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Electrochemical microelectrodes for improved spatial and temporal characterization of aqueous environments around calcium phosphate cements

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ABSTRACT

Calcium phosphate compounds can potentially influence cellular fate through ionic substitutions. However, to be able to turn such solution-mediated processes into successful directors of cellular response, a perfect understanding of the material-induced chemical reactions in situ is required. We therefore report on the application of home-made electrochemical microelectrodes, tested as pH and chloride sensors, for precise spatial and temporal characterization of different aqueous environments around calcium phosphate-based biomaterials prepared from α-tricalcium phosphate using clinically relevant liquid to powder ratios. The small size of the electrodes allowed for online measurements in traditionally inaccessible in vitro environments, such as the immediate material–liquid interface and the interior of curing bone cement. The kinetic data obtained has been compared to theoretical sorption models, confirming that the proposed setup can provide key information for improved understanding of the biochemical environment imposed by chemically reactive biomaterials.

1. Introduction

Enabling tools that provide accurate spatial and temporal information on cellular fate and/or material performance find numerous applications in biomaterials and tissue engineering research [1]. Ion and pH sensors are examples of enabling tools that can reveal information on both tissue development and material activity. For example, general cellular respiration tends to provoke acidification of the extracellular environment [2], and in bone tissue engineering applications specific cellular activity may further influence the extracellular pH, as well as the ionic environment with respect to calcium and phosphate [3–5]. In parallel, many scaffold biomaterials used in bone tissue engineering are based on calcium phosphate compounds [6] which often undergo ion-exchange processes when immersed in aqueous environments [7,8]. Such solution-mediated reactions may simultaneously influence pH and the concentration of many extracellular ions, which in turn can affect cellular behaviour both positively and negatively [9–12].

To control or turn such material-induced ionic interactions into a powerful tool that can promote or suppress certain cellular activity, one first has to understand the nature of the reactions, and determine their magnitude in biologically relevant volumes and environments. Of particular interest are environments created at the immediate interface between biomaterials and biological substances, as well as in the interior of scaffolds. Detailed characterizations of such environments are still scarce [13–14], but recent efforts to develop biocompatible optical microparticle sensors may improve our understanding of the instantaneous composition of local microenvironments at the cell–material interface [15,16]. A different method to approach local environments at the material interface includes the use of miniaturized electrochemical sensors. Electrochemical sensors do not only have a long history of applications in complex chemical environments, but are also relatively easy to modify for the detection of many different analytes and in different environments, including opaque ones where optical sensors may not be used.

In this study we have focused on the use of electrochemical sensors for spatial and temporal evaluation of small-volume environments created around ion-reactive calcium phosphate cements. For this purpose, we present how miniaturized electrodes were prepared from iridium oxide (IrO_2) or silver/silver chloride (Ag/AgCl) to obtain sensors for pH or chloride ions, respectively, and how those sensors were subsequently used in standard in vitro environments containing ion-reactive biomaterials. As a model biomaterial we used α-tricalcium phosphate (α-TCP), which

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