NIH Award from the National Institute of Allergy and Infectious Diseases

Principal investigator: Aaron Packman, civil and environmental engineering
McCormick School of Engineering and Applied Science

- Project: Synchrotron imaging of crystalline biofilms in urinary catheters
- Start Date: June 1, 2009
- Total Award Amount: $222,896

How the results of this project will benefit society:
Proteus is an extremely common pathogen in urinary tract infections, and is particularly problematic in patients subject to long-term urinary catheterization. Catheter blockage from Proteus infections still represents a major, ongoing, and serious problem for patients and for long-term care facilities. P. mirabilis hydrolyzes urea, leading to an increase in the pH of urine and the formation of mineral deposits within the urinary tract. These deposits form stones and encrustations in the bladder and kidneys, as well as encrustations on inserted devices such as catheters and ureteral stents. A lack of understanding of the structure and composition of crystalline biofilms, or slime layers that develop naturally when bacteria congregate on surfaces, has hindered the development of new treatments to prevent catheter infections and control catheter blockage. The project results will indicate how the crystalline structure influences the development of Proteus biofilms on urinary catheters and suggest improved strategies for treating these infections and for preventing catheter blockage.

The problem the project is trying to solve:
A suite of synchrotron-based x-ray imaging methodologies will be used to assess the development of crystalline biofilms formed by Proteus mirabilis in urinary catheters. Approximately half of patients with long-term urinary catheters develop catheter blockage as a result of these infections. Blockage incidents can cause serious acute symptoms and are a contributing factor to morbidity and mortality in catheterized patients. The need to monitor and replace urinary catheters also presents a substantial burden for long-term management of these patients.

How this project will work:
One major challenge in understanding the development of crystalline biofilms and the associated catheter blockage is that the mineral deposits prevent use of optical methods such as confocal microscopy. To overcome this limitation, Proteus biofilms within urinary catheters will be imaged using sophisticated synchrotron-based methods that we have recently developed for non-invasive investigations of mineral samples. Synchrotron x-ray computed micro-tomography will be used to image the pore structure of Proteus biofilms in three dimensions with near-micron-scale resolution, and synchrotron x-ray diffraction will also be used to assess the distribution of different mineral phases within the biofilms. In addition, environmental scanning electron microscopy will be used to assess cell distributions within biofilms, and analytical electron microscopy will be performed using energy-dispersive spectrometry and electron diffraction to determine chemical distributions within the crystalline deposits. Analyses will be performed on intact catheters containing crystalline biofilms grown in vitro using a model bladder system, as well as on blocked catheters retrieved from patients. Quantitative descriptions of the biofilm pore structure will be developed using image analysis methods, and the internal transport environment within each biofilm will be evaluated by using the tomographic data in conjunction with lattice Boltzmann simulations of pore fluid flow. Results obtained for different Proteus strains and different growth durations will be compared in order to assess the interplay of pore structure, internal transport conditions, and crystalline biofilm development, as well as the overall effects of biofilm growth on catheter blockage.

This award is funded under the American Recovery and Reinvestment Act of 2009, NIH Award number: 1R21AI079640-01A1.