



## Faculty of Engineering and Applied Science Chemical Engineering Seminar Series



# Viscous Liquid Biodegradable Polymer Strategies for Therapeutic Protein Delivery

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### ABSTRACT

Proteins are an important drug class because of their potential to treat a wide range of conditions. Compared to small drug entities, protein therapeutics are highly specific in their action, and are expected to be less toxic than synthetically derived molecules as well as to behave more predictably *in vivo*. They thus represent a significant potential market. Because of the stability requirements of proteins and the barriers to their absorption by other conventional routes such as oral, nasal, buccal, and transdermal, the route of administration for many therapeutic proteins is currently parenteral. However, parenteral delivery may not be suitable for a number of protein drugs. Most therapeutic proteins have a short *in vivo* half-life and, upon injection, are unevenly distributed in the interstitial fluid and unable to reach the desired physiologic sites. They may also bind unselectively to cellular receptors and thus cause undesirable side effects. Furthermore, many therapeutic proteins are produced locally to act on cells in the immediate environment. These proteins are often active at very low concentrations, of from  $10^{-9}$  to  $10^{-11}$  M, and are required at the local tissue site for a prolonged period of time. Thus, administration regimens typically consist of multiple injections, often at supraphysiologic concentrations, which presents potential problems with patient compliance and possible complications when administered in a non-clinical setting. A long-term continuous and localized protein drug delivery depot could therefore provide numerous and distinct advantages, both therapeutic and financial, for many therapeutic proteins, and, in many cases, are required for their clinical application. Numerous biodegradable polymer formulations have been proposed and examined for such a purpose. An effective formulation for protein delivery must possess a number of features. The protein structure and bioactivity must be retained during fabrication, storage, and following release, as patient safety and drug efficacy can be compromised if even a small fraction of the protein molecules is degraded. An appropriate release rate must be generated, in terms of local concentration and duration, to achieve the desired therapeutic response. The protein must also be completely released from the device. Finally, the formulation should be capable of

being manufactured in relatively large-scale so as to yield a reproducible, sterile product. It is also often desirable for the formulation to be capable of administration via simple injection through standard gauge needles for minimally invasive localization to the desired site of action. In this talk I will discuss the potential of utilizing biodegradable polymers in the format of viscous liquids to fulfill the requirements of an effective therapeutic protein formulation for long-term delivery.