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BioInterface Perspective

Establishing ultimate biointerfaces covered with phosphorylcholine groups

Junji Watanabe[a,b], Kazuhiko Ishihara[c,d,e,*]

[a] Department of Applied Chemistry, Graduate School of Engineering, Osaka University, 2-1 Yamada-oka, Suita, Osaka 565-0871, Japan
[b] 21st Century COE Program "Center for Integrated Cell and Tissue Regulation", Graduate School of Engineering, Osaka University, 2-1 Yamada-oka, Suita, Osaka 565-0871, Japan
[c] Department of Materials Engineering, School of Engineering, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan
[d] Center for NanoBio Integration, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan
[e] Department of Bioengineering, School of Engineering, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan

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ABSTRACT

The phospholipid molecule is a typical component of the cell membrane. In particular, the phosphorylcholine polar group is an electrically neutral head group. 2-Methacryloyloxyethyl phosphorylcholine (MPC) comprising a phosphorylcholine group side chain was designed with the cell membrane as an inspiration. Versatile polymers comprising MPC could be synthesized, and their specific biofunctions were evaluated. Establishing an ultimate biointerface with multiple functions is important from the viewpoint of biomaterials science. Nonspecific protein adsorption is essential for achieving versatile biomedical applications. Simultaneously, bioconjugation and retention of its biofunction are crucial for a high-performance biointerface. In this review article, a tunable biointerface comprising MPCs was introduced. In particular, the use of nanoparticles and polymer brushes as biointerfaces was described along with the perspective versatility of their biological applications.

1. Inspiration from cell membranes

The cell is the minimum unit of life in our living system, and it is surrounded by a cell membrane that helps it adapt to the versatile physiological environment. Cell membranes have been present in nature since ancient times. The bacterium, which is a primitive living thing, also contains a nanoscale bilayer. Nature produces versatile and complex cell membranes, and most of them have a hierarchical structure with versatile functions. Therefore, the cell membrane is a good candidate for constructing a biointerface platform. Understanding the cell membrane facilitates the engineering of an advanced biointerface with highly controlled properties and functions. Cell membrane formation in nature is highly regulated and finely tuned at the molecular level. Therefore, we have focused on the biomimetic approach as one of the strategies for creating an artificial biointerface.

McConnell et al. reported the construction of a lipid monolayer with dipalmitoyl phosphatidylcholine on an alkylated glass substrate [1]. This is a typical cell membrane model, and it facilitates the investigation of pure physical chemistry at the air–water interface. Moreover, the monolayer is appropriate as a target membrane in the study of cellular immune response, which strongly depends on the incorporation of specific antigens, lipid haptens, and antibodies [2]. Sackmann reported another approach that involved the membrane supported on a substrate [3]. Lipid bilayers can be separated from the substrate by ultrathin layers of water or soft polymer cushions. In this system, membrane structure and its dynamic mobility are maintained. Moreover, it enables the creation of artificial biointerfaces to explore the interplay of receptor-ligand binding involved in cell adhesion [4]. Recently, this supported membrane was integrated with microfabrication and/or nanofabrication, and a suspended biomimetic bilayer was formed on the silicon substrate with submicron pores [5]. The resulting biointerface facilitates the investigation of ion channel function. With regard to industrial and medical application, high versatility and robust biointerface are key issues. Taking these biomimetic approaches into account, we should embark on a new investigation by using polymeric materials with a bioinspired approach.

The fundamental strategy of a bioinspired approach is to clearly understand the principles of the cell membrane functions. Fig. 1 shows the typical illustration of a cell membrane along with some functions. Numerous biomolecules are embedded in the phospholipid bilayer, e.g., antibodies, glycoproteins, enzymes, and receptors. The favorable biofunctions are inertness of the capsule, biological affinity, enzymatic reaction, etc. These are fundamental biomolecules that play important roles. In the bioinspired approach, molecular components were assembled to perform these selected biofunctions. For example, phospholipids comprise a polar

* Corresponding author at: Department of Materials Engineering, School of Engineering, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan. Tel.: +81 3 5841 7124; fax: +81 3 5841 8647.
E-mail address: ishihara@mpc.t.u-tokyo.ac.jp (K. Ishihara).

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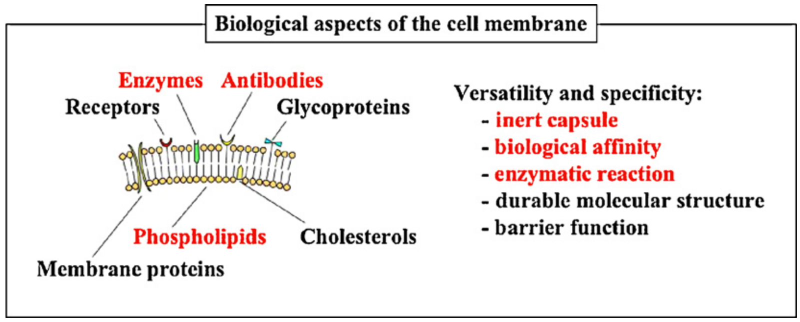

Fig. 1. Schematic illustration of the cell membrane with versatile biomolecules. Typical biomolecules and their fundamental aspects are indicated in red letters. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

head group and alkyl tail group. However, surface enrichment of phospholipid polar groups is essential for preparing the biointerface. In other words, the entire phospholipid molecule is not necessary for formation of the biointerface. This is the concept of a fundamental bioinspired approach, and in the next chapter, we introduce polymer materials to create the essential biointerface along with the related perspectives.

The requirements of establishing ultimate biointerfaces are (i) bioinertness, (ii) easy fabrication, (iii) immobilization of biomolecules under mild condition, (iv) retention of higher biofunctions, and (v) easy accessibility of target molecules without any barrier. In this review, MPC is utilized as a key material for constructing a biointerface platform. MPC allows versatile polymerization techniques with appropriate comonomers: conventional radical, living radical, atom transfer radical polymerizations. Therefore, precisely designed polymers comprising 2-methacryloyloxyethyl phosphorylcholine (MPC) are easily synthesized; herein, the ultimate biointerfaces by MPC is introduced along with recent excellent results.

2. Tunable biointerface covered with phosphorylcholine groups

In the medical field, studies on blood compatibility, biological sensing, regenerative medicine, and medical diagnosis focus on the development of high-performance biointerfaces. Fig. 2 shows one of the applications of the biointerface, along with its functions. This is a typical protocol for molecular diagnosis in the medical field. Human blood and serum contain a considerable number of biomolecules such as phospholipids and proteins, antibodies, and enzymes, in addition to blood corpuscles and platelets. Multiple processes are required to detect specific biomolecules. If each process, i.e., affinity separation, biological sensing, and medical diagnosis, is simultaneously performed at the surface of the devices, this technology based on materials science could be essential from the viewpoint of medical welfare. Polymeric materials facilitate the creation of multipurpose interface between biological circumstances and materials, that is biointerfaces. Moreover, they facilitate the application of versatile substrates independent of the compositions and morphologies of the materials.

In 1990, Ishihara et al. reported the biological potentials of phospholipid polymer materials, and successfully synthesized phospholipid monomers with higher yield and excellent purity [6]. The monomer, MPC, is a methacrylate comprising a phosphorylcholine (PC) polar group as the side chain. Originally, Nakabayashi et al. designed and synthesized the monomer in 1978 [7]. However, the potential of the polymer having the MPC units as biomaterials could not be observed because synthetic route of the MPC was not optimized, and the monomer yield and its purity were not so good. Thus, versatile researches regarding the biointerface were not conducted. Now, MPC is produced industrial scale by one of the Japanese chemical companies. And biointerface research with MPC and its polymers has been conducted worldwide. It has opened up new avenues for investigation, particularly in the field of life science research. Biomaterial researches employing MPC and its polymers are increasing every year due to its excellent polymerization ability with other vinyl compounds to obtain various functional polymers. Some of the MPC polymers have been already applied in clinically. The synthesized polymers comprising MPC are versatile: polymer solution, hydrogel, polymer-coated surface, and

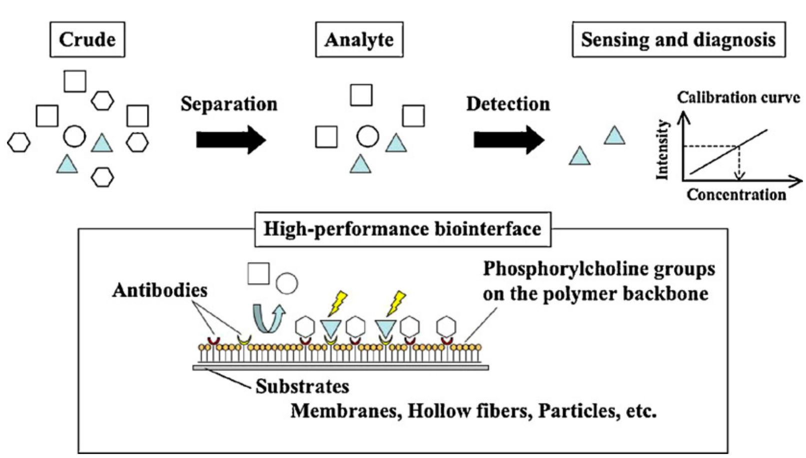

Fig. 2. An ultimate biointerface covered with phosphorylcholine groups on a polymer backbone simultaneously facilitates affinity separation, biological sensing, and medical diagnosis.