166c Membrane Science and Intelligent Therapeutics

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Recent advances in the discovery and delivery of drugs to cure chronic diseases are achieved by combination of intelligent membrane design with advances in nanotechnology. Since many drugs act as protagonists or antagonists to different chemicals in the body, a delivery system that can respond to the concentrations of certain molecules in the body is invaluable. For this purpose, intelligent therapeutics or "smart drug delivery" calls for the design of the newest generation of sensitive membranes based on molecular recognition.

Biomimetic polymeric membranes can be prepared by designing interactions between the building blocks of biocompatible networks and the desired specific ligands and by stabilizing these interactions by a three-dimensional structure. These structures are at the same time flexible enough to allow for diffusion of solvent and ligand into and out of the networks. Synthetic networks that can be designed to recognize and bind biologically significant molecules are of great importance and influence a number of emerging technologies. These artificial materials can be used as unique systems or incorporated into existing drug delivery technologies that can aid in the removal or delivery of biomolecules and restore the natural profiles of compounds in the body.

In this review we address important aspects of the use of principles of bionanotechnology in the development of membranes for drug delivery and modern therapeutics. Special emphasis was placed on the importance of biomimetic systems and intelligent substrates in truly innovative drug delivery systems. In recent years, there has been considerable work in preparing materials and finding new uses for nanoscale structures based on biomaterials. Uses such as carriers for controlled and targeted drug delivery, micropatterned devices, systems for biological recognition, have shown the versatility of these biopolymeric materials as indicated by Langer and Peppas [1].

Of specific interest are applications requiring the patterning of vinyls, methacrylates and acrylates during reaction allowing for the formation of nanoscale three-dimensional structures. These micropatterned structures may be used for a host of applications including cell adhesion, separation processes, the so called "factory-on-a-chip" microscale reactors, and microfluidic devices.

Electronic devices have now reached a stage of dimensions comparable to those of biological macromolecules. This raises exciting possibilities for combining microelectronics and biotechnology to develop new technologies with unprecedented power and versatility. While molecular electronics use the unique self-assembly, switching and dynamic capabilities of molecules to miniaturize electronic devices, nanoscale biosystems use the power of microelectronics to design ultrafast/ultrasmall biocompatible devices, including implants, that can revolutionize the field of bioengineering.

Thus, in recent years we have seen an explosion in the field of materials or membranes incorporated in novel microfabricated and nanofabricated devices for drug delivery. Such devices seek to develop a platform of well controlled functions in the micro- or nano-level. They include nanoparticulate systems, recognitive molecular systems, biosensing devices, and microfabricated and microelectronic devices.

In addition, biomimetic methods are now used to build biohybrid systems or even biomimetic materials (mimicking biological recognition) for drug delivery, drug targeting, and tissue engineering devices [2]. The synthesis and characterization of biomimetic gels and molecularly imprinted drug release and protein delivery systems is a significant focus of recent research. We concentrate on configurational biomimetic imprinting processes of important analytes on intelligent gels that can lead to preparation of new biomaterials that not only recognize the analyte but also act therapeutically by locally or systemically releasing an appropriate drug.

The design of a precise macromolecular chemical architecture that can recognize target molecules from an ensemble of closely related molecules has a large number of potential applications [3].

There are numerous techniques for microfabrication of patterned polymer surfaces and microchips for drug delivery. While silicon has been the choice material for much of the research done with MEMS, the methacrylates and acrylates provide a rapid and inexpensive base for future work. Several applications have already been suggested including patterned surfaces for cell adhesion, biosensors, microfluidic devices, and arrays for chemical screening.

Using intelligent polymers, it is now possible to design new devices for intelligent therapeutics. Such systems can be employed for auto-feedback drug delivery, whereby the hydrogel will be connected to a biosensor and will respond to fast changes in the external biological conditions. This idea may be used to develop novel insulin delivery systems. Another particularly novel use of these systems is for the release of human calcitonin. The physicochemical understanding of such hydrogels under the conditions of application is neither simple nor well developed. Considering that all these carriers are ionic hydrogels, and that several ionic and macromolecular components are involved, with associated thermodynamically non-ideal interactions, it is evident that analysis and prediction of the swelling and drug delivery behavior is rather complex. In this volume, our research group has provided two reviews on related subjects.

These recent developments in the field of drug delivery could not be predicted twenty years ago when the emphasis of all controlled release work was on the "adjustment" of the drug release rate. But they could not have been possible without the integration of the field and without the contributions of many scientists and engineers from other areas. I hope you will enjoy this volume and that you will find its contributions thought-provoking.

References

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