

Medical Engineering Spring 2006 Course on Biomaterials and Biocompatibility
Class on Proteins at Interfaces by T. Horbett
Monday, April 17

Outline of Class:

Lecture A: "Basic Lecture on Protein Adsorption"

- 1. Experimental demonstration of protein adsorption effects on interfaces**
- 2. Introductory overview and summary of the importance of protein adsorption in biomaterials**
- 3. Overall properties of proteins relevant to adsorption, including structure**
- 4. Concepts and principles of protein adsorption in single solutions**

Lecture B: "The role of adsorbed adhesion proteins in cellular recognition of polymeric biomaterials"

- 1. Adhesion proteins and cell recognition.**
- 2. Adsorption from complex mixtures**
- 3. The integrin receptors on cells that allow recognition of adsorbed adhesion proteins**
- 4. Differential affinity: the amount of an adhesion protein adsorbed to a surface varies, depending on the chemical composition of the surface**
- 5. Modulation: the cell adhesive activity of adhesion proteins varies and depends on the type of surface they are adsorbed to.**
- 6. Substrate activation: adsorbed adhesion proteins are often more biologically active than soluble adhesion proteins**

THE ROLE OF ADSORBED ADHESION PROTEINS IN CELLULAR RECOGNITION OF POLYMERIC BIOMATERIALS

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The “fouling” of foreign surfaces often involves cell attachment that is mediated by the prior adsorption of specialized adhesion proteins to the surface. These adhesion proteins act as ligands specifically recognized by the cell’s adhesion receptors. Therefore, the role of adsorbed adhesion proteins in mediating cellular interactions with biomaterials will be the primary focus of my presentation. The ability of the adhesion proteins to support cell interactions with surfaces will be illustrated with examples from my lab and the literature.

A complex mixture of adhesion promoting and adhesion inhibiting proteins adsorbs rapidly to surfaces exposed to cells because the media typically contains many different proteins with large differences in their affinity for surfaces. Thus, the composition of the adsorbed layer on each biomaterial is different. The principles underlying protein adsorption to biomaterials from complex protein mixtures will therefore be presented. Variations in surface affinity and protein concentration in the context of a limit on adsorption (the monolayer) lead to selectivity in adsorption.

The integrins are the only class of cell receptors known to be important in adhesion to foreign surfaces. Fibrinogen, fibronectin, vitronectin, and von Willebrand’s factor all act as ligands for integrins in various cells and thus mediate adhesion when adsorbed. Examples illustrating the role of the integrins and the adhesion proteins in cell attachment will be given. Three major mechanisms underlying the role of the adsorbed adhesion proteins in cell interactions are the differential affinity for surfaces, modulation of the biological activity of the adsorbed adhesion protein by the surface, and substrate activation of adhesion proteins.

Differential affinity will be illustrated with studies of the adsorption behavior of the adhesion proteins fibrinogen, fibronectin and vitronectin from complex protein mixtures onto synthetic substrates. Selective depletion of adhesion proteins is a powerful tool that has identified vitronectin as opposed to fibronectin in mediating attachment and spreading of anchorage dependent cells on some surfaces. Depletion has also shown the important role that adsorbed fibrinogen plays in the adhesion of platelets and neutrophils.

Surfaces with similar amounts of adsorbed adhesion proteins sometimes exhibit differences in cell attachment and spreading, suggesting that the substrate properties modulate the biological activity of the adhesion protein. Examples illustrating modulation in the interaction of platelets with fibrinogen adsorbed on a series of polyurethanes and fibronectin interaction with several cell types will be given.

“Substrate activation” refers to the idea that adsorption of adhesion proteins appears to potentiate their adhesive properties. Substrate activation may be partly due to the exposure of novel binding sites in the adsorbed protein that are normally hidden in the soluble protein. The binding of monoclonal antibodies to adsorbed fibrinogen and fibronectin will be used to illustrate this phenomenon.