NON-TOXIC ANTI-FOULING SOLUTIONS: SHARKLET

Antifouling and Biomimicry

Sharklet Technologies uses an engineered microscopic topography inspired by sharkskin to reduce the ability of bacteria to adhere to surfaces without the use of biocidal toxic chemicals. Bacterial fouling is a major challenge in a large number of industries, ranging from marine shipping to healthcare, and tens of billions of dollars are spent annually on antifouling strategies. Many of these involve constant reapplication of toxic chemicals, yielding diminishing effects and carrying negative environmental and health impacts. Sharklet™ focuses primarily on biological fouling, or biofouling, in healthcare, targeting surfaces and devices that see frequent human contact, especially in hospitals where more than 1.7 million people per year acquire infections after being admitted in the US. These infections are often caused by bacteria which which form films on surfaces/areas that see frequent use, such as countertops, hospital beds, and medical devices. Sharklet's goal is to reduce the use of toxic chemicals in antibacterial applications, and to prevent the evolution of antibiotic-resistant bacteria by applying a nature-inspired strategy that has been effective in antifouling for millions of years. This case study will cover biofouling and the antifouling strategies used to combat it, as well as the creation of Sharklet™ Technologies as an industry leader in clinical antifouling technologies.

The Problem: Biofouling

Docks covered in mussels and ships returning to port covered in algae and barnacles are common sights around the world and indicative of the struggle with fouling. Biofouling can occur anywhere, including on countertops and door handles in hospitals, on machines in factories, and on massive ship hulls. The fouling

Dr.Brennan was inspired by sharks natural ability to prevent fouling on their skin to develop antifouling materials for hospitals which reduce bacteria build-up and help prevent the spread of infections.

process occurs in a similar manner regardless of the surface or scale, but is often facilitated when the surface is wetted from exposure to water or oils. It begins when bacteria adhere to a surface in order to gain a measure of stability, to access a steady supply of accumulated food, or to attach to a specific targeted surface. Once established, they begin excreting a variety of proteins, lipids, and polysaccharides known as extracellular polymeric substances (EPS), creating both a structure to secure the organism in place and a stratum upon which other organisms can attach. New organisms attach, and the established ones reproduce, causing an exponential increase in population. The time it takes many bacteria to replicate is roughly 20 minutes, so in one day a single bacterium can multiply into more than 16 million individuals. Many other organisms, including barnacles and algae, can then take advantage of the bacterial foothold.

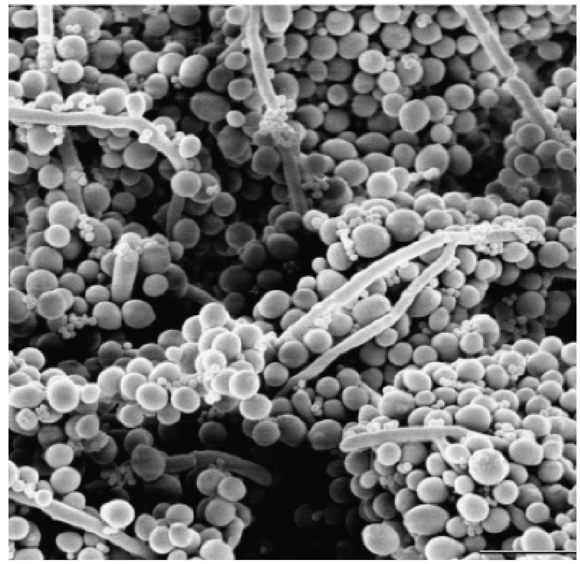
Biofouling: A biofilm of barnacles, algae, and bacteria encrusting a ship hull.

Biofouling has enormous health and economic impacts, primarily in the marine shipping and healthcare industries. A coating of algae and barnacles on a ship can cause a 16%-86% decrease in power efficiency, dramatically impacting energy and fuel use as well as reducing cruising speeds. The U.S. Navy, which constitutes roughly 0.5% of the world's fleet, incurs around $260 million in annual costs associated with biofouling. In the marine shipping industry, which spends an estimated $60 billion annually combating biofouling, there is strong demand for effective, low-cost, environmentally-friendly products.

Early marine antifouling strategies by Europeans involved the use of copper cladding on ships, which was toxic to many organisms and either deterred attachment or was lethal to those that did attach. While the materials have changed, the fundamental strategy remains the same: kill the organisms that attach to a ship's hull using biocidal compounds instead of preventing the attachment in the first place. Many metal-based strategies work when the metal ions inhibit various enzymes within the organism, disrupting essential metabolic activities. Over time, the coatings slough off, exposing additional metal ions. This strategy is expensive and results in metals leaching into the environment.

Current marine antifouling techniques involve the use of toxic materials to remove algae and barnacles from a ships hull.

Biomimetic antifouling solutions for marine biofouling are beginning to emerge, with companies designing products which do not use toxic chemicals. One company, Luritek, uses a counterintuitive approach, triggering the formation of a biofilm to repel other biofilms. The company produces a nutrient-rich hull coating that bacteria use as a food source. These bacteria attach and form a biofilm. Through a process known as negative allelopathy, the bacteria then repel other organisms seeking to attach to the hull, such as algae and barnacles. The bacterial biofilm produces much less drag than one composed of larger organisms, and in some cases the bacteria act as a lubricating layer, reducing drag and improving fuel performance.



Microscopic view of an established bacterial biofilm, which can lead to potentially deadly infections that are becoming increasingly difficult to treat.

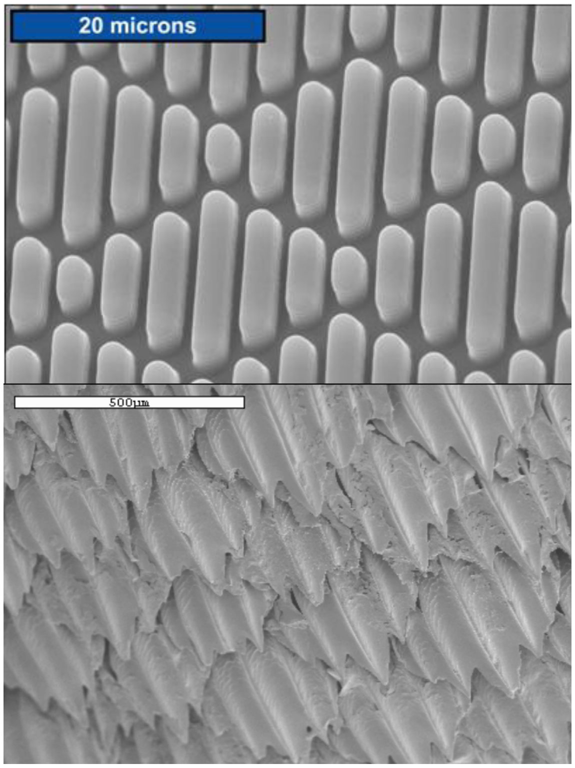
Biofouling is not limited to aquatic environments as the majority of research on antifouling strategies focuses on the healthcare industry where biofouling can be lethal. Effective antifouling technologies have the potential to save billions of dollars in hospital care and reduce the amount of antibacterial chemicals used to sanitize surfaces and devices.

All large organisms rely on microorganisms to function, but many microbes can cause detrimental health effects. Some bacteria strains, known as "superbugs", have evolved to be resistant to many antibiotics making them extremely difficult to eradicate. Superbugs are increasingly common in hospitals and clinical settings. Hospitals also have a multitude of surfaces that many people touch during the course of a day, allowing for easy transmission of infectious bacteria. Routine operations and procedures are riskier due to hospital-acquired infection (HAI). According to the CDC, in the United States around 271 people die daily from such infections and there are more than 2 million documented HAIs annually. The economic cost exceeds $30 billion annually in the United States alone.

Clinical antifouling research has led to a wide variety of preventative strategies for hospitals and clinics, such as coatings or new surface topologies for high-touch surfaces to prevent bacteria from adhering and forming biofilms. Many researchers have looked to nature for inspiration, examining organisms which are able to combat microbial fouling. Antifouling chemicals produced by some seaweed species have been successfully replicated, but questions remain about their efficacy and widespread use, especially in sterile or high-traffic environments.

Sharklet: Inspired by Ancient Predators

Sharks are unique in that they accumulate virtually no biofilms. The topography of their dermal denticles, or scale ridges, display a distinct ridged diamond pattern which make it very hard for microbes to attach.



Top: The Sharklet pattern.

Bottom: Shark skin composed of overlapping dermal denticles.

The work that led to the formation of Sharklet Technologies began in 2002 when company founder and University of Florida professor, Dr. Anthony Brennan, was performing antifouling research for the U.S. Office of Naval Research. The Navy sought a way to reduce the buildup of algae on ship hulls that did not involve toxic paints and reduced maintenance and dry dock costs. The Navy's techniques at the time, mentioned previously in this case study, leached large amounts of toxins into the water, requiring the Navy to constantly work to remove biofilms that formed on their hulls. This strategy also led to evolutionary pressures for microbes, since the individual organisms that are most resistant to the toxins can persist on the hulls and reproduce, making the following generations of algae and bacteria tougher to eradicate and future cleaning more difficult and costly. Brennan realized that the most effective solution was to prevent fouling in the first place, rather than cleaning it up after it occurred.

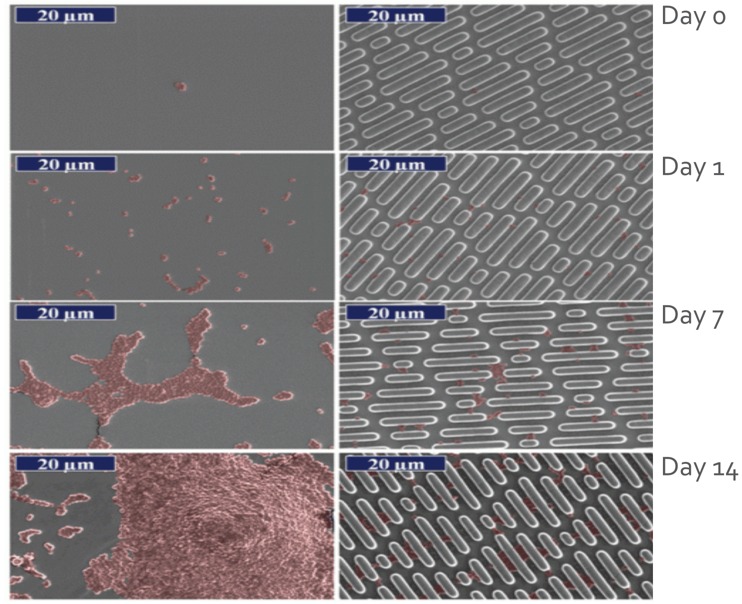
After observing submarines returning to port covered in algae, Brennan decided that replicating an antifouling strategy found in nature could yield promising results while also minimizing the environmental impact. Additional research showed that using microtopography, where the surface is designed to impede microbial attachment, would be the most effective nontoxic way to combat fouling. Brennan looked at the animals that faced the same fouling problems submarines and boats did: large slow-moving marine animals. Out of all his observations the one animal that had virtually no fouling problems was the shark.

Shark scales, or dermal denticles, are structurally different than most fish scales. They are covered in enamel that is analogous to human teeth and can repel more than 85% of algae that comes in contact with the scales. Brennan took an impression of shark dermal denticles and examined it under a scanning electron microscope. The scales had a distinct topography comprised of microscopic ridges arranged in diamond patterns, something lacking in most other large marine animals such as whales. Brennan spent several years mimicking sharkskin, culminating in the development of an artificial pattern of diamond-shaped scales and contours similar to that of sharkskin. This became known as Sharklet™.

From the Ocean to the Hospital

An experiment conducted in Brennan's laboratory opened a new realm of possibilities for applications of material mimicking shark skin. One of his students was trying to grow bacteria on a petri dish lined with sharkskin. To everyone's surprise, the bacteria failed to grow, opening a new avenue of research beyond the marine industry applications. While the shark-inspired patterning upon which Sharklet was originally created was extremely effective against algae, preventing 87% of algae and 97% of barnacles from attaching to ships, Brennan now envisioned widespread use in clinical environments where the microtopography would be used to prevent fouling in hospitals, homes, and offices, and could thus lead to thousands of lives and billions of dollars saved.

During testing, the key to the pattern's success was identified: the pattern dramatically increases the energy required for bacteria to colonize a surface. The cells have to suspend over the gaps between ridges or bend to the surface's contours. Both place significant tension and stress on the cell membrane and reduce the area of contact. To adhere and stay attached under such stress increases the energy required, forcing bacteria to either seek another place to grow or die. While success rates differed between bacterial species, the Sharklet™ pattern proved highly effective, preventing more than 90% of bacterial attachment and proving especially effective against both gram-positive and gram-negative bacterial strains antagonistic to humans, such as Escherichia coli, Staphylococcus aureus, and Pseudomonas aeruginosa.



Testing of the Sharklet material proved to drastically reduce the amount of bacteria growth on a surface. This testing is the result of 14 day growth of bacteria.

The University of Florida wanted Brennan to commercialize his topography, and he was interested in entrepreneurship and wanted his shark-inspired pattern to be used to improve the healthcare industry. He invited his friend, businessman Greg Garvis and close colleague Joe Bagan. They instantly recognized the breakthrough. In 2007, Sharklet™ Technologies was formed, backed by $1.2 million in investments. Joe Bagan became chairman of the board and the first CEO, Garvis a member of the board and close business advisor and Brennan a board member and the Chief Technology Officer.

Scaling the Product

While the Sharklet™ design showed immense potential, the new company needed to continue testing the technology's efficacy. Experiments were conducted over the company's first few years to determine the bacterial species inhibited by the technology and to demonstrate how effective the design was against the various species. Through many experiments, the patterns which produced strong antifouling effects against many species were established, increasing the design's/technology's value to the medical community.

With its unique biologically-inspired topography, Sharklet™ Technologies had to overcome many hurdles in manufacturing and scalability before they could achieve commercial success. The pattern's ridges are 3μm in length and 2μm wide, and few companies had the capability to create textured materials at this scale. Sharklet™ Technologies had two business goals, each with its own manufacturing requirements and challenges: the formation of licensing model where companies paid to use the Sharklet™ surface and the creation of their own medical product lines. In 2008, with the company still struggling with scalability and the company's survival in question, current CEO Mark Spiecker was contacted by FlexCon, a Massachusetts-based company specializing in adhesive coating and laminating. FlexCon was able to successfully develop a way to produce Sharklet-patterned materials in industrial sheets. Spiecker made arrangements with Chicago-based 10x Microstructures who agreed to manufacture tools for molded parts with Sharklet™ texturing being manufactured by FlexCon.

To produce a Sharklet-patterned item, the first step is the production of a master mold. The molds are produced in silicon wafers, similar to the production of modern electronics, and are patterned using laser lithography. The typical master mold is 4″x4″ but can be as large as 9″x9″. Sharklet™ first picks a pattern depending on the intended use from two base patterns: standard and inverted. The standard protruding pattern works best for limiting bacterial migration and is therefore primarily used for medical devices and implants such as catheter tubes. Sharklet's inverted pattern, where the ridges are indented, is more effective on high-touch surfaces where the inverted ridges are protected from wear and the surface can maintain its efficacy for a longer period of time. The master pattern is used by 10x Microstructures to create a patterned mold produced using a nickel electroforming process. Electroforming allows for high consistency and fidelity because the surface topography is replicated at the atomic level. The resulting mold can then be used in a standard injection molding process, where heated plastic is forced into the mold cavity and solidifies in the Sharklet™ pattern. The master pattern is also used by FlexCon in the manufacture of patterned sheets for adhesion to existing surfaces and equipment. With these partnerships, Sharklet™ can produce patterned films for use on existing items and surfaces, as well as pieces where the pattern is molded directly into the surface, opening up the technology to numerous commercial possibilities.

Commercial Results

As the company acquired the means to manufacture their texture at scale word spread rapidly. The company secured $4 million in funding, including a $1.4 million Small Business Innovation Research (SBIR) grant from the National Institutes of Health (NIH) to adapt the pattern to reduce urinary catheter infections and $2 million for the development of vascular tubes. In 2011, Sharklet™ entered into a licensing deal with LG International (LGI), with LGI incorporating Sharklet™ texturing into their Tactivex® line of bacterial inhibition covers. This provided Sharklet™ with an excellent market entry into healthcare and clinical antifouling. Furthermore, Sharklet's "no-kill" functionality reduced the likelihood of superbugs forming, since it prevented microbial adhesion rather than creating an evolutionary pressure.

The NIH SBIR grant allowed Sharklet™ to focus on the development of patterned urinary catheters to alleviate common problems caused by infection and bacterial migration. The urinary catheter market is valued at over $2 billion annually and is expected to grow as the US population ages. Urinary catheter infections constitute more than 40% of hospital-acquired infections, create additional healthcare costs of more than $565 million in the U.S. annually, and are not covered by MediCare. Sharklet technology has the potential to greatly impact this healthcare problem. In addition, Sharklet™ is designing medical equipment to treat other areas where there is a critical need for antifouling capabilities, such as endotracheal tubes and vascular-access devices.

While Sharklet™ has not yet conducted human medical trials to prove its efficacy in medical settings, the company had a successful year in 2012 with more than $1 million in sales. The company is currently working on obtaining funding for research on the effectiveness of the pattern in hospitals settings. Sharklet™'s patterned products are comparably priced to similar products without the pattern and the company foresees a drop in price as they scale their operations.

Sharklet™ continues to collaborate with companies and expand its product offerings. The company has 12 joint development agreements to develop products for medical markets, working with companies such as Cook Medical. These agreements are being used to help scale manufacturing and reduce costs. In addition to continuing development of their urinary catheters, the company plans to work with Steelcase in 2014, providing Sharklet-patterned desks and other furniture for shared office environments, college classrooms, and meeting areas. With their biomimetic suite of products, Sharklet™ Technologies hopes to establish their antifouling technology as an effective tool to reduce the development of biofilms and the outbreak of deadly superbug bacterial strains.

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Source Notes:

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