

Biofilms

Pharmaceutical Microbiology

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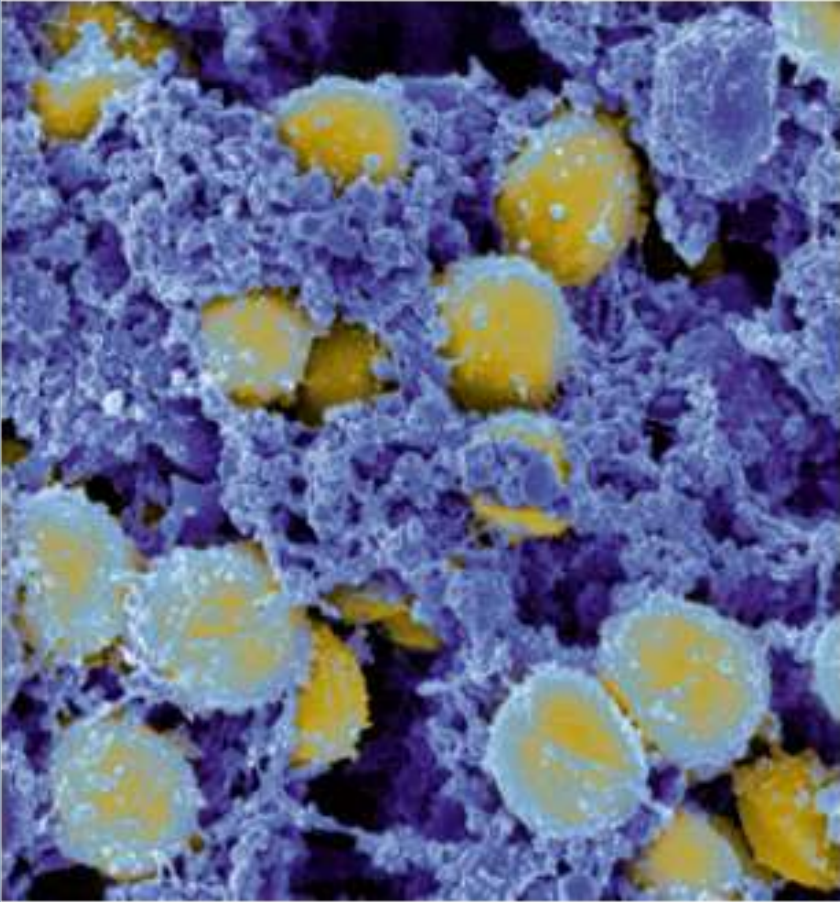
Definition

- Biofilms are communities of surface-associated microorganisms encased in a self-produced extracellular matrix.
- Biofilm formation is a nearly universal bacterial trait, and biofilms are found on almost all natural and artificial surfaces.
- Some examples of biofilms are the plaque that forms on teeth and the slime that forms on surfaces in watery areas.

Examples of biofilms



- Biofilms science and technology has been an active field of study since the late seventies when the first definition of biofilms was brought to public attention by Bill Costerton and coworkers in 1978
- **Significance: Protect and allow bacteria to survive and thrive in hostile environments.** Withstand host immune responses, much less susceptible to antibiotics and disinfectants.



High-resolution scanning electron microscopy image of a community associated methicillin-resistant *Staphylococcus aureus* biofilm embedded in extracellular matrix, formed on implanted catheter tubing during experimental biofilm infection

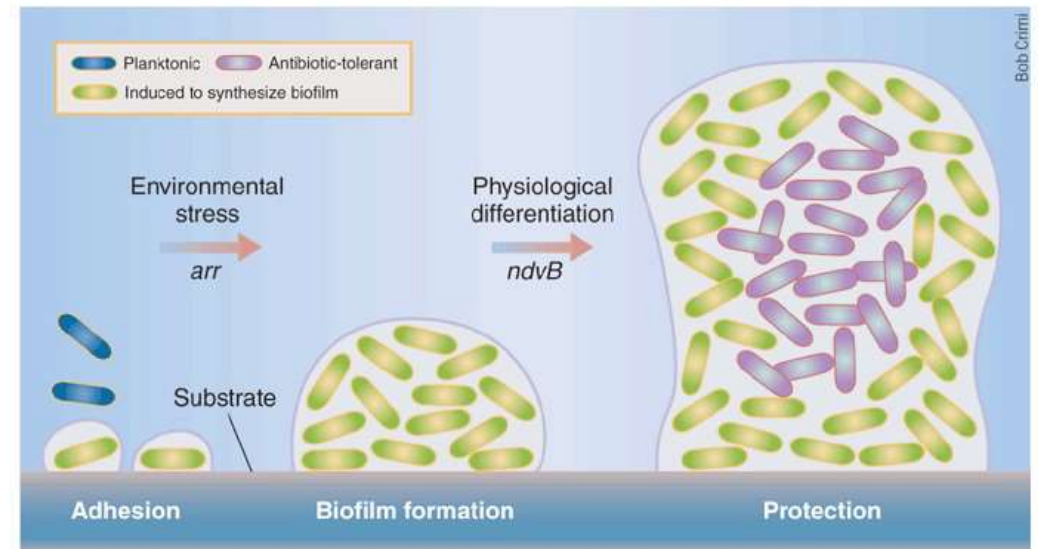
Human Infections linked to biofilms

Table 1. Partial list of human infections involving biofilms.

Infection or disease	Common biofilm bacterial species
Dental caries	Acidogenic Gram-positive cocci (e.g., <i>Streptococcus</i>)
Periodontitis	Gram-negative anaerobic oral bacteria
Otitis media	Nontypable strains of <i>Haemophilus influenzae</i>
Musculoskeletal infections	Gram-positive cocci (e.g., staphylococci)
Necrotizing fasciitis	Group A streptococci
Biliary tract infection	Enteric bacteria (e.g., <i>Escherichia coli</i>)
Osteomyelitis	Various bacterial and fungal species—often mixed
Bacterial prostatitis	<i>E. coli</i> and other Gram-negative bacteria
Native valve endocarditis	Viridans group streptococci
Cystic fibrosis pneumonia	<i>P. aeruginosa</i> and <i>Burkholderia cepacia</i>
Meloidosis	<i>Pseudomonas pseudomallei</i>
Nosocomial infections	
ICU pneumonia	Gram-negative rods
Sutures	<i>Staphylococcus epidermidis</i> and <i>S. aureus</i>
Exit sites	<i>S. epidermidis</i> and <i>S. aureus</i>
Arteriovenous shunts	<i>S. epidermidis</i> and <i>S. aureus</i>
Scleral buckles	Gram-positive cocci
Contact lens	<i>P. aeruginosa</i> and Gram-positive cocci
Urinary catheter cystitis	<i>E. coli</i> and other Gram-negative rods
Peritoneal dialysis (CAPD) peritonitis	A variety of bacteria and fungi
IUDs	<i>Actinomyces israelii</i> and many others
Endotracheal tubes	A variety of bacteria and fungi
Hickman catheters	<i>S. epidermidis</i> and <i>C. albicans</i>
Central venous catheters	<i>S. epidermidis</i> and others
Mechanical heart valves	<i>S. aureus</i> and <i>S. epidermidis</i>
Vascular grafts	Gram-positive cocci
Biliary stent blockage	A variety of enteric bacteria and fungi
Orthopedic devices	<i>S. aureus</i> and <i>S. epidermidis</i>
Penile prostheses	<i>S. aureus</i> and <i>S. epidermidis</i>

Biofilm formation and growth

- Basic structural unit of a biofilm is the **microcolonies or cell cluster** formed by the surface adherent bacterial cells.
- **IMPORTANT FACTORS IN BIOFILM FORMATION**
- **Cell attachment**
- **Extracellular polysaccharides (EPS)**
- **Cell-cell communication (Quorum sensing)**



Basic units of biofilm

- **Microcolonies of homogenous or heterogenous bacterial species.**
- **Matrix :** A glycocalyx matrix made up of extracellular polymeric substance(EPS) surrounds the microcolonies and anchors the bacterial cell to the substrate.
- **Functions:**
 - Maintains the integrity of biofilms
 - Prevents desiccation.
 - Resists antimicrobial agents
 - Create a nutritionally rich environment

Quorum sensing

- is a **communication mechanism between bacteria** that allows specific processes to be controlled.
- Involves the regulation of expression of specific genes through the accumulation of signaling compounds that mediate intercellular communication.
- Dependent on cell density and mediated through signaling compounds.
- The signals are thought to allow **cross-talk** between species, causing them to **increase their production of** **exo-polysaccharide** and the **factors that increase their virulence**.

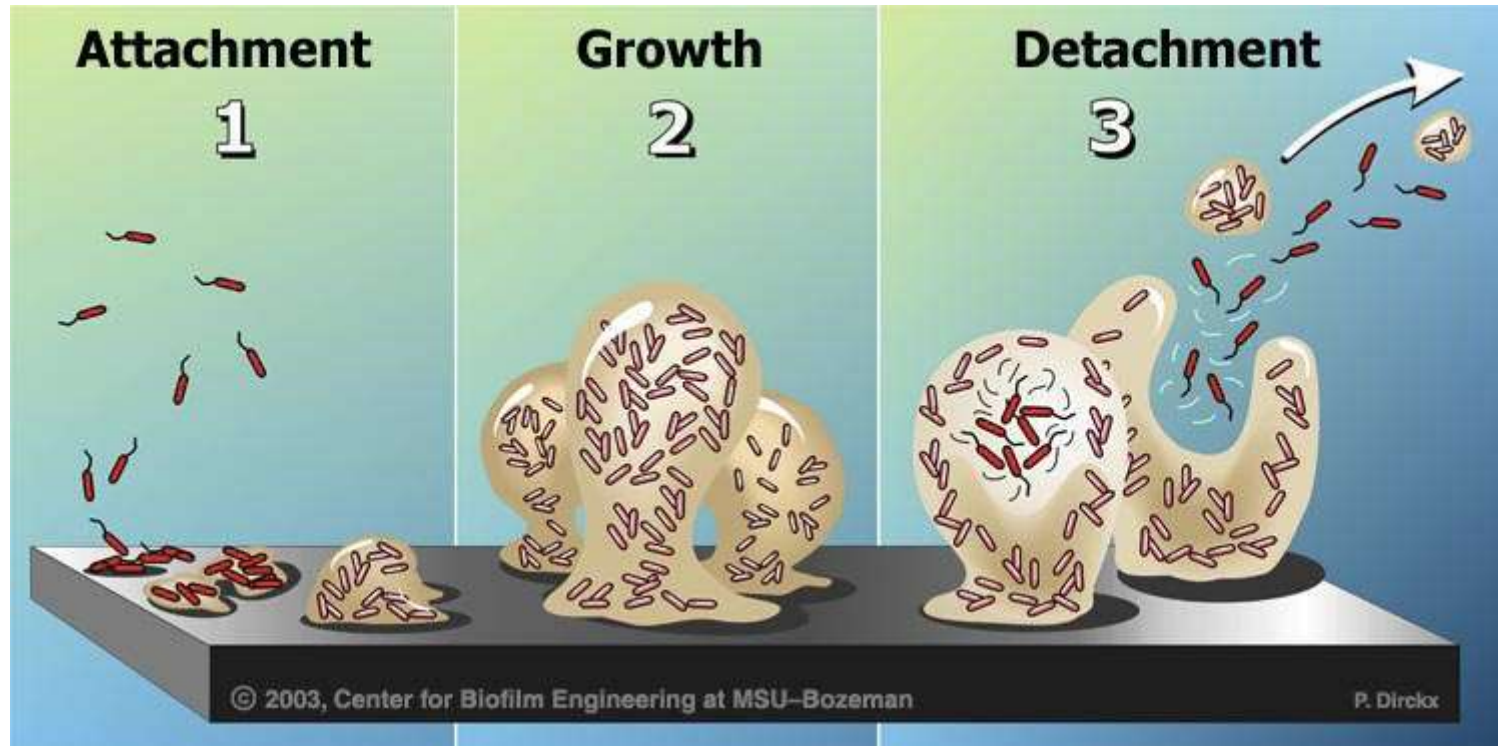
Mechanisms of Biofilm formation



- **Formation of a biofilm begins with the attachment of free-floating microorganisms to a surface. These first colonists adhere to the surface initially through weak, reversible van der Waals forces. If the colonists are not immediately separated from the surface, they can anchor themselves more permanently using cell adhesion structures such as pili**

Stages of Biofilm Formation

Bacteria switch from a free-floating (**planktonic**) state where they function as individuals to a sessile state where they function as communities.



STAGE 1

- Adsorption of inorganic and organic molecules to the solid surface, forming a thin layer termed as conditioning layer.



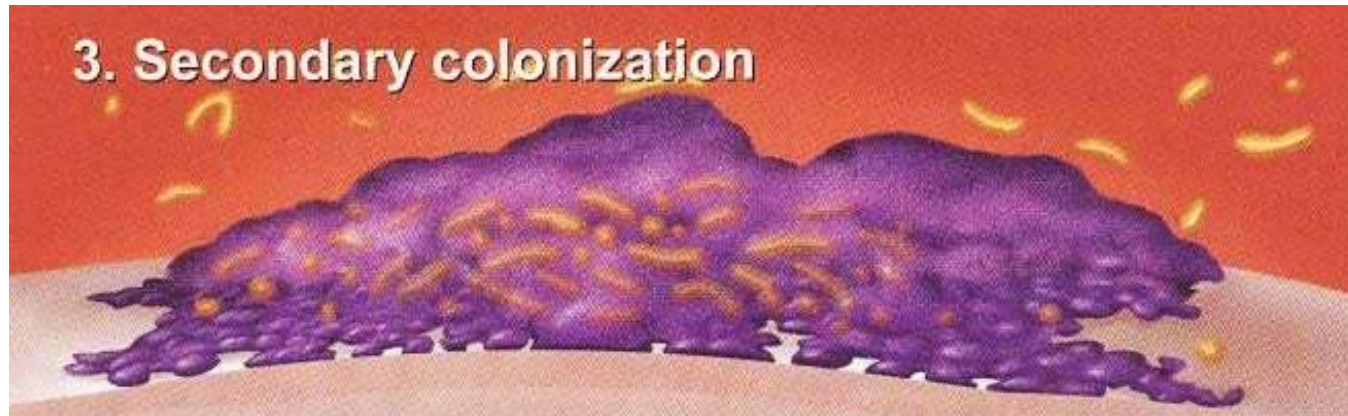
STAGE 2

- Adhesion of microbial cells to this layer.
 - Phase 1 - Transport of microbes to surface.
 - Phase 2 - Initial non specific microbial-substrate adherence phase.
 - Phase 3 - Specific microbial-substrate adherence phase.



STAGE 3

- Bacterial growth and expansion.
- Monolayer of microbes attracts secondary colonizers forming microcolony, and the collection of microcolonies gives rise to the final structure of biofilm.

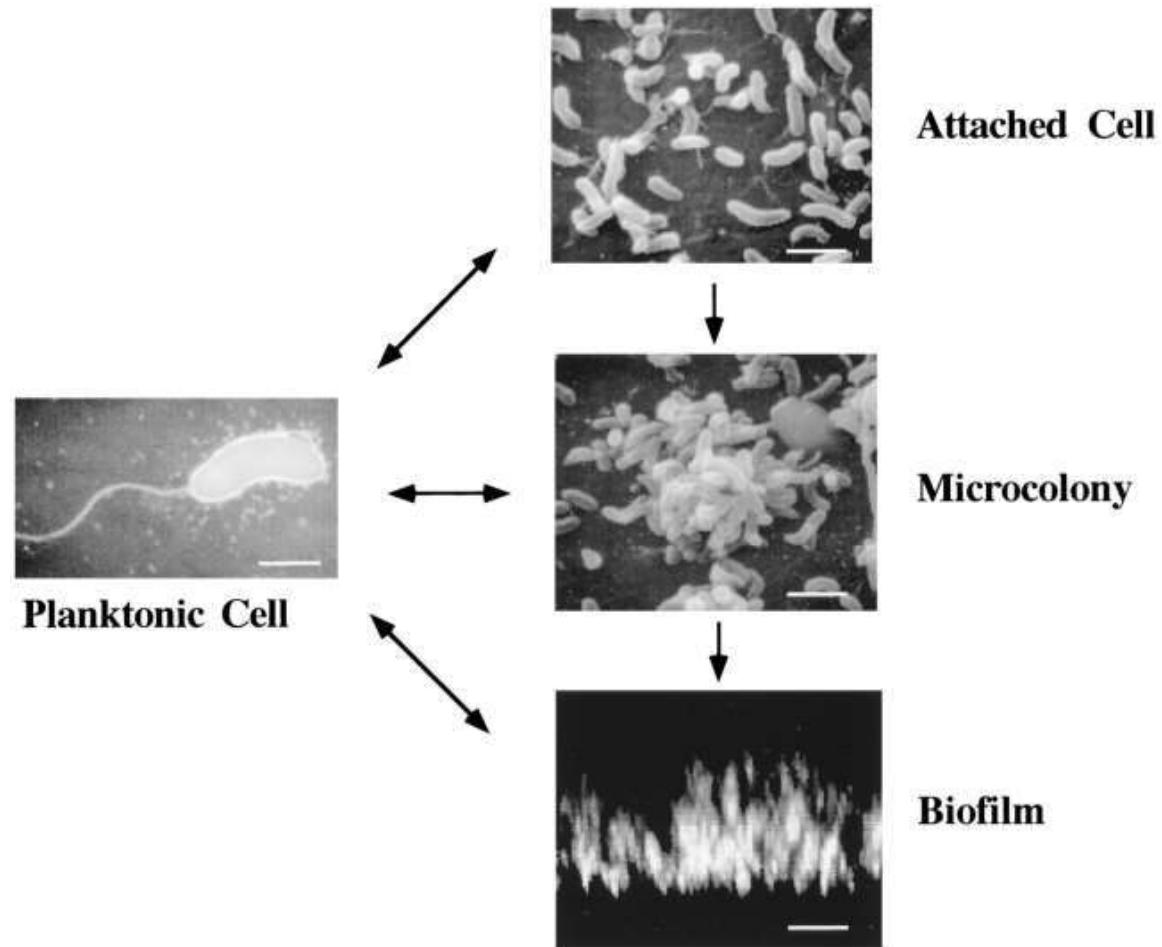


STAGE 3

- A mature biofilm will be a metabolically active community of microorganisms where individuals share duties and benefits.
- Some microorganisms help in adhering to the solid support, while some others create bridges between different species.



Biofilm formation in *Vibrio cholerae*

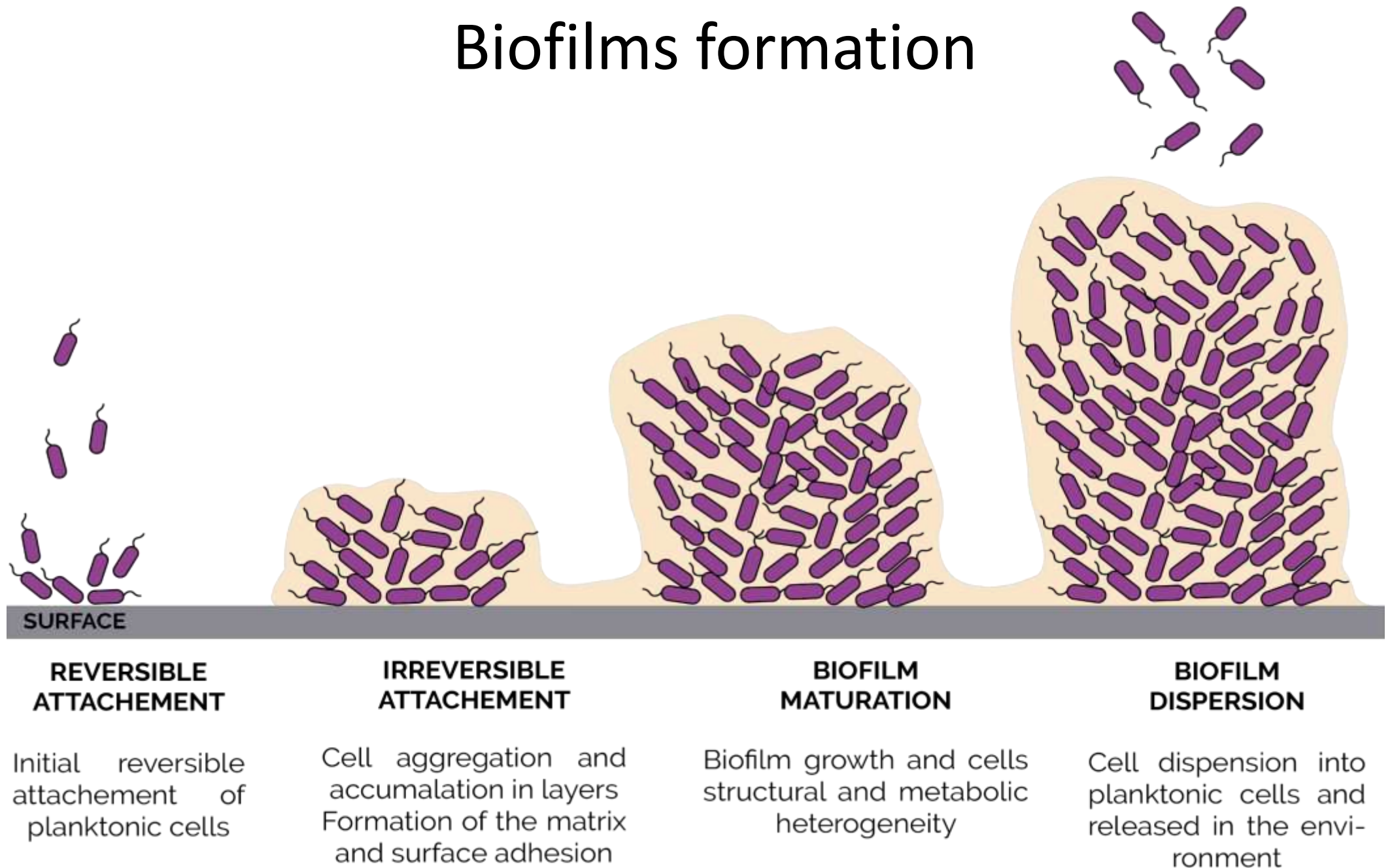


STAGE 4 : Detachment / Dispersion

- During detachment, as a strategy of bacterial cells to leave biofilms and continue another biofilm life cycle
- Detachment plays an important role in shaping the morphological characteristics and structure of mature biofilm.



Biofilms formation



Benefits Of Biofilm To Microbes

- Helps the bacteria to survive in unfavorable environmental and nutritional conditions.
- Resistance to antimicrobial agents.
- Opportunity of genetic material exchange.
- Ability to communicate between bacterial population of same and or different species.
- Produce growth factors across species boundaries.

Role of biofilms in antibiotic resistance

- Delayed penetration of the antimicrobial agent----EPS diffusional barrier ; delays rate of transport of drugs
- Bacteria intact in biofilms more resistant than single cells
- Altered growth rate of organisms in biofilms----organisms grow more slowly in biofilms---Slow uptake of antimicrobials----Actively growing and dividing cells are required for drug action

Biofilms a Great threat to Implants

- A significant number of people are affected by biofilm infections which develop on medical devices implanted in the body such as catheters (tubes used to conduct fluids in or out of the body), artificial joints, and mechanical heart valves.
- When implanted material becomes colonized by microorganisms, a slow developing but persistent infection results

Endocarditis and Biofilms

- Microorganisms may attach and develop biofilms on components of mechanical heart valves and surrounding tissues of the heart, leading to a condition known as prosthetic valve endocarditis.
- The primary organisms responsible for this condition are *S. epidermidis*, *S. aureus*, *Streptococcus spp.*, gram-negative bacilli, enterococci, and *Candida spp.*
- These organisms may originate from the skin, other indwelling devices such as central venous catheters, or dental work.

Urinary catheters and Biofilms

- Urinary catheters are tubular latex or silicone devices, which when inserted may readily acquire biofilms on the inner or outer surfaces.
- The organisms commonly contaminating these devices and developing biofilms are **S. epidermidis**, **Enterococcus faecalis**, **E. coli**, **Proteus mirabilis**, **P. aeruginosa**, **K. pneumoniae**, and other **gram-negative** organisms.
- The longer the urinary catheter remains in place, the greater the tendency of these organisms to develop biofilms and result in urinary tract infections

