

## **Thinfilms Biomaterials: Toward Biomedical Implant Applications**

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Nanoscale films formed via the layer-by-layer (LbL) assembly of oppositely charged macromolecular species [1] are promising materials for biomedicine [2, 3]. LbL films are easy to fabricate on a variety of flat or irregularly shaped objects (only simple solution exposures are required) and are amenable to fine control over physicochemical properties (through choice of polymers, solution conditions, and post-formation steps). Bioactivity may be conferred through the facile incorporation of biomolecular species, making LbL films excellent candidates for biomaterial applications, e.g. cell culture, tissue engineering, and biomedical implants [4-7].

Controlling the cellular response is a key challenge in biomaterials science. Material charge, hydrophobicity, topography, mechanical rigidity, and bioactivity are all known to be important factors. Ideally, each of these properties would be independently optimized toward a desired cell response. In practice, bioactivity and mechanical rigidity are often difficult to decouple, and in fact typically inversely correlated.

Through a recent collaboration [8-14], Profs. Pauthe and Van Tassel have developed unique approaches toward nanofilm biomaterials with independently tunable mechanical rigidity and bioactivity. The main idea is based on creation of pore space within the film, where the polymer portion may be “hardened” via standard chemical cross-linking methods, and the pore space then filled with bioactive species, both to independently controllable extents. One approach toward porous films has been “Nanoparticle (NP) templating”, where film formation occurs in the presence of spherical latex NP, followed by chemical cross-linking to control film rigidity and “lock in” a porous morphology, and finally by removal of the NP via dissolution (Fig. 1C). Another approach has been “solution shock”, where a sudden change in solution conditions (e.g. pH) follows film formation, resulting in the creation of a porous network that is then “locked in” through cross-linking (Fig. 1D). This work has led to a series of papers [11, 12, 14], in which proof of concept has been established and some early material characterization undertaken. Although certainly motivated by important applications in biomedicine, these ideas have not as yet been directed toward applications.

We propose here a sabbatical stay by Prof. Van Tassel in the lab ERRMECe, during Fall 2016, whose goal would be to develop the nanofilm biomaterial strategies described above toward a biomedical implant application. A key challenge in bone applications involves osseointegration between the implant material and the contacting bone tissue. We hypothesize that porous nanofilm biomaterials, of tailored mechanics and loaded with the growth factor bone morphogenetic protein (BMP), when coated onto the surface of a biomedical (e.g. titanium) implant, may significantly improve osseointegration. We propose to test this hypothesis first in vitro, by measuring the attachment, spreading, and proliferation of MC3T3-E1 pre-osteoblasts under controlled culture conditions, and then in vivo by measuring the extent of osseointegration within a murine model. Key variables to be investigated include film mechanical rigidity, BMP loading, and BMP release kinetics – all properties controllable by varying the film formation process. The significance will be a nanofilm biomaterial platform to optimize the tissue integration of common bone implant materials.

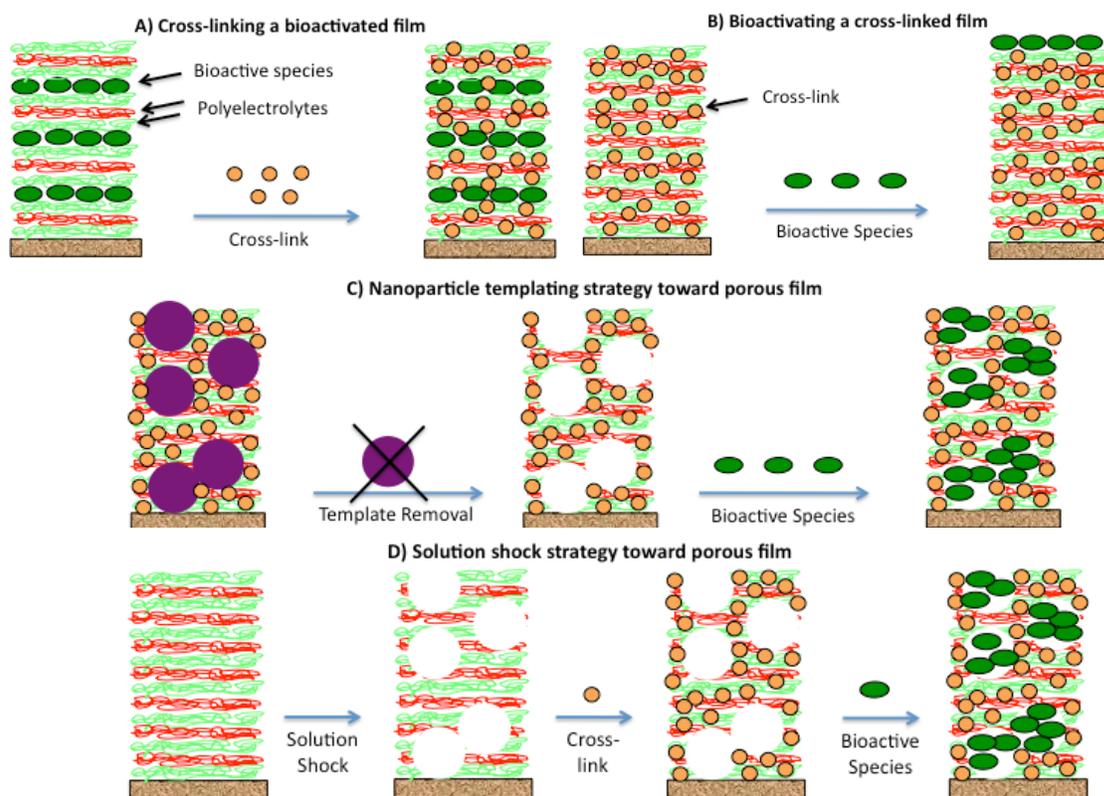


Figure 1: A) Bioactive species within an LbL film (left) may interact with contacting cells either through intra-film diffusion or film degradation. Chemical cross-linking (right), while increasing mechanical rigidity, acts to suppress bioactive species diffusion and film degradation, and so also generally suppresses bioactivity. B) A chemically cross-linked LbL film may be bioactivated via adsorption of biomolecules. However, cross-links diminish film permeability, limiting biomolecular adsorption to the film's surface region. In both A) and B), film rigidity is inversely coupled to bioactivity. C) Nanoparticle (NP) templating strategy, where following layer-by-layer assembly of charged polymers and NP, films are first cross-linked and then the NP are removed by dissolution. Bioactive species may then be loaded within the film by passive adsorption. D) Solution shock strategy, where following layer-by-layer assembly of charged polymers, solution conditions are abruptly changed (e.g. pH), resulting in a partial spinodal decomposition and a porous film. The film is then cross-linked to lock in the porous structure, and bioactive species adsorb upon solution exposure. (Cross-links are amide bonds between free amines and carboxyl groups, and so involve no additional chemical groups being added to the film. The layered structure of the films is exaggerated; in fact, considerable interpenetration among the polymer layers occurs [15, 16].)

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