Measuring Nanoparticle Interactions using Surface Plasmon Resonance

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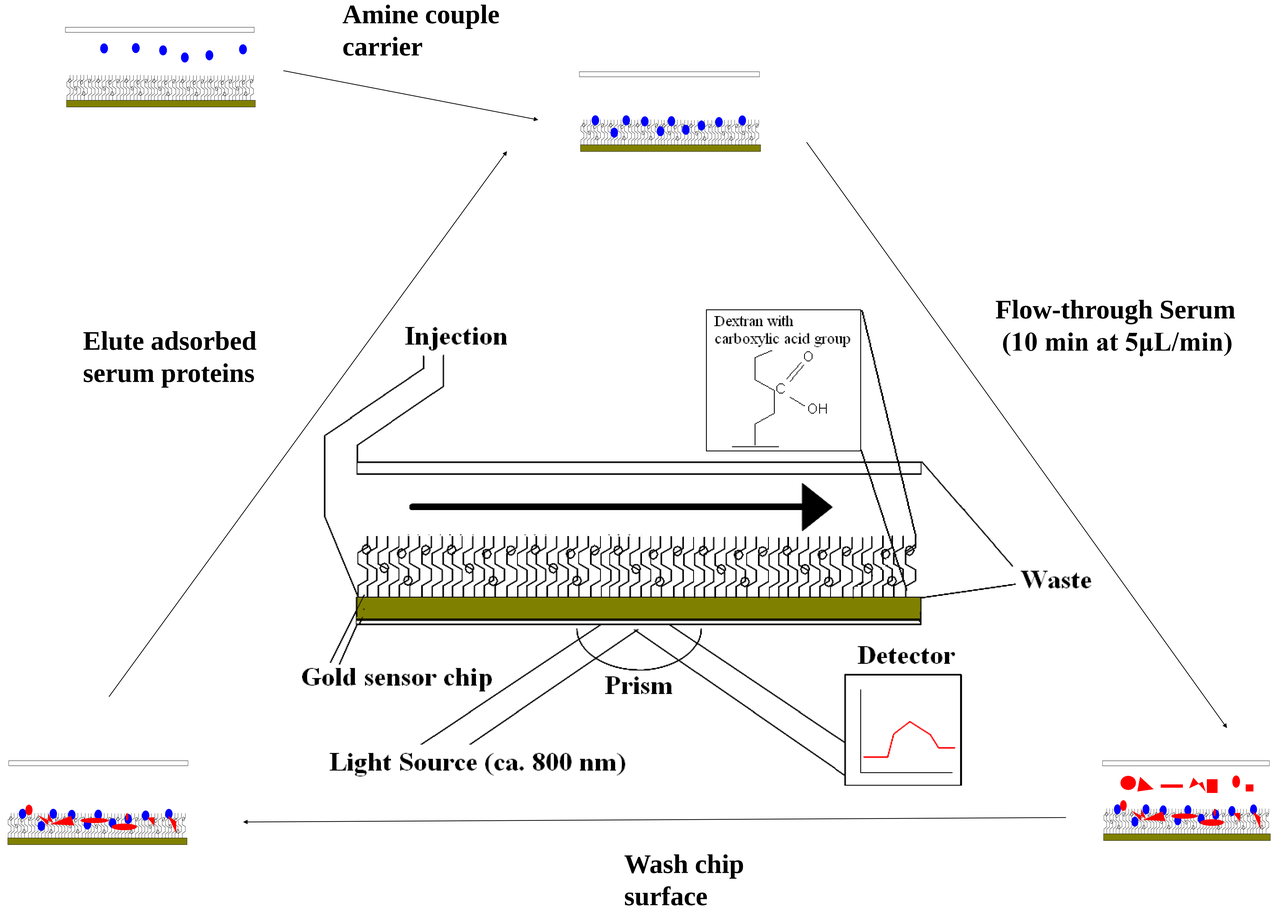
Nebraska IN-BRE NIH grant #P20RR16469-05

Project goal

Develop *in vitro* techniques for determining *in vivo* biodistribution, by studying the interfacial interactions between drug delivery vehicles and serum proteins—specifically using Surface Plasmon Resonance.

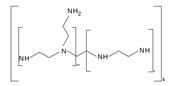
Abstract

Finding tools to study pharmacokinetic properties of drug delivery vehicles (DDVs) is becoming increasingly important in today's drug delivery efforts. Understanding of these properties should facilitate design of more effective DDVs.
In this study, polyethyleneimine (PEI) and nanogel—a recently developed polymeric nanoparticle—were applied in a novel drug delivery screening approach, which utilized Surface Plasmon Resonance (SPR) technology. The two nanoparticles were amine coupled to a biosensor chip and screened for interactions with human serum proteins. Preliminary results showed serum protein adsorption to PEI, but no adsorption to nanogels. These adsorbed proteins could be eluted by treatment with chaotropic reagents. Thus, *proof of principle* was demonstrated via protein adsorption to and desorption off of PEI. Additionally, this study employed an innovative approach to DDV screening in that rather than immobilizing serum proteins to the biosensor chip, the nanoparticles were immobilized. The serum proteins were subsequently injected over the sensor chip. Furthermore, the novel nanogel particle displayed inert properties that should support its progression through DDV development. Future research will involve combining SPR with MALDI MS to collect and identify the interacting serum proteins.

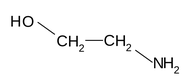


Project Design

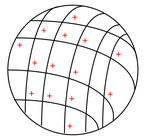
1. Couple polyethyleneimine particles (positive control) to the sensor chip surface, using an amine coupling reaction (Graph 1).
2. Screen for interactions between serum proteins and sensor chip-bound polyethyleneimine particles by injecting serum proteins over the SPR surface; subsequently, elute bound serum proteins off of the polyethyleneimine particles using various regeneration cocktails (Graphs 2 and 3).
3. Couple unloaded and loaded nanogel (an effective, hydrophilic drug carrier) to the sensor chip surface, using an amine coupling reaction (Graphs 4 and 5).
4. Screen for interactions between serum proteins/nucleic acids and sensor chip-bound nanogel particles by injecting these solutions over the SPR surface (Graph 6).



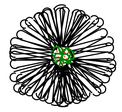
Polyethyleneimine (PEI)



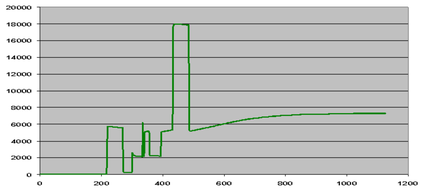
Ethanolamine



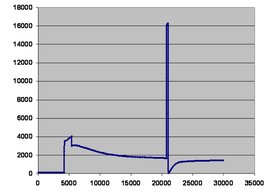
Unloaded nanogel



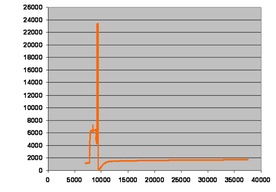
DNA-loaded nanogel



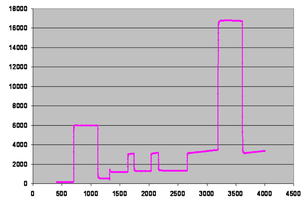
Graph 1: Sensorgram of PEI coupling



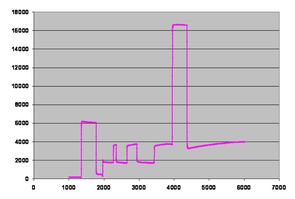
Graph 2: Sensorgram of serum proteins adsorbing to PEI, followed by slow elution



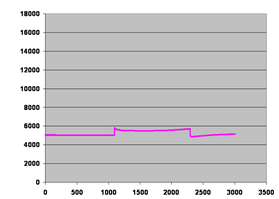
Graph 3: Sensorgram of serum proteins adsorbing to PEI, followed by fast elution



Graph 4: Sensorgram of loaded nanogel coupling



Graph 5: Sensorgram of unloaded nanogel coupling



Graph 6: Sensorgram of human serum protein injection over unloaded nanogel

Conclusions

- PEI, and unloaded and loaded nanogels were coupled to a sensor chip SPR surface (Refer to graphs 1, 4, and 5)
- "Proof of Principle" was demonstrated via binding and elution of serum proteins bound to amine coupled PEI (Refer to graphs 2 and 3)
- PEI – serum interaction is primarily ionic, although multifaceted (Refer to graphs 2 and 3)
- Thus far, no interactions were observed between nanogels, and DNA, siRNA, and serum proteins (Refer to graph 6)

Benefits of SPR Approach

In drug delivery research, Surface Plasmon Resonance technology can be used to determine three different parameters in a real-time, interactive fashion:
(1): presence of binding between carrier and serum proteins;
(2): specific interfacial interactions between carrier and serum proteins, using regeneration cocktails; and
(3): specific interaction partners in the serum solution that adsorb to drug carriers.

Future Directions

1. Develop positive control for nanogel binding
2. Optimize the coupling reaction (pH, temperature)
3. Complete the proof of principle by eluting and identifying targets, by combining SPR with MALDI MS
4. Verify with another technique (size exclusion or column chromatography)
5. Design different SPR approaches
   - Couple PEI and flow-through DNA
   - Couple DNA and flow-through nanogels and PEI
   - Couple "sticky" substance, IgG or albumin, and flow-through carriers
   - Couple a modified nanogel and flow-through a specific interaction partner.