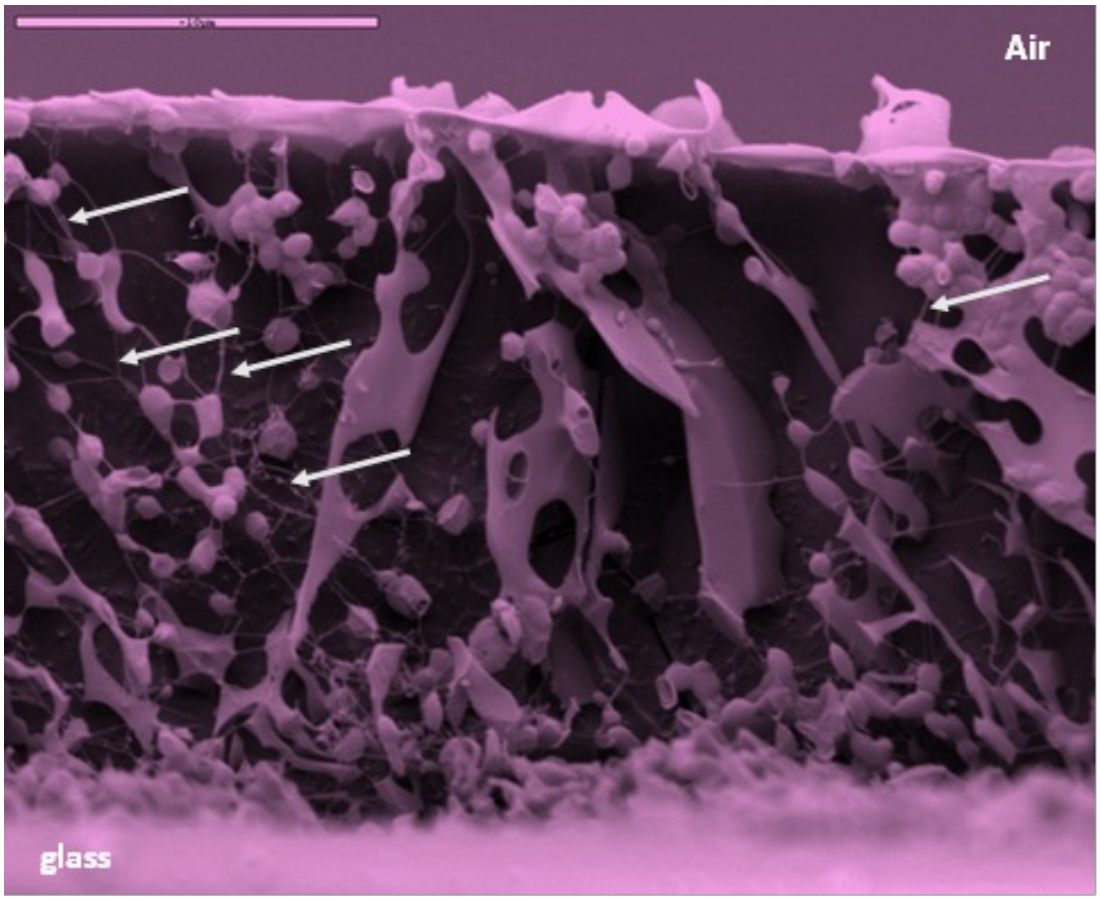
Antimicrobial Resistance Gallery

Biofilms

(Julio Sempere and Mirian Domenech)



Biofilm "Bacterial city"- Image obtained by a Low Temperature Scanning Electron Microscope of a *Streptococcus pneumoniae* biofilm formed on the surface of a glass coverslip. Filamentous material or matrixome (the "housing", indicated by arrows) links the pneumococcal cells to one another. The reticular nature of the intercellular matrix can be observed. Courtesy of Miriam Moscoso, Ernesto García and Mirian Domenech.

Biofilms: microbially-created extracellular physical barriers that protect against harmful agents

Although we often think of microbes as single-celled organisms, floating around in the sea or rivers (i.e. "planktonic" microbes), most of them, most of the time live in communities on surfaces as *biofilms*. These surfaces can be inanimate, like stones in a river or the drain of a shower, or a living tissue, like the walls of our intestines. The microbes in such communities work together and divide up their tasks among themselves. Depending on their size, biofilms can represent small microbial *bunkers*, *forts* or large *fortified cities* that provide protection against their enemies, such as predators, and harmful substances, that free-living individual microbes don't enjoy. The biofilm lifestyle gives microbes cool benefits, such as being less susceptible to antimicrobial treatments, better evasion of the host's immune system, or maintaining viability despite adverse conditions such as nutrient scarcity.

Biofilms are found essentially everywhere in nature

Biofilms are the predominant mode of life of microbes, so practically everywhere microbes exist, biofilms exist. For example, all forms of life are covered with microbes – their microbiomes – and most of these live in biofilms. Seaweed is covered with microbial biofilms, as are the rocks in rockpools on the beach or stones in rivers. The microbes in wastewater treatment plants that remove the nasty materials in the wastewaters from our toilets and showers live in biofilms on the surfaces of stones in trickling filter systems, or in "flocs" – they join together to form their own surfaces – in activated sludge systems. They form biofilms on the difficult-to-clean parts of our shower and wash basin drains. Even on the surfaces of buildings, statues, and other structures created by humans, we can see biofilms, sometimes as green slime. Microbial life is mostly biofilm life!

The biofilm matrix

The microbes in a biofilm do not live as a single layer on a surface, but build a multi-dimensional structure that can be so big that we can see and feel (and sometimes smell) it: e.g. the shower drain biofilm. They do this by creating a matrix made, not of the construction wood, plaster and bricks we use, but of biopolymers they make themselves, which can vary in composition depending on the environment, the specific microorganisms involved, and the surfaces where the biofilms form.

These polymers are mainly made up of sugar molecules (exopolysaccharides), proteins, DNA, and RNA. The "housing" part of the biofilm is called the *matrixome*. The matrixome is full of water (highly hydrated) and possesses various important functions. It

- contributes to the biofilm architecture by mediating its adhesion to the surface and holds the microorganisms together (cell-cell cohesion),
- controls what goes in and out, like nutrients and signals for communication between microorganisms inside and outside the biofilm,
- acts as a semipermeable barrier, protecting microorganisms from external aggressions, since the matrixome is often negatively charged or very viscous, and
- protects microorganisms against both the host's immune system and antimicrobial agents.

The matrixome is thought to act both as a dispersal system for nutrients present in the medium in which the biofilm is attached, and a filtering system that prevents certain compounds from penetrating into the interior of the biofilm, in addition to having channels to eliminate the "*city*'s" waste.

The importance of biofilms for infections

The biofilm lifestyle is the normal lifestyle of microbes, but when it occurs on a body tissue or organ surface, it affects the activity and behaviour of that tissue. And if the microbes in the biofilm are pathogens, they can damage the tissue and cause disease. These are sometimes called pathogenic biofilms. When bacteria live in biofilms, they behave differently than when they're floating around on their own. They use energy slower (slower metabolism) and produce a different set of proteins. This can make them up to 1000 times harder to kill with antibiotics

because slow-growing cells are generally much less vulnerable to cell damage than fast-growing cells.

Moreover, some harmful bacteria, like *S. pneumoniae* or *Staphylococcus aureus*, can form biofilms that are more difficult to identify by our immune system: the immune cells responsible for eliminating them do not "see" them. The immune system works by a system of recognition: it is trained to distinguish the cells and cellular products of its own body as "self" structures that are not to be attacked, from "non-self" or "foreign" structures, like pathogenic microbes, that are potentially dangerous and to be attacked and destroyed. Some pathogens, for example the human pathogen *S. pneumoniae* mentioned above, interfere with the recognition system by camouflaging themselves. They do this by recruiting and covering themselves with host proteins, so that the immune system is not able to recognise them as "foreign". To achieve this, such bacteria express special proteins on their surface that recruit specific host proteins to cover their own "foreign" surface structures and make them appear as "self". Because these bacteria cannot be identified as harmful, they are not attacked by the immune system and the infection can continue.

How can we help our bodies fight off biofilm infections?

Pathogenic biofilms are gaining in importance. As people live longer, they increasingly need medical interventions, some of which involve the insertion of "indwelling devices", such as catheters and stents – plastic or metal tubes that for example provide channels for the free flow of fluids, like blood or urine, in our organs. Sooner or later, the surfaces of these indwelling devices may become colonised by biofilm-producing microbes, some of which may block the tubes and some of which may cause infections that are difficult to treat.

Since biofilms cause so many problems, knowing the foundations of biofilm formation and learning how to knock them down or prevent their construction is essential. Many biofilm research groups focus on identifying the components of the matrixome, studying their functions within the "city", and seeking new treatments both to prevent biofilm formation and to destroy them once formed.

The importance of biofilms for us

Natural biofilms significantly impact human, animal and plant health, sometimes positively, for example, on plant roots by promoting plant growth and protecting from root infections, and sometimes negatively, for example by their resistance to antibiotic treatment (One Health), or by contributing to the chronicity of some infectious diseases. In industry, biofilms are responsible for pipeline blockages in refineries. On the other hand, designed-engineered microbial biofilms are at the heart of many biotechnological processes – we mentioned wastewater treatment above – but also of processes for the production of valuable chemicals including medicaments. So: biofilms are for us, on one hand serious problems and, on the other, serious solutions to problems!