calculates its speed. Using the real-time speed of the larvae, improved the ejection success rate and reduced the time to fill a multi-well plate to about 4 minutes.

Currently, the built-in machine-learning classifier is being trained with early stages of fertilized Zebrafish eggs with the goal to automatically differentiate between fertilized eggs in the 2- and 4-cell state (which corresponds to the first hour past fertilization) and to dispense the latter into a multi-well plate for further processing. This greatly improves the efficiency of post treatment procedures of the fertilized eggs, as required by end-users that CSEM is in contact with.

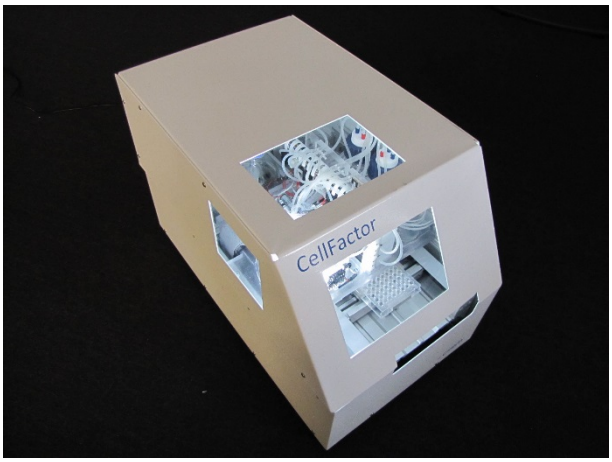

Figure 1: CellFactor in its newest form for analysis and sorting of small model organisms.

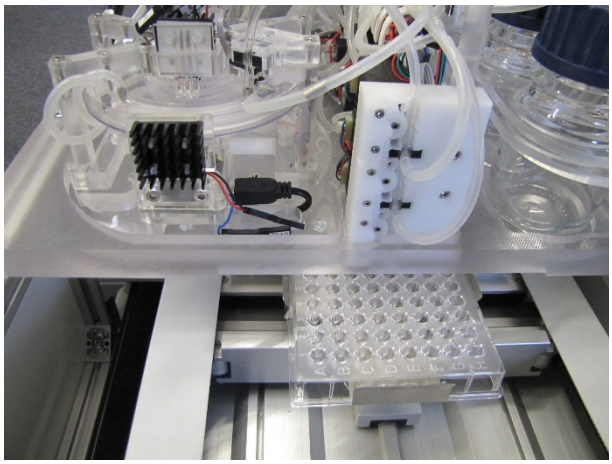

Figure 2: CellFactor interior. (top left) sorting module, (bottom) well-plate handler, (top right, white) dispensing module.

CSEM would like to thank the Swiss Federation and the MCCS Micro Center Central Switzerland for their financial support.

[1] S. F. Graf, *et al*., "muTish–Tools to monitor and handle medium sized biological entities", in this report, page 18.

[2] S. F. Graf, N. Schmid, H. F. Knapp, "Device, System and Method for Storing and Sorting Cellular Samples". U.S. Patent 8,940,541, issued Jan 27, 2015.