Drug Delivery Control at the Molecular Level

The objective of this exploratory project was the development of nanostructured drug delivery films with applications in glaucoma treatment. This intends to be a potentially alternative solution to the current therapeutics where the drugs can be released directly into the eye using intraocular devices coated by the proposed nanostructured films.

**GENERAL MOTIVATION AND OBJECTIVES**

The glaucoma (GL) is one of the most troubling diseases, globally considered the second leading cause of blindness by the World Health Organisation. This disease is associated with elevated intraocular pressure (IOP), in which damage to the eye optic nerve can lead to loss of vision and even blindness. Its treatment consists in a surgical technique where an artificial valve is implanted in the eye in order to decrease the IOP. In addition to this surgery, the patient needs to administrate ocular drops composed of drugs that will also contribute to decrease the IOP. However, this method has strong limitations such as, only 20% of the active drug in a droplet achieves the ocular anterior chamber; the remaining is drained through the nasolacrimal duct or run down the chin.

Another problem relates to the patient noncompliance since half of glaucoma patients do not use their ophthalmic medication properly. This project established an important bridge between the drug delivery (DD) monolayers and the optimization of the proposed films. The MOLDELIV project contributed to the development of self-assembled monolayers that can coat the intracellular devices and incorporating the same drugs as those used in the conventional therapeutics.

**WORK DESCRIPTION AND ACHIEVEMENTS**

This project was developed by the following two main tasks:

Glucuronic acid (GlcA) monolayer – The first task of the project consisted on the preparation of a GlcA monolayer on graphite using STM at the solid/liquid interface. The method was focused on a droplet of an isolated and inert solvent that was injected between the STM tip and the substrate. Into this droplet, the molecules that correspond to the GlcA monolayer were co-adsorbed with heptanoic acid on graphite surface. This project was prepared using a layer-by-layer technique and their growth was characterized by STM and spectroscopy. The kinetic of drug release was also studied by immersing the films in a solution similar to the human biological fluids and the amount of drug delivered to the solution was monitored with spectroscopy. The films were developed by the following two main tasks:

- **Monolayer with glucuronic acid and heptanoic acid on graphite**

**Fig. 1** Sequential STM images of a self-assembled monolayer of glucuronic acid (GlcA) co-adsorbed with heptanoic acid on graphite surface.

**Fig. 2** High resolution STM image (scan size: 200 x 200 nm²) which shows a lamellar structure with bright features surrounded by dark troughs. The bright features correspond to two heptanoic acid molecules arranged in a tail-to-tail fashion whereas in the dark troughs two distinct molecular conformations of glucuronic acid molecules can be distinguished in figure b.

**CHALLENGE**

The main challenge of MOLDELIV was the development of the nanostructured films at molecular scale where scanning tunneling microscopy (STM) was used to control the process of fabrication. More specifically, biocompatible monolayers with a subunit of heparine were assembled on graphite surface. This monolayer could work as a platform to adsorb cyclodextrins (CDs) with drugs used in GL treatment.