Center for Manufacturing Innovation

The Fraunhofer Center for Manufacturing Innovation (CMI), together with its partner Boston University, conducts advanced research and development leading to engineering solutions for a broad range of industries, including biotech/biomedical, photonics, and renewable energy. Fraunhofer engineers, faculty and students scale up basic research into advanced technologies for client companies in the U.S. and abroad. CMI's primary focus is on next-generation, high-precision automation systems as well as medical devices and instruments that lie at the intersection of engineering and biology.

During 2011, CMI was successful in acquiring a number of contracts from industry in the area of manufacturing automation. The specific applications ranged from high speed manufacture of disposable products, to highly sophisticated, intelligent automation for genetically engineered products. In the biotech/biomedical space, CMI worked on innovative ways of assessing antibiotic susceptibility, novel in-vivo cancer detection medical devices, and the automation of sample processing, a recognized bottleneck in the automation of biological assays.

In-Vacuum Positioning System

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Fraunhofer CMI has developed a space and environment-optimized in-vacuum positioning system for the use in custom spectometry instruments. These research tools require precise placement of test samples in the demanding environment of a vacuum chamber. Current designs utilize commercial, "off-the-shelf" linear positioning hardware that is modified to work under vacuum conditions. However, this commercial equipment is not space efficient and requires a working volume much larger than the sample positioning volume. As a consequence, the vacuum chambers are larger than fundamentally necessary, resulting in higher cost, and longer times to draw vacuum. Furthermore, since these positioning devices were not specifically designed for use in vacuum, their reliability is sub-optimal.

The in-vacuum position system developed by CMI is extremely compact with respect to their maximum travel. This allows the customer to use the in-vacuum space more effectively and specify a smaller vacuum chamber for reduced cycle times. The stages have an X/Y travel of 125 x 125 mm with an external envelope of 200 x 200 x 63 mm. All necessary instrumentation, including encoders, limit switches, motors, etc. are packaged within the envelope of the stage.

In addition to minimizing space requirements, the positioning system is capable of high positioning accuracy on the order of microns. Since the system must operate inside a vacuum, special attention was paid to removing the heat generated by the motor through the housing of the stages without interfering with the positioning accuracy. Additionally, the system provides an electrical vacuum feed-through that allows the electrical signals to be passed through the wall of the vacuum chamber. The positioning system is driven by an external controller, and can be interfaced with other control hardware using Ethernet.

CMI Automated Winder for Fiber Optic Gyroscope Production

Advanced Metrology and Guiding for Fiber-Optic Coil Winding

Fiber-optic gyroscopes, also called Sagnac interferometers, are highly precise sensors for the detection of angular motions. By measuring the phase shift between two synchronous light signals traveling in opposite directions around a fiber coil, large and highly dynamic rotations as well as small angular shifts can be detected reliably over long periods of time. Such gyroscopes are used for navigation and guidance in airplanes, ships, satellites, submarines, missiles, and other vehicles.

The heart of a fiber optic gyroscope is its coil, which has to be wound starting from the center of its fiber length using exact winding patterns in order to guarantee a symmetrical optical path for both optical signals. The winding requires precise fiber placement as well as close control of the winding tension. These requirements, combined with typical coil length of multiple kilometers of fiber, makes automating the winding a necessity for the economical production of high-quality gyroscopes.

CMI has been a pioneer in the development of automated fiber optic winders for gyroscope production. During 2011, CMI has taken these winders to new heights with the development of a real-time metrology system that allows the machines to map out and wind different size coils with no change-over time, thereby facilitating production of a wider variety of gyroscopes on one machine, as well as making the overall process more cost-effective. Furthermore, the development of an improved fiber guiding system has further reduced the already minimal operation involvement, while increasing the quality of the wind.

Accelerated Antibiotic Resistance Testing

Fraunhofer CMI, in collaboration with Harvard Medical School/Brigham and Women's Hospital, has developed and implemented a novel and rapid diagnostic platform for determining the antibiotic resistance of bacteria. Over the past twenty years, antibiotic resistance has developed into a public health crisis. Medications that were once considered the 'drugs of last resort' are now proving to be ineffective against certain infections. In fact, sixty percent of Staphylococcus aureus, or 'staph', infections are now resistant to methicillin, a close relative of penicillin.

It is critical to accurately diagnose these resistant S. aureus, or MRSA, infections in order to prescribe the proper medications to patients. However, current diagnostic methods rely on the growth of bacteria in the presence of antibiotics, and thus suffer from long wait times – 18 to 24 hours at minimum. These slow tests force physicians to prescribe one drug and then later transfer patients to other more effective medications. This pattern of care is only exacerbating the problem of resistance.

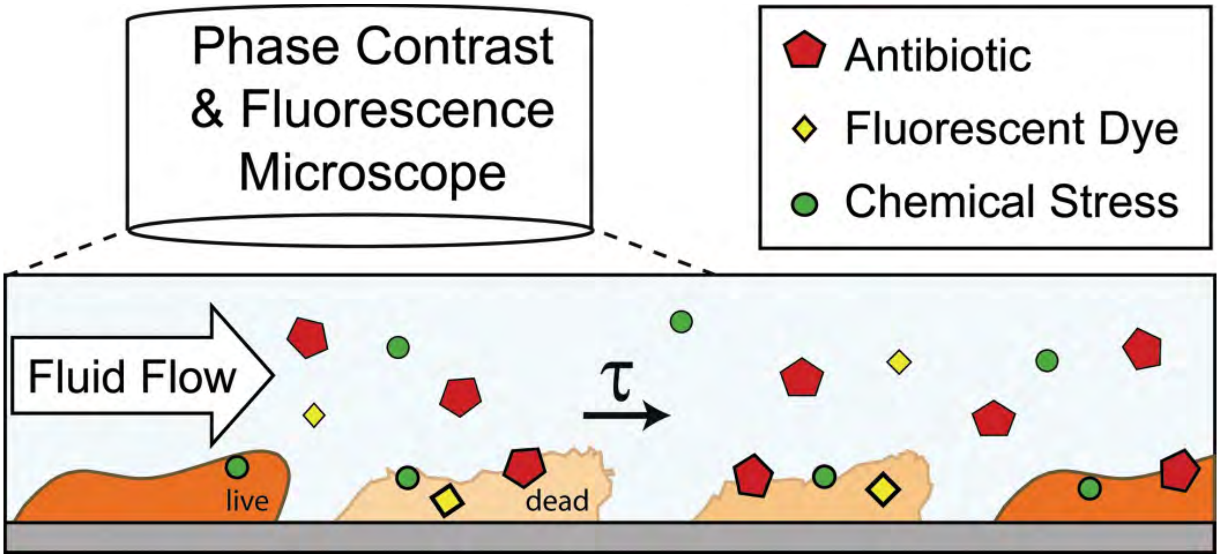
The diagnostic test developed at Fraunhofer CMI compares the percentage of dying bacteria, over time, within microfluidic channels that either contain or do not contain an antibiotic of interest. Susceptible strains are killed in the presence of antibiotic while resistant strains are able to survive. Because our method does not rely on the growth of bacteria as a read-out, it can deliver results within an hour.

Bacteria are immobilized on a glass slide, which is incorporated into a flow cell that utilizes PDMS to create the walls of four microfluidic channels. Fluids containing both culture media (± antibiotic) and an additional optional chemical stress agent are then pumped through the channels applying mechanical stress to the bacteria. The chemical stress alone does not kill the bacteria, but we see an increase in signal for susceptible bacteria when it is included. Once flow has begun, two images of each microfluidic channel are taken every two minutes: one phase contrast image (to determine the number of total cells) and one fluorescent image (to measure the number of dead cells). For rapid and reproducible testing, we have automated the microscope stage movement, the image collection, and the image analysis.

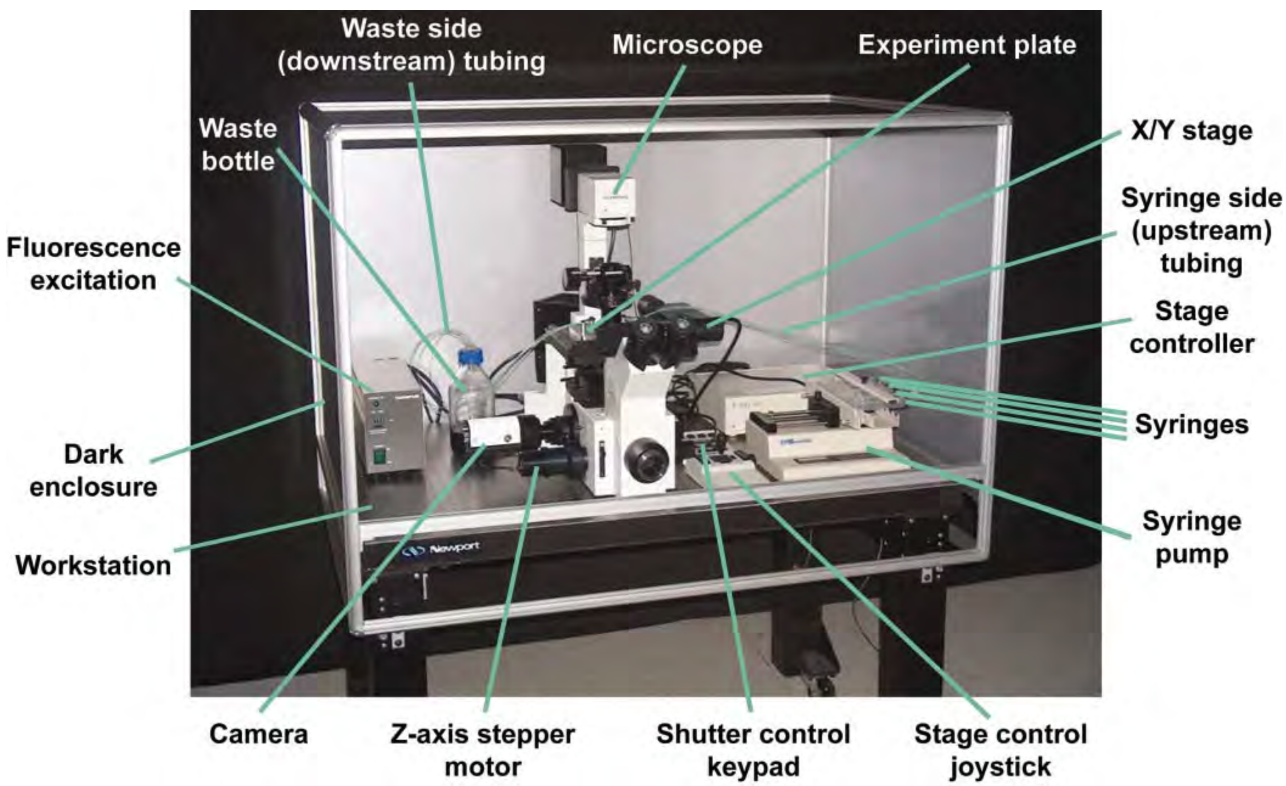
We established our experimental conditions by comparing the rates of killing of a methicillin-susceptible and a methicillin-resistant S. aureus strain. Testing these strains multiple times allowed us to develop phenotype separation criteria based on the percentages of dead cells after 60 minutes of exposure to stress and antibiotic. These criteria proved effective. Subsequently, we successfully determined the susceptibility of 16 clinically important S. aureus strains in a blinded study, demonstrating the clinical utility of our rapid diagnostic method. In the near future, we envision that our platform can be adapted to test other bacterial species with different antibiotics.

CMI Internship Program

CMI's internship program continues to thrive, providing a global experience to 12 European interns per year. Since its inception, the program has hosted over 150 interns, mostly from Germany. Interns are provided with housing and a stipend, and are encouraged to experience not only the American workplace, but the American culture as well. The program has been tremendous success, receiving rave reviews from all involved. These students are subsequently highly recruited in Europe, as they bring a global perspective to the job.



Rapid microfluidic antibiotic susceptibility concept. Fluid containing antibiotic, fluorescent dye, and chemical stress is flowed over immobilized bacterial cells. Bacteria that are resistant to the antibiotic survive the test while those that are susceptible die and become fluorescent.



Experimental set-up. The system is designed to automatically collect time-resolved fluorescence and phase contrast microscopic images while maintaining a constant flow rate.

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