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Challenges in developing antimicrobial polymers

A NAMRIP pump-priming project

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Aim of our Research Project

- **NAMRIP** funded a short "pump priming" project
- The aim was to make a type of polymer (plastic) for urinary catheters that could **prevent bacteria growing** on them
- Polymers must be:
  - **Effective against bacterial biofilm growth**
  - **Suitable for catheters** (i.e. flexible, low friction)
  - **Harmless** to sensitive human tissue
  - **Low cost**

If it was EASY someone would have done it!

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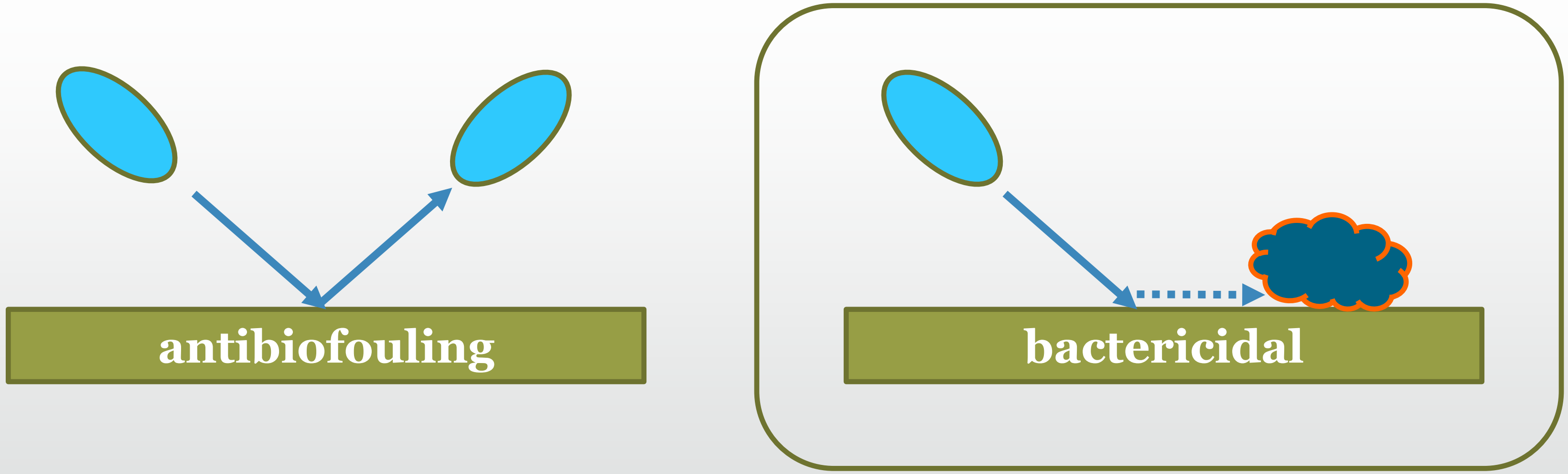
Antibacterial Surfaces

- "Antibacterial surfaces may repel or resist the initial attachment of bacteria by either exhibiting an **antibiofouling** affect or by inactivating any cells coming into contact with the surface, causing cell death, therefore exhibiting a **bactericidal** effect"



Hasan, J., et al. (2013). "Antibacterial surfaces: the quest for a new generation of biomaterials." Trends in Biotechnology **31(5): 295-304.**

Bactericidal Surfaces

- Easiest way is to **add** something **toxic** to the plastic:

SILVER: effective, depends on leaching of Ag^{+} ions

Silver is applied to textiles, wound dressings

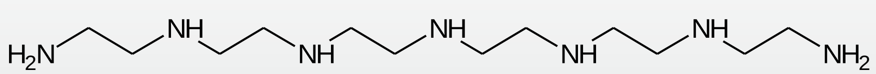
QUATS: quaternary ammonium compounds

Well-known as biocides and disinfectants

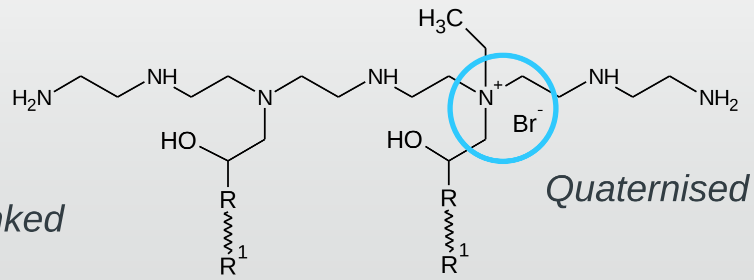
- However, **toxic** materials mixed in to the plastic are slowly released to kill bacteria – could also be harmful to the user

QPEI

- **Can the polymer itself be made to kill bacteria?**
  - ***Polyethyleneimine*** is a syrupy liquid polyamine that dissolves in water: *crosslink* the polymer to make it insoluble
  - *Crosslinked quaternised polyethyleneimine* [**QPEI**] has been claimed as an antibacterial material e.g. for use in dental fillings
  - Attraction between the cationic polymer and the bacterial cell wall leads to disruption of the membrane and death of the cell



Polyethyleneimine



Crosslinked

Quaternised

Challenge no 1 – MAKING THE POLYMER

- **Followed a published literature method*** for making **quaternised polyethyleneimine** which is crosslinked by **epoxy** compounds and claimed to be tough and flexible

- Soon found out that the published method didn't work – ***and couldn't work!***

  e.g. "heat with ethyl bromide for 1 hour at 60° C"

  – but the *boiling point* of ethyl bromide is 38° C

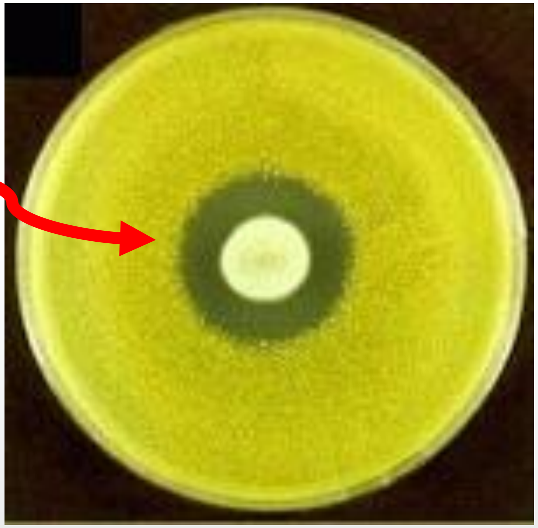
- Devised a **new synthetic route** to make these polymers

* Chachulski, B., et al., *Properties of a polyethyleneimine-based sensor for measuring medium and high relative humidity. Measuring Science Technology, 2006.* ***17: p. 12-16.***

Challenge no 2 – **TESTING THE POLYMER**

Any **ZONE OF INHIBITON** around an antibacterial polymer shows that ***something is leaching out of the sample***

If you see this in a research paper it should set off warning bells!



http://archive.bio.ed.ac.uk/jdeacon/microbes/penithum.jpg

Polymers must be rigorously washed to remove ***impurities*** that could give misleading results (*we did this*)

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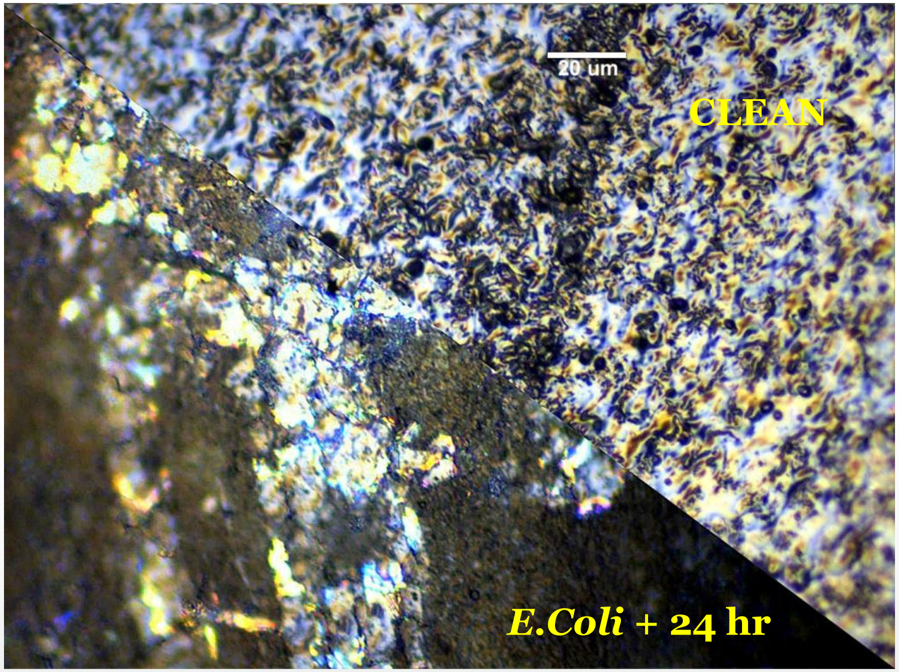
Polymer Test Results

- Not successful (Sandra Wilks)
- CLEAN polymer has *rough surface texture* when hydrated



RAISES MANY QUESTIONS:

Are the bacteria LIVE or DEAD?
Is surface texture important?
Change the quaternary type??

More questions than answers...

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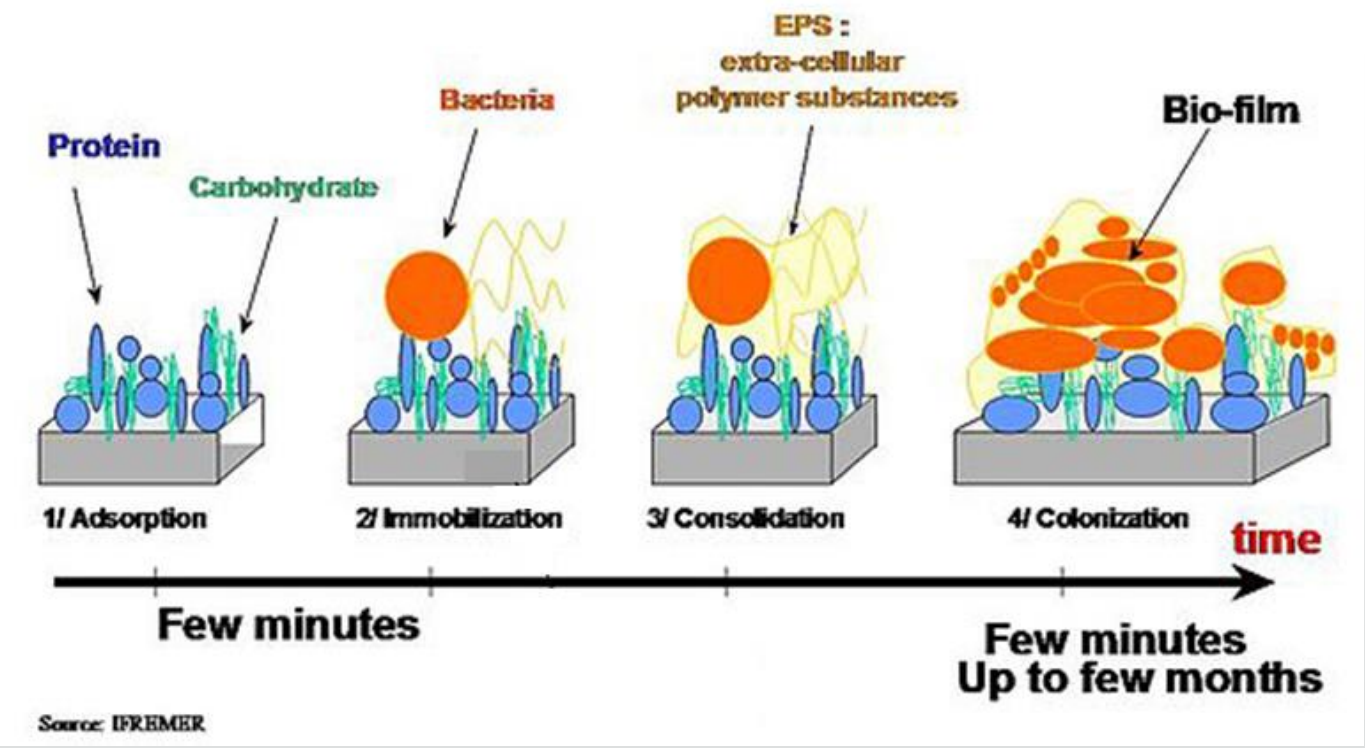
Another complication…

- ***Bacteria never encounter a pure polymer surface***
- The first things to fasten immediately on the surface are **PROTEINS** and **CARBOHYDRATES** which can also blanket the biocidal groups



The Fundamental Question…

- ***How effective CAN bactericidal polymer surfaces ever really BE?***

- The polymer does not dissolve in water so it cannot enter the bacterial cell – it must kill bacteria when they simply settle on it (by disrupting the cell wall)
- If the polymer surface ***DOES KILL bacteria on contact***, the dead bacteria will remain there covering the surface and provide a base for further bacteria to settle and grow on

Summary:

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- A way of making crosslinked quaternised polyethylenimine with good mechanical properties was developed
- The polymer was cleaned of impurities before testing
- Initial testing did not show anti-biofilm activity
- Further variations of the polymer are available

- *CAN this approach be made to work?*

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Thanks for listening!