Monitoring Low Volume Liquid Handling in High Throughput Screening

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Introduction

We present a computer vision based liquid handler monitoring application. It is aimed at microtiterplate based high throughput applications and at detecting low volumes (<10µl) in shortest time-frames. It is possible to screen a plate in <10s. Its hardware costs are low, such that a robot (see **fig. 1** for an impression) can be equipped with multiple sensors if required. The aspired future application of the system is online monitoring of liquid handling operation to detect errors early and efficiently.

System Concept

We investigated the use of two flatbed-scanners (CCD/CIS) and a camera system as hardware base (**fig. 3,4**). While the scanners provide a good uniform image of all wells of the plate, the camera system suffers from distortion and changing perspective (see **fig. 5**), but offers instant image acquisition. For initial development, we focused on the flatbed scanners.

Labware Compatibility

The system can be configured to work with different microtiterplates. The system is tested to work with 96 and 384 well plates, different shapes (V,U, Flat) and the materials Polypropylene and Polystyrene (PP/PS).

GUI for Setup and Plate Evaluation

A GUI is included that implements all functionality provided to the process control system and adds setup and batch-operation functionality. It is used to configure the system for new labware or to investigate previously recorded data.

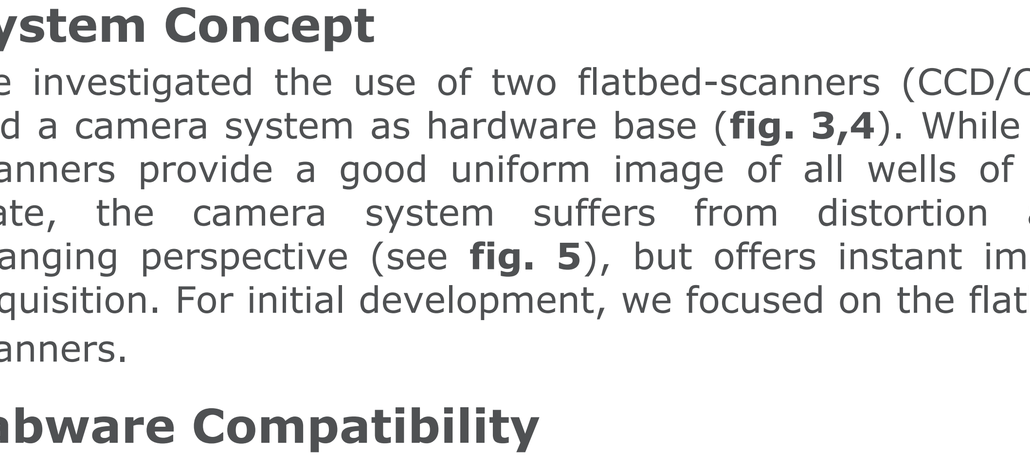


Figure 1: Visual Alp on flatbed scanner base

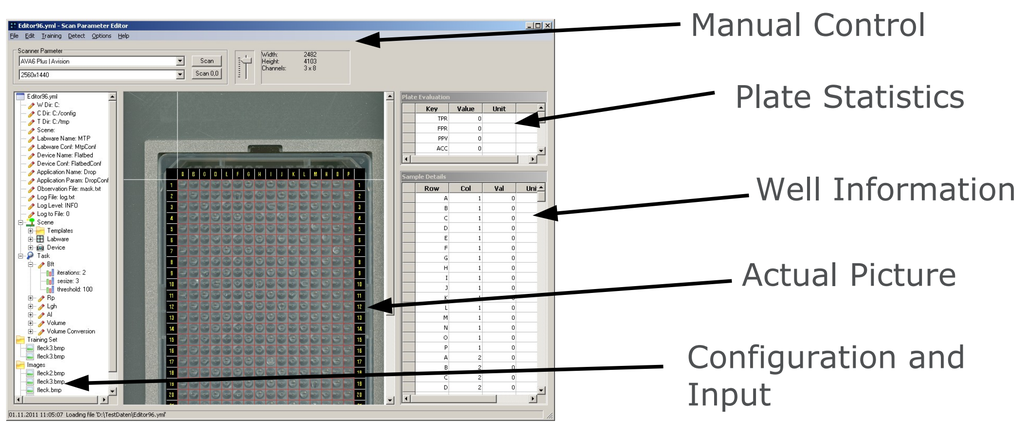


Figure 2: GUI for Setup and Plate Evaluation

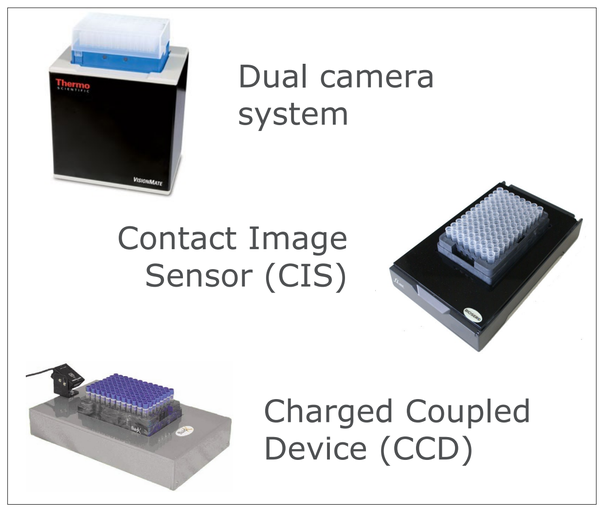


Figure 3: Imaging devices, t.t.b.: Cam, CIS/CCD scanner

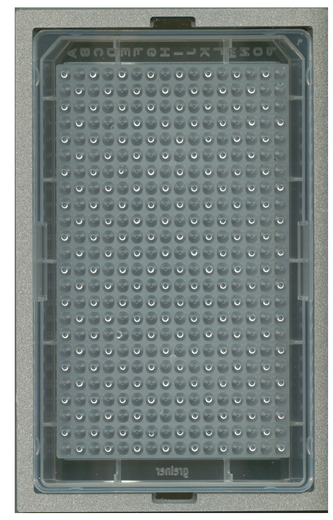
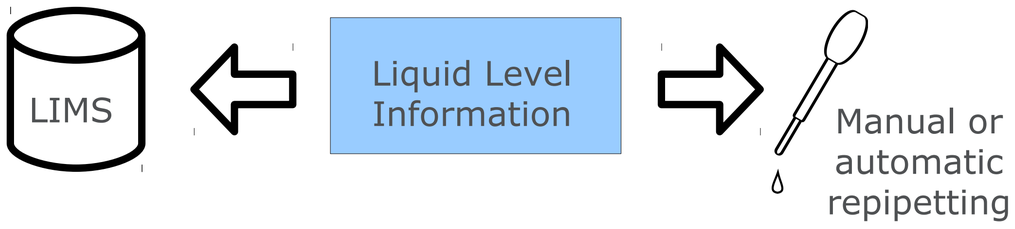


Figure 4: Example picture, 2µl, CCD scanner

Application Liquid Handler Monitoring

The system can be configured in different ways to react on the measurement results. For example, they can be passed to a Laboratory Information Management System (LIMS) for documentation. By observing trends, such as an increase in erroneous empty wells, it is possible to detect errors early. It would also be possible to pass the results to the pipettor to repipette the erroneous well.



Results

The qualitative performance is shown in **fig. 5**. A covering lid was considered to investigate the effect of ambient light. The first quantitative evaluation shown in **fig. 6** shows acceptable results below 3µl. **Fig. 7** shows a cause for the decreasing performance with growing sample volume.

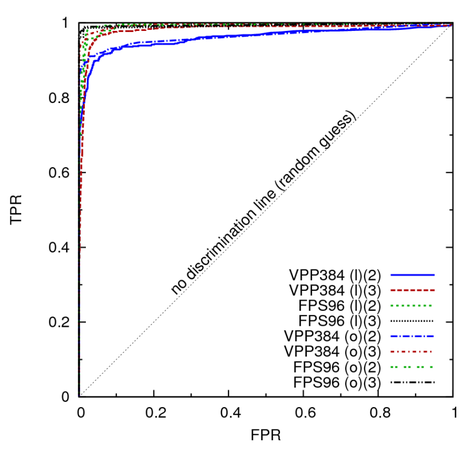


Figure 5: Qualitative Results with (l) and without lid (o), CCD

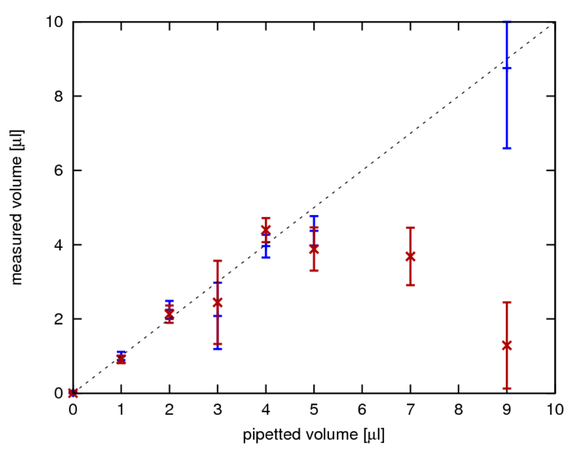


Figure 6: Quantitative evaluation possible up to 4µl

Conclusion & Outlook

Our validation test proved effective qualitative drop detection. The future work will focus on improving quantitative evaluation and to enlarge the operating range.

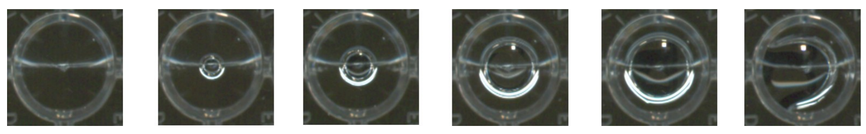


Figure 7: A growing drop clinging to the wall

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