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Doctoral School: SEVAB
First year registration: 2018
Funding: University grant (UPS)

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DEVELOPMENT OF QUORUM SENSING INHIBITORS FOR COMPLEX BIOFILMS CONTROL

Développements d'inhibiteurs du Quorum Sensing pour le contrôle de la formation de biofilms complexes

Microbial biofilms pose major problems in many industrial sectors because of equipment damage, biocorrosion, energy loss, contaminations. In the medical area, they are responsible for 65% of nosocomial infections. They also colonize water systems and are the major cause of biofouling.
Biofilms are aggregated microorganisms attached to surfaces and embedded in a self-produced matrix (EPS). Bacteria in biofilms have higher protection against antimicrobials and are more tolerant to disinfectants. The mechanism behind biofilm formation is called Quorum Sensing (QS), a communication system where bacterial cells produce, detect and respond to small molecules called auto-inducers. Since auto-inducers are the key factor in the processes leading to biofilms, they are a promising target to control their formation.
The thesis project is focused on developing synthetic analogs of the native auto-inducers, capable of interfering with the QS and disrupt the cell-to-cell communication to inhibit biofilm formation. The main originality of this work is to target inter-species Quorum Sensing and therefore control the formation of multi-species biofilms.
A major part of the project will be focused on the design (by molecular docking), chemical synthesis, and characterization of heterocyclic compounds as new analogs of the QS auto-inducers. The second part will be dedicated to the evaluation of their anti-biofilm activity, on pure bacterial strains and on multi-species biofilms in order to select the best inhibitors. Another objective of the thesis will be to use the selected inhibitors as molecular tools to get insights on the mechanisms involved in the Quorum Sensing of multi-species biofilms, in static conditions and under flow, using molecular biology techniques.