Membrane Science, Engineering and Technology Center (MAST)

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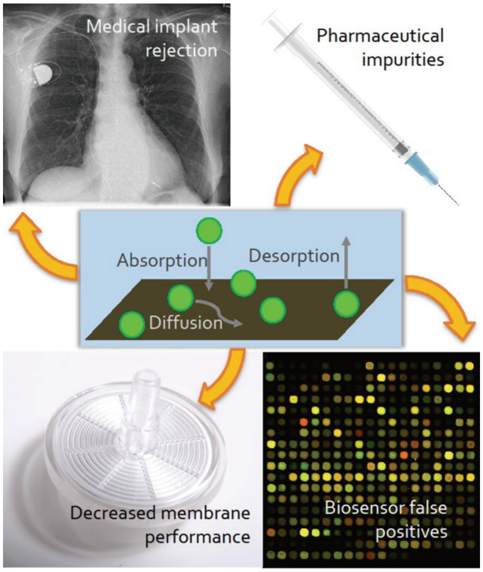
Single Molecule Protein Interactions with Surfaces



The ability to observe individual protein molecules attach to (adsorb), detach from (desorb), and move around (diffuse) on material surfaces will allow industry to develop improved materials that are not readily fouled by protein layers. This will decrease production costs and improve performance, product quality, and safety in a variety of industries where proteins are critical components.

The understanding of what occurs when protein molecules approach surfaces has many practical applications for the biopharmaceutical industry and for therapeutics for more that half a million Americans annually. As one important example, associated advances in knowledge guide the development of materials that do not foul (or that are easily cleaned) when filtering, transporting, or storing pharmaceuticals, foods, and beverages. These advances increase patient safety, reduce the production costs of numerous pharmaceutical products, and increase product quality and shelf life. In other industries it helps in the development of packaging materials that do not alter the effectiveness or taste of the package contents.

Researchers at the University of Colorado Boulder have refined a way to monitor individual protein molecules as they attach to and detach from solid surfaces. This work represents a major advance over the previous state of the art because it facilitates a detailed mechanistic understanding of how individual molecules interact with surfaces rather than simply measuring overall rates of fouling or cleaning in an empirical, trial-and-error manner. It also enables researchers to better study how proteins interact with a fouled surface after attempted surface cleaning; something that is very difficult to achieve with other methods.

In this breakthrough approach, surfaces of interest are irradiated with lasers during exposure to solutions of proteins that are tagged so that they glow (i.e., fluoresce) when they become attached to surfaces. The proteins stop glowing when they detach from surfaces. The appearances and disappearances of each glowing protein molecule are recorded with a sensitive camera through a microscope so that millions of individual molecules may be separately observed in a given experiment. Specialized custom-written software computes the rates of attachment and detachment of different proteins from the surfaces studied.

This work literally provides improved pictures of the mechanisms of surface fouling and the nature of the surfaces after cleaning compared to what had previously been available. The information obtained aids in the design of materials and coatings that are not readily fouled and can be quickly and repeatedly cleaned for re-use. The method impacts the design of filters, packaging, drugs, foods, medical devices, and biomedical implants.

The research that began in the IUCRC is now completed and is being expanded through a private contract from industry to further extend the capabilities. The work has already led to a follow-on private research contract with the Principal Investigator to further develop the technique. Future work will likely bring this kind of work in-house.

> **Economic Impact**: Biopharmaceutical therapies are becoming increasingly important for treating a variety of diseases including cystic fibrosis, skin and breast cancers, tuberculosis, and leukemia. Biopharmaceutical purification (e.g., filtration) accounts for 50-80% of all manufacturing costs. The ability to rationally design non-fouling and cleanable filtration materials will lead to safer, more efficient product purification. Reducing the cost of filtration will also help grow new business in cost-sensitive applications where good filtration is currently considered too expensive to be economical. Similarly, the rational design of protein-resistant materials for shipping, storage, and delivery will lead to greater product stability and efficacy. The implications of this work for medical therapies are major and many of these will have significant economic ramifications. For example, anticoagulation therapies that accompany implanted stents or heart valve procedures are often costly and dangerous (e.g., can result in excessive bleeding).
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> Each year more than half a million Americans receive coronary stent implants. Designing smarter materials that prevent pathological material-blood interactions can reduce the need for such treatments, thereby reducing the economic burden on the health care system. Biosensors have wide applications in medical (e.g., detecting disease markers, sugar or insulin levels in the blood of diabetics) as well as important environmental applications (e.g., identifying toxins or organic compounds in groundwater). Non-specific protein adsorption presents major challenges in biosensing applications. These can lead to poor detection limits and false positives in state-of-the-art medical diagnostic devices, all of which have major economic impacts, most of which are almost impossible to estimate. Understanding and reducing non-specific binding can greatly increase the speed and sensitivity of such analyses, allowing more information to be collected with fewer sensors and enabling portable devices for use in the field.

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High-Recovery Desalination Process for Brackish Groundwater

The first-generation desalination pilot plant.

Many regions of the world including the Middle East are plagued by a severe scarcity of fresh water sources. As a result, seawater has been the most commonly used raw water source for desalination. Desalination is a well-established process that uses reverse osmosis (RO) for the removal of salt from seawater or other brackish (salt-containing) water sources. RO is a pressure-driven process in which water is forced through a polymeric membrane while salts are retained. A major barrier to efficient desalination processes is the potential for the precipitation by sparingly soluble salts on the surface of the membrane, a process termed scaling. Scaling is of immense practical importance since it significantly degrades membrane performance and/or water quality and hence increases the cost of desalination.

Current approaches for control of scaling include addition of antiscalants, base softening, or adjusting the pH. These approaches, however, involve relatively high chemical costs and/or increase the complexity of the overall desalination process. The innovation in this work is that it delays the onset of scaling through a unique combination of the flow-reversal technology developed at Ben Gurion University and the ultrasonic sensor technology developed by the NSF Center for Membrane Science, Engineering and Technology (MAST) at the University of Colorado Boulder. This new sensor-based separation process could significantly lower the cost of brackish water desalination. Since its inception, the project has received support from the NATO Science for Peace (SfP) Program, the Middle East Desalination Research Center (MEDRC), and ROTEC, a small start-up company specifically formed to commercialize this technology.

The Middle East is plagued by a severe scarcity of fresh water sources. There, seawater has been the most commonly used raw water source for desalination. However, for those countries of the region that are mostly or completely landlocked, such as Jordan, brackish water is a potential major resource. This project enabled the design and fabrication of a pilot demonstration desalination plant based on RO using brackish groundwater that is configured for this new technology. The ability to exploit brackish groundwater for the successful operation of a demonstration plant would encourage development of these marginal water sources in countries in the region as well as globally in those countries with similar water characteristics. In addition, sensor-based flow reversal has significant potential for increasing recovery from RO for boron reduction in seawater desalination for direct or indirect agricultural use.

> **Economic Impact:** This new sensor-based separation process has the potential to significantly reduce costs associated with brackish water (BW) desalination, which is expected to have a global market value of $30 billion by 2015 with a growth rate of 10%/year. This technology enables higher recovery so that there is more fresh water and less salt produced per unit of feed water. For example, adding the technology to a 1200 m^3/day BW-RO plant (80% fresh water recovery) would enable operation at 92% recovery thus generating 1380 m3/day of fresh water. The total cost for adding the technology would be about $11,000/year. The additional water produced is valued at about $31,000/year, a significant economic benefit. This cost reduction becomes quite

significant given that the expected annual investment in desalination in the United States is currently estimated at $4.5 billion. In addition to the favorable economics, implementation of the technology will relieve pressure on existing water sources thereby reducing friction and facilitating cooperation between affected countries as they attempt to cope with dwindling freshwater supplies. This technology should help make it possible for water scarcity to become less of a driver of future conflict. It is difficult to overestimate impacts of avoiding the economic and human costs that would be associated with diminishing such future conflicts.

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