

Modeling of Medical Device-Biological Interactions

Uses of biomedical devices have been very successful in treating diseases, especially chronic diseases where pharmaceutical approaches are less effective^{1,2}. The successes of biomedical devices are due, in large part, to the effective uses of biomaterials. A good example is the treatment of the abnormal narrowing of blood vessels (Figure 1). The most effective treatment procedure is to use a high strength plastic balloon to open the narrowed vessel and leave behind a tiny metal mesh (stent) with an antiproliferation drug to prevent the vessel from re-narrowing. Materials to make balloons, stents, and drug carriers are among the key components that contribute to this successful therapy.

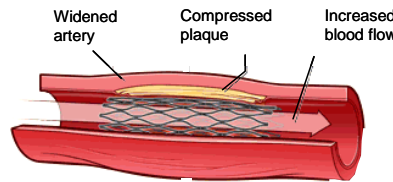


Fig 1. Stent prop opens vessel.

A critical effort in the development of medical devices is to find ways to manage the device-biological interactions, a large part of which are due to the materials of devices. Acceptable interactions allow the medical devices to perform their functions. Adverse interactions can cause serious side effects on the bodies as well as damages to the devices. This is commonly referred to as biocompatibility.

We propose three research topics. The first one is protein-material interactions. Different from protein folding, in protein-material interactions, folded proteins unfold and are absorbed to the materials' surface. This process is fast. The consequence is proteins denature and serve as a primer for a cascade of more complicated events. Physically, adsorption of proteins at the surface can be treated as a special protein unfolding problem. We are interested in protein absorption thermodynamics and dynamics and its relationships with protein structures, surface properties, and application conditions. Protein folding has been studied extensively. The physical concepts and mathematical tools developed in that area may be useful for studying protein adsorption at surface.

A second area of interest is interactions of cells with the materials' surface. Cells sense chemistry, topology, and mechanical properties of materials and respond by doing attachment, migration, growth, differentiation, necrosis, or other things. These can result in various physiological consequences. We are interested in understanding these processes at the molecular and cellular levels so that we can control wound healing and tissue regeneration. Quantitative modeling in this area has not been well developed. This is a challenge but an opportunity as well.

A third area of interest is related to the technologies for delivering drug through medical devices. There are a number of successful examples proving the effectiveness of these technologies. However, these technologies also add new dimensions to the traditional frame to study performance and pharmacological activity of drugs. This is due to a few reasons: (1) the delivery of drug from medical devices has extra release control (liberation) compared to that delivered from traditional dose forms such as oral pills, (2) drugs' interactions with biological systems are coupled with the device-biological interactions, and (3) drug and devices interact with themselves as well. These new interactions play critical roles in determining the success of drug-eluting medical devices. The exiting pharmacokinetics is not sufficient to address this new case. We need to develop a new approach to describe and predict the pharmacological performance of drug eluting medical devices.

References

1. Ratner, B. et al. Biomaterials science: an introduction to materials in medicine. Academic Press, San Diego (2004).
2. Shmulewitz, A. & Langer, R. Nature Biotechnology 24, 277-280 (2006).