

EXECUTIVE SUMMARY : In treatment of some tumors, bacterial infections, or bone regeneration, local drug delivery is the method of choice. In some of these cases the required dose of a drug is so high that it could be fatal on a systemic level. In addition it might be necessary to maintain a high local drug concentration for many hours. In the latter case the drug can be “trapped” in the delivering matrix and released by slow progressive diffusion. Thus the drug needs to be weakly and reversibly bound to the matrix. Two main forces responsible for interactions of drugs with the matrix are hydrophobic and electrostatic interactions. While several literature reports address electrostatic interactions, less is known about hydrophobic interactions. I propose a new technique that will enable the quantitative assessment of the hydrophobic domains within the collagen matrix. The technique is based on the electrochemical measurement of time-of-flight of a non-metal redox probe within the matrix. The probes are small molecules specifically designed to vary their hydrophobicity in a systematic way. At the same time the collagen matrix will be systematically modified with a crosslinking agent to create different strength of interactions between the small molecules and the matrix. As a result of these studies I hope to answer several questions concerning local environments (i.e. the existence and size of hydrophobic pockets) within the collagen matrix. These local hydrophobic pockets can promote preferential binding of hydrophobic drugs and slow down their release. The knowledge gained from these studies will contribute to an understanding of the mechanics of the collagen matrix and will lead to release profiles useful for physicians.