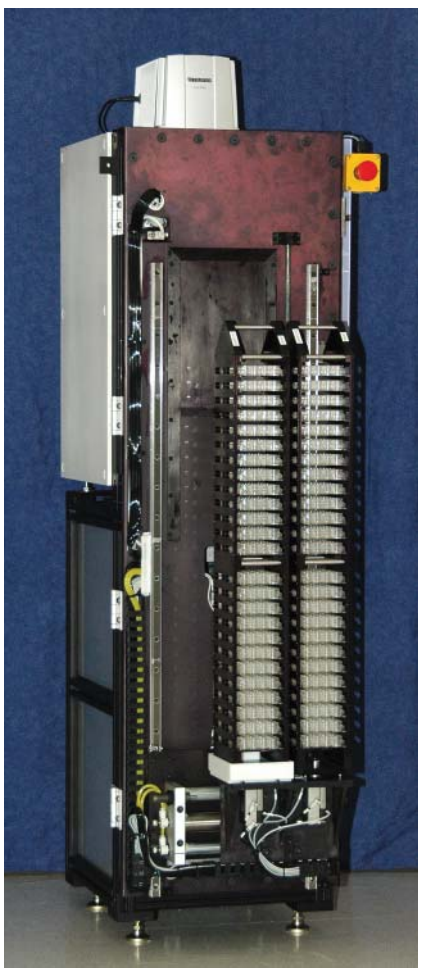
Fraunhofer USA

Center for Manufacturing Innovation

In collaboration with Boston University, the Fraunhofer Center for Manufacturing Innovation provides manufacturing solutions to a broad range of industries, including optoelectronics, biotechnology and semiconductor, with a focus on high precision, next-generation automation systems and instruments. Engineers at CMI develop novel machines, devices and instruments for clients launching new products or who need to improve existing manufacturing operations. CMI also forms engineering "partnerships" with clients, providing product development assistance and objective bench-marking against industry best practices.



Automated Microtiter Plate Imager
Installed at a customer's site.

During 2006, CMI worked on and deployed a number of systems including a laser-interference lithography tool for the manufacture of large optical gratings. Two other representative projects are detailed here.

CMI is working with a a large pharmaceutical company to automate the loading of individual micro-titer plates, from a queue, into a Fujifilm LAS-3000 Imaging System for optical analysis. The goal was to accomplish this objective with a cost-effective, highly reliable solution, employing best-practice principles of automation that took up very little laboratory space and could be easy utilized by chemists, not engineers.

The customer runs an assay in which the final content analysis is performed by the Fujifilm LAS-3000 Imaging System. This system scans one micro-titer plate at a time, and requires several minutes for scanning and analyzing the data. Consequently, an operator is continuously engaged, loading and unloading micro-titer plates. Since there can be hundreds of micro-titer plates processed in one day, the current approach keeps an operator busy the entire day performing a mundane operation instead of analyzing the data generated by the process. Furthermore, since incubation, the operation upstream, is a batch process in which many micro-titer plates can be incubated at once, a labor bottleneck occurs at the imaging station. This is because it is a serial process, in which individual micro-titer plates are scanned.

The customer wanted to automate the loading of the Imaging System such that a large number of micro-titer plates could be queued, thus freeing the operator for significant periods of time. It had to do this in a very cost-effective manner, retrofitting the imaging/analysis operation with minimal impact on the rest of the operation, both in terms of processing and required floor-space.

Fraunhofer CMI has a wealth of experience developing custom automation equipment for the photonics, biomedical, and semiconductor industries, and was uniquely positioned to undertake this work.

Fraunhofer CMI proposed a system to minimize the number of transfer points “handoffs” as well as the number of operations required to achieve the task. In a unique approach, the micro-titer plate is not loaded and left in the chamber and consequently picked up and unloaded. Rather, the arm/gripper assembly that picks up the micro-titer plates from the queue, actually holds on to the micro-titer plate during imaging. Thus, the micro-titer plates will not be placed on a “shelf” contained in the photo chamber. This eliminates a handoff operation, which like all handoffs has a non-zero probability of failure.

In this approach, the entire loading/unloading mechanism, including the magazines in which the micro-titer plates are queued, are all attached to what became a new door of the chamber. As can be seen in the picture on page 20, the load/unload mechanism is actually attached to the inside of the door, thus resides inside the chamber. It is very similar in concept to a CD/DVD load/unload mechanism, augmented by three (only two shown in the figure for clarity) magazines, attached to the outside of the door, in which the micro-titer plates are queued. Since the entire mechanism is attached to door, the Imaging chambers can be easily retrofitted by simply removing the current doors and bolting on the new door with the mechanism all integrated in. Thus, there is no additional floor space required and no need for additional framing to support stand-alone carousels, robots, etc.

The new door has a pneumatically actuated flap covering and uncovering the slot through which the micro-titer plates are loaded and unloaded, thus, blocking out any ambient light during imaging. Hence, the new door with the integrated mechanism will only be opened for maintenance needs.

Except for the magazine’s vertical motion for loading/unloading a particular micro-titer plate, all the other actuators are pneumatic (in order to reduce cost), as they toggle between only two positions. The magazine vertical motion was accomplished through servo motor drives to facilitate the required precision motion. Thus, in operation, the system will cycle through one magazine, and then the next magazine will be indexed into load/unload position. The inactive magazines can be loaded or unloaded while the system is working.

The queue held no less than an hour’s worth of micro-titer plates supply, but could easily be increased, to accommodate future increased requirements. The loading/unloading can be performed while the Imaging system is processing the data it collected after the scan; thus, the current cycle times were also decreased. Fraunhofer also had to develop a custom interface to the FUJI Imaging system software.

This prototype device may have application to other areas of drug discovery that require similar imaging analysis.

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Automated Psoriasis Treatment

Millions of people around the world have psoriasis, a chronic disease characterized by sharply demarcated erythematous plaque with a silvery white scale. Psoriasis effects 3 to 5 million Americans and up to 3 percent of populations worldwide. Most common sites of involvement are scalp, elbows and knees, followed by nails, hands, feet and trunk. Most patients with psoriasis tend to have the disease for life. While psoriasis is not typically life threatening, it can greatly affect appearance, self-esteem and overall quality of life.

A large number of the patients with psoriasis can be treated using UV light exposure. Laser emitting in UVB wavelengths within the action spectrum of psoriasis have enhanced the range of phototherapy devices utilized. The best example of the enhancement of the phototherapy treatment of psoriasis has been the use of the 308 nm excimer laser, which is starting to have a more prominent role in psoriasis treatment. The laser allows treatment on only the affected skin, thus considerably higher doses of UVB can be administered to the psoriatic plaque at a given treatment compared with traditional phototherapy.

Although the currently available 308 nanometer excimer laser allows the treatment to be given only at the specific lesion as compared to the conventional narrow band UVB, it still exposes some of the healthy skin around the treatment area to harmful UV radiation. It also requires manual application by qualified personnel, which can be expensive and time consuming. Also, since the laser pulse has to be manually given one after another, there will always be minimal areas of the psoriasis lesion left untreated. And at the same time, there will always be the risk of stacking the pulses onto the same area, thus over-exposing the area. The system currently under development at Fraunhofer CMI will eliminate the above problems of the laser-based system.

The Fraunhofer USA Center for Manufacturing Innovation (CMI), together with Wellman Center for Photomedicine at Massachusetts General Hospital and Boston Array Technologies, Inc., are developing an Automated Psoriasis Treatment System based on recent Micro Electro Mechanical Systems (MEMS) technological developments.

The goal of this NIH-funded project is to develop a stand-alone working Automated Psoriasis Treatment prototype instrument. The device will be able to use monochromatic UVB light (308 nm) to selectively treat psoriasis lesions and minimize healthy skin exposure to UV light.

In the core of the instrument being developed is the Digital Micromirror Device (DMD) by Texas Instruments and a machine vision system.

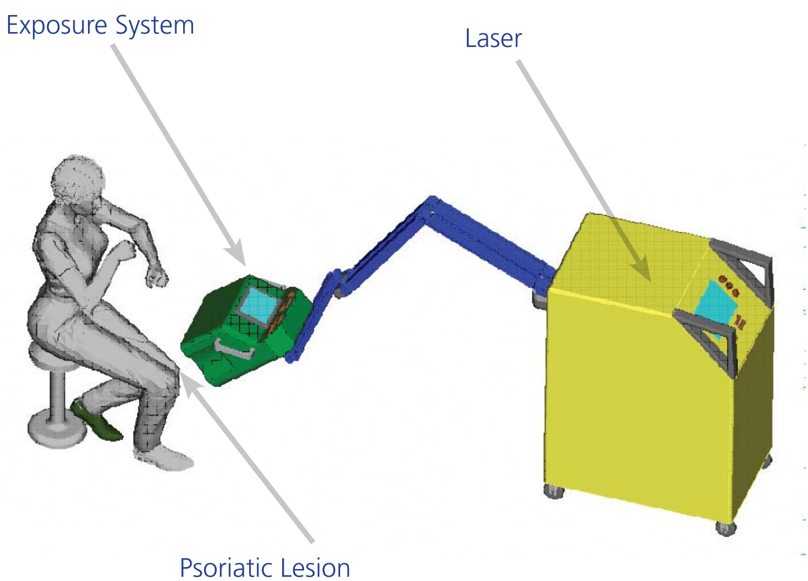

Figure 1. The overall view of the instrument under development.

The Automated Psoriasis Treatment System will eliminate exposure of healthy skin by using virtual masks where a large number of small individually addressable mirrors will be used to selectively illuminate only the lesion areas. To create a virtual mask, a vision system will image the lesion area, analyze the image and activate those mirrors necessary to illuminate only the lesion. In addition, the vision system will be able to adjust the illumination in real time if the patient moves slightly.

Image analysis software is the key element of the system. It needs to be capable of acquiring and analyzing images of psoriatic lesions in real time and generating correct virtual masks for exposure. The main requirement for the exposure system is to minimize the exposure of the healthy skin while treating the lesions. Figure 2 illustrates the current level of the software development.

The Fraunhofer USA Center for Manufacturing Innovation hopes that success in development of this Automated Psoriasis Treatment System and its eventual commercialization will improve lives of millions of psoriasis patients

Partner Statement

Our collaboration with Fraunhofer over the last 10 years has been highly productive both in terms of research and education. On the research side, we have collaborated on a number of projects, ranging from DNA array fabrication for medical diagnostics, to micro-cryogenic pumps for on-board satellite electronics. While the College of Engineering at Boston University is well known for being on the forefront of academic research in several areas of national importance, Fraunhofer's close ties to industry have helped the College establish itself as a valuable resource for Industry as well.

On the educational side, Fraunhofer provides engineering students with a most-valuable, out-of-classroom experience by engaging them in real industrial projects while still in school. Not only does this hands-on experience excite the students about their chosen profession, but it also makes them highly marketable upon graduation.

We are very excited about our new Alliance with Fraunhofer for the development of medical devices, instrumentation, and diagnostics, and look forward to continued collaboration into the future.

Dr. Kenneth Lutchen, Dean
College of Engineering
Boston University

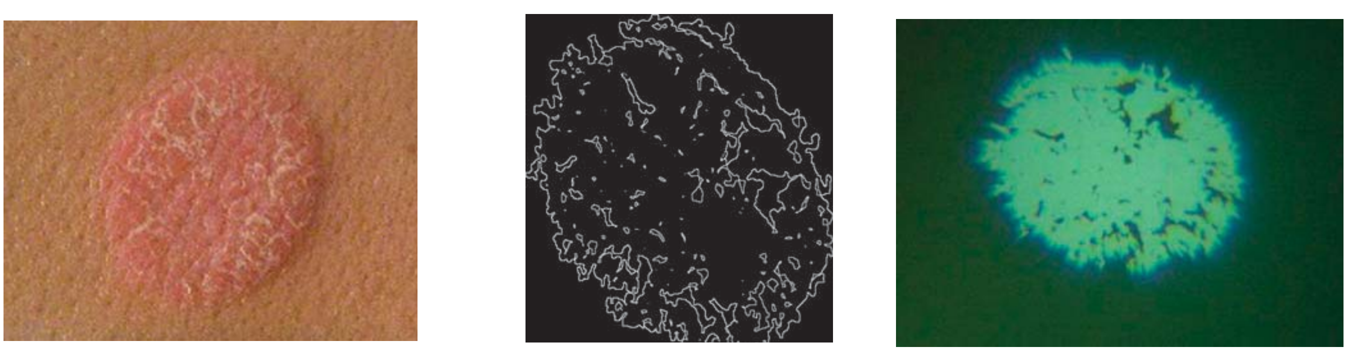

Figure 2. Psoriasis lesion image (left); result of automated image recognition algorithm (center) and an image generated using UV light (right, scale is approximately 8.5 centimeters)