“This book describes a new family of in situ in vivo produced bioceramics with high potential within dentistry and orthopedics. The importance of nanostructural properties is thrilling, and thoroughly described.”

Prof. Roger Narayan
North Carolina State University, USA

Biomaterials are produced in situ and in vivo in the body using mainly hydration reactions, that is, reactions between phosphates, silicates or aluminates, and water. The nanostructural integration of these biomaterials in the body is controlled by six mechanisms. The biomaterial interaction with body liquid results in bioactivity and total closure of the contact zone between the biomaterial and hard tissue.

This book describes the new biomaterials based on nanostructural chemically bonded bioceramics and discusses their general and specific properties. It presents an overview of the nanostructural chemically bonded bioceramics, including their processing aspects, properties, integration with tissues, relation to other bioceramics and biomaterials, and nanostructural integration in different dental and orthopaedic applications. The book also describes the potential application areas for these new chemically bonded bioceramics.

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NANOOSTRUCTURAL
BIOCERAMICS
NANOSTRUCTURAL BIOCERAMICS
Advances in Chemically Bonded Ceramics

Leif Hermansson
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Preface

It is a great honor to present this book on ‘nanostructural chemically bonded bioceramics’. The direct opportunity of this opened up after a speech on ‘Why even difficult to avoid nanostructures in chemically bonded calcium aluminate–based biomaterials’. The invitation to write this book from Pan Stanford Publishing is thankfully acknowledged.

Writing a book, which covers a whole new technology within biomaterials science (materials, processing, properties, biological response, clinical evaluation, new applications, etc.), is of course not one person’s work. I would like to acknowledge the following people contributing to the thinking in this book. I will start with my wife Irmeli, a dental technician, who challenged the author some decades ago with the question ‘Why don’t you from your ceramic platform do something which makes sense?’ She wanted a substitute for amalgam. This started a work at Karolinska Institute at the former Center for Dental Technology and Biomaterials, Stockholm University, Sweden. Prof. Rune Söremark, late Associate Prof. Folke Sundström, and Associate Prof. Yangio Li are specifically acknowledged. The input from CEO Torgny Nilsson of KRISS, Sweden, was fundamental for the start of the new activities. After some turbulent years, the author met his ‘positive anti-picture,’ Dan Markusson, who has been of great general help in understanding biomaterials product development. Dan is now CEO of Peptonic Medical AB, Sweden. The work at Karolinska Institute, and later at Uppsala University, Sweden, have contributed enormously to the understanding of nanostructural chemically bonded biomaterials. The work by Prof. Håkan Enqvist, Tech. Drs. Lars Kraft and Jesper Lööf, and Associate Prof. Erik Adolfsson are thankfully acknowledged. Early cooperation with Prof. Roger Carlsson and Associated Prof. Elis Carlström and colleagues at Swedish Ceramic Institute (now within IVF-SWEREA), Prof. Richard Bradt, Pennsylvania State University, USA, and Prof. Hans Larker at former ABB Cerama AB (now Saint Gobain Advanced Ceramics AB), Sweden, have been fundamental for basic understanding of materials science. The author would like to thank all personnel within Doxa AB,
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Leif Hermansson
Summer 2014
Chapter 1

Introduction to Nanostructural Chemically Bonded Bioceramics

This chapter gives an introduction to chemically bonded bioceramics (CBBCs) and the position of CBBCs in relation to other biomaterials based on metals, polymers, and other bioceramics. A detailed description of CBBCs will be presented in the subsequent chapters.

1.1 Chemically Bonded Bioceramics: An Overview

Biomaterials in general are based on the materials’ groups’ metals, polymers, and ceramics [1]. Typical metallic biomaterials are based on stainless steel, cobalt-based alloys, and titanium or titanium alloys and amalgam alloys. Polymeric biomaterial composites from monomers are based on amides, ethylene, propylene, styrene, methacrylates, and/or methyl methacrylates. Biomaterials based on ceramics are found within all the classical ceramic families: traditional ceramics, special ceramics, glasses, glass-ceramics, coatings, and chemically bonded ceramics (CBCs) [2, 3]. Examples are given in Table 1.1.
Table 1.1 Examples of bioceramics

<table>
<thead>
<tr>
<th>Ceramics: classification</th>
<th>Examples of bioceramics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traditional ceramics</td>
<td>Dental porcelain, leucite-based ceramics</td>
</tr>
<tr>
<td>Special ceramics</td>
<td>Al, Zr, and Ti oxides</td>
</tr>
<tr>
<td>Glass</td>
<td>Bioglass (Na₂O–CaO–P₂O₅–SiO₂)</td>
</tr>
<tr>
<td>Glass ceramics</td>
<td>Apatite–wollastonite, Li-silicate-based</td>
</tr>
<tr>
<td>CBCs</td>
<td>Phosphates, aluminates, silicates, and sulphates</td>
</tr>
</tbody>
</table>

CBCs are widely used as general construction materials but have found new applications as biomaterials. The following CBC systems have been proposed or are already used as biomaterials: Ca-phosphates, Ca-silicates, Ca-aluminates, Ca-sulphates, and Ca-carbonates (see Table 1.2).

Table 1.2 CBBC systems

<table>
<thead>
<tr>
<th>Group/name</th>
<th>Basic system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium silicates</td>
<td>CSH(^a)</td>
</tr>
<tr>
<td>Calcium aluminates</td>
<td>CAH(^b)</td>
</tr>
<tr>
<td>Calcium phosphates</td>
<td>CPH(^c)</td>
</tr>
<tr>
<td>Calcium sulphates</td>
<td>CaSO₄–H₂O</td>
</tr>
<tr>
<td>Calcium carbonates</td>
<td>CaO–CO₂</td>
</tr>
</tbody>
</table>

\(^a\)CSH = CaO–SiO₂–H₂O (calcium silicate hydrate).  
\(^b\)CAH = CaO–Al₂O₃–H₂O (calcium aluminate hydrate).  
\(^c\)CPH = CaO–P₂O₅–H₂O (calcium phosphate hydrate).

Most ceramics are formed at high temperatures through a sintering process. By using chemical reactions, the biomaterials in the chemically bonded bioceramic (CBBC) systems can be produced at low temperatures (body temperature), which is attractive from several perspectives: cost, avoidance of temperature gradients, (thermal stress), dimensional stability, and minimal negative effect on the system with which the material interacts. Notable is that the hard tissue of bone and teeth (apatite, a Ca-phosphate-based material) also is formed via a biological chemical reaction and close in composition to some of the CBBCs. The proposed CBBC systems have in general favourable biocompatible properties. The
The chemistry of these systems is similar to that of the hard tissue found in living organisms. These are based on different types of apatites and carbonates. The bioactivity aspects of CBBCs will be treated separately in Chapters 3 and 8.

One of the first ceramics to be proposed as a biomaterial was gypsum, \( \text{CaSO}_4 \cdot \frac{1}{2} \text{H}_2 \text{O} \). The first cement to be proposed and used was a Zn-phosphate, which is still used as a dental cement. Examples of typical phases formed in CBC systems are presented in Table 1.3.

### Table 1.3 CBC systems

<table>
<thead>
<tr>
<th>Group/name</th>
<th>Basic system</th>
<th>Typical phases formed</th>
</tr>
</thead>
<tbody>
<tr>
<td>OPC(^a)</td>
<td>CSH</td>
<td>Amorphous CSH, tobermorite</td>
</tr>
<tr>
<td>CAC(^b)</td>
<td>CAH</td>
<td>Katoite and gibbsite</td>
</tr>
<tr>
<td>Gypsum plaster</td>
<td>Ca-sulphates</td>
<td>( \text{CaSO}_4 \cdot 2\text{H}_2 \text{O} )</td>
</tr>
<tr>
<td>Sorel</td>
<td>MgO–H(_2)O (Cl)</td>
<td>MgOCl</td>
</tr>
<tr>
<td>Bioglasses</td>
<td>CaO–Na(_2)O–SiO(_2)–P(_2)O(_5)</td>
<td>Carbohydroxyapatite</td>
</tr>
<tr>
<td>Phosphates</td>
<td>CPH</td>
<td>Apaties, brushite, monetite</td>
</tr>
<tr>
<td>Carbonates</td>
<td>CaO–CO(_2)–H(_2)O</td>
<td>Calcite, aragonite</td>
</tr>
<tr>
<td>Geopolymers(^c)</td>
<td>Aluminosilicates, metakaolin</td>
<td>Amorphous phases</td>
</tr>
</tbody>
</table>

\(^a\)OPC = ordinary Portland cement  
\(^b\)CAC = high-alumina cement: C\(_3\)A, C\(_{12}\)A\(_7\), CA, etc.  
\(^c\)Geopolymers = metakaolin or synthetic aluminosilicates

CBCs constitute ceramics which are being formed due to chemical reactions. Often the precursor material is a ceramic powder (e.g., Ca-silicate or Ca-aluminate), which is ‘activated’ in a water-based liquid. A chemical reaction takes place, in which the initial powder is partly or completely dissolved and new phases precipitate. The precipitated phases are composed of species from both the liquid and the precursor powder. The precipitates can be formed in situ, in vivo, often in the nanoscale due to low solubility of the phases formed (see Chapter 6 for details). The nanostructural CBBCs are especially found within the Ca-phosphate, Ca-aluminate, and Ca-silicate systems. The large pores between the original dissolving precursor powders are filled, and the material hardens. The dissolution speed and solubility products of the formed hydrate phases determine the
nanosize, setting time, and final curing (hardening) of the material. The setting time can be controlled by selection of the precursor grain size and/or by addition of accelerating or retarding substances. Since the material can be formed from a precursor powder mixed with a liquid, the material can be made mouldable simply by controlling the amount of liquid (in relation to the powder) and by the possible addition of small amounts of polymers in the liquid. This makes CBBCs useful as injectable biomaterials, where the final biomaterial is formed in situ, in vivo. This will be treated in detail in Chapter 3 and Chapters 6–8. Also worth mentioning is a relatively new group of ceramics called geopolymers [4–6]. These are also produced by chemical reactions but do not involve hydration, that is, new uptake of water. The geopolymerisation is thus not a hydration process, in which water is consumed. Instead the water resides in the pores but plays an active role as a dissolution medium during the reaction, an inorganic polymerisation.

CBBCs can further be divided into two main groups, resorbable and stable biomaterials. This will be described next.

1.2 Stable and Resorbable Chemically Bonded Ceramics

Ca-aluminate-based biomaterials and to some extent Ca-silicates are stable materials after hydration and can favourably be used for load-bearing applications. The Ca-phosphates, Ca-sulphates, and Ca-carbonates are known to be resorbable or slowly resorbable when inserted in the body, and their main applications are within bone void-filling with low mechanical stress upon the biomaterial. The resorbable materials are after various times depending on the specific chemical composition replaced by new bone tissue. This can start immediately after injection, and the material can be completely dissolved after months and in some cases after a few years [7].

1.2.1 Stable Chemically Bonded Bioceramics

The chemistry and phases in stable CBBCs are presented in Fig. 1.1 [8]. The actual phases, using the cement abbreviation system (C=CaO, A=Al₂O₃, S=SiO₂, H=H₂O, etc. [9]) in the Ca-aluminate system
are C₃A, C₁₂A₇, CA, and CA₂ and in the Ca-silicate system are C₃S and C₂S. The reactivity of all these phases increases with the content of CaO. When these phases are used as biomaterials, precaution must be taken in the hydration reactions, which are exothermic reactions. The temperature increase during the setting and initial hardening can be controlled by selection of the phases and volumes involved and by processing agents.

The Ca-aluminate and Ca-silicate reaction mechanisms differ in one respect considerably from those of Ca-phosphate reactions and other reactions of resorbable chemically bonded materials. This has to do with the amount of water involved in the hydration reactions, and this can easily be seen when comparing the chemical formula of the phases formed in the curing reactions (see Table 1.4). An example of the water involved in the hydration of a given reaction is shown here:

\[
3\text{CaO} \cdot \text{Al}_2\text{O}_3 + 12 \text{H}_2\text{O} \rightarrow \text{Ca}_3[\text{Al(OH)}_4]_2(\text{OH})_4 + 4\text{Al(OH)}_3
\]

Ca-aluminate Water Katoite Gibbsite
The water content of the final chemical products has great influence upon the optimisation of the water-to-cement (w/c) ratio with regard to handling properties and the final microstructure, especially the residual porosity, which can be reduced substantially for the systems where the water consumption is high. The inherent high water uptake of stable CBBCs in comparison to resorbable ones yields benefits such as higher mechanical strength; extended possibility to add fillers, for example, for improved radio-opacity; and tuneable handling properties.

Table 1.4 The water involved in the hydration of three CBBC systems [2]

<table>
<thead>
<tr>
<th>System</th>
<th>Typical phase(s)</th>
<th>Oxide formula</th>
<th>Mol. % H₂O</th>
<th>Wt.% in hydrated products</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca-phosphate</td>
<td>Apatite</td>
<td>10CaO·3P₂O₅·H₂O</td>
<td>7</td>
<td>Approx. 5</td>
</tr>
<tr>
<td>Ca-aluminate</td>
<td>Katoite + gibbsite</td>
<td>3CaO·Al₂O₃·6H₂O + Al₂O₃·2H₂O</td>
<td>&gt;60</td>
<td>Approx. 25</td>
</tr>
<tr>
<td>Ca-silicate</td>
<td>Tobermorite + amorphous phases</td>
<td>5CaO·6SiO₂·5H₂O + Ca, SiH₂O</td>
<td>&gt;30</td>
<td>Approx. 20</td>
</tr>
</tbody>
</table>

A typical hydrated area in Ca-aluminate is shown in Fig. 1.2. High-resolution transmission electron microscopy (HRTEM) reveals nanosize porosity <3 nm, often 1–2 nm, and hydrates in the size range of 20–50 nm [10, 11] (see Fig. 1.3).

1.2.2 Resorbable Chemically Bonded Bioceramics

Ceramic biomaterials are often based on phosphate-containing soluble glasses and various calcium phosphate salts. These materials can be made to cure in vivo and react in situ with the surrounding tissue and are attractive as replacements for the natural calcium phosphates of mineralised tissues. Ca-phosphate products are gaining ground in orthopaedics as resorbable bone substitutes. Other resorbable ceramics are based on Ca-sulphates or combinations of Ca-sulphates and Ca-phosphates. So far most bioceramic applications have dealt with bone replacement using phosphates. The scientific
work and literature deal almost extensively with Ca-phosphate-based biomaterials [12].

Figure 1.2 The hydrated area of a Ca-aluminate-based material (white bar = 50 nm).

Figure 1.3 HRTEM picture of hydrated Ca-aluminate (white bar = 10 nm).

These materials are often designed in combination with implants with porosity or channels, into which the resorbable materials are introduced. The resorbable materials are supposed to be exchanged by new bone tissue. Therefore their mechanical properties are not
constant and change over time. Resorbable as well as stable CBBCs can also be used as coatings on implants materials (metals or ceramics) for permanent use or as replacements.

Table 1.5 summarises the most frequently used resorbable CBBC systems [13, 14].

<table>
<thead>
<tr>
<th>System</th>
<th>Initial phases</th>
<th>Final phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca-sulphate a</td>
<td>CaSO$_4$·1/2H$_2$O</td>
<td>CaSO$_4$·2H$_2$O (gypsum)</td>
</tr>
<tr>
<td>Ca-sulphate b</td>
<td>CaSO$_4$·1/2H$_2$O</td>
<td>CaSO$_4$·2H$_2$O (gypsum)</td>
</tr>
<tr>
<td>Ca-phosphate b</td>
<td>b-TCP + mono-Ca-phosphate</td>
<td>CaHPO$_4$ (monetite)</td>
</tr>
<tr>
<td>Ca-phosphate a</td>
<td>Solution of Ca$^{2+}$ and PO$_4^{3-}$</td>
<td>Ca$_5$(PO$_4$)$_3$(OH) (apatite)</td>
</tr>
<tr>
<td>Ca-phosphate a</td>
<td>a-tricalcium phosphate</td>
<td>(CaHPO$_4$)$_2$H$_2$O (brushite)</td>
</tr>
</tbody>
</table>

1.3 Summary and Conclusions

- Most ceramics are formed at high temperatures through a sintering process. By using chemical reactions, CBBCs can be produced at low temperatures (body temperature), in situ, in vivo.
- The chemistry of these systems is similar to that of the hard tissue found in living organisms. These are based on different types of apatites and carbonates. CBBCs easily form nanostructures with crystal sizes similar to those found in hard tissue.
- Both stable and resorbable CBBCs can be produced. The stable phases are found within the CAH and CSH systems, while resorbable phases are seen within the CPH system and within sulphate systems.

In summary CBCs have advantages related to many other biomaterials, including sintered bioceramics, with respect to:

- the possibility of in situ–, in vivo–formed biomaterials;
- reaction temperatures close to those of tissues;
- similarity in chemistry and physics to hard tissue;
- tolerance for moist conditions;
- closure of contact zones;
• nanostructural integration; and
• bone and dental void–filling possibilities.

Acknowledgement

The author thanks the personnel at Doxa Company, Sweden, and the Materials Science Department at Uppsala University for valuable inputs during a two-decade period.

References


Chapter 2

Structures of Hard Tissue and the Importance of in situ–, in vivo–Formed Bioceramics

This chapter presents the structure of hard tissues—enamel, dentine, and bone tissue—and how chemically bonded bioceramics (CBBCs) interact with hard tissues. The features of CBBCs as injectable in situ–, in vivo–formed biomaterials will be treated in some detail. A detailed description of CBBC materials will be presented in Chapters 3 and 6–8.

2.1 Hard Body Tissue Structures: An Overview

Hard tissue is basically divided into three major groups: enamel, dentine, and bone structures [compact and spongy (trabecular or cancellous)] [1]. The main purpose of hard tissue is to carry loads or have the ability to withstand mechanical pressure or stress. For the dental tissues, enamel and dentine, resistance against wear and chemical attack are also important features. The hard chemical component in all hard tissues is apatite. Apatite can appear in nature and in living beings in several modifications, as the basic structure hydroxyapatite (HA), \( \text{Ca}_5\{\text{PO}_4\}_3\{\text{OH}\} \) easily forms solid solutions [2]. Examples are in Table 2.1.
Table 2.1 Examples of solid solutions of HA as minerals and biological apatites

<table>
<thead>
<tr>
<th>Type of apatite</th>
<th>Main formula</th>
<th>Major substituent(s)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>HA</td>
<td>$\text{Ca}_5\text{(PO}_4\text{)}_3\text{(OH)}$</td>
<td>–</td>
<td>Basic structure</td>
</tr>
<tr>
<td>F-aptite</td>
<td>$\text{Ca}_5\text{(PO}_4\text{)}_3\text{(OH,F)}$</td>
<td>F</td>
<td>Mineral</td>
</tr>
<tr>
<td>Mineral OH-apatite</td>
<td>$\text{Ca}_5\text{(PO}_4\text{)}_3\text{(OH)}$</td>
<td>–</td>
<td>Mineral</td>
</tr>
<tr>
<td>Dahllite</td>
<td>$\text{Ca}_5\text{(PO}_4\text{, CO}_3\text{)}_x\text{(OH)}_y$</td>
<td>$\text{CO}_3$</td>
<td>Mineral</td>
</tr>
<tr>
<td>Staffelite</td>
<td>$\text{Ca}_3\text{(PO}_4\text{, CO}_3\text{)}_x\text{(OH,F)}_y$</td>
<td>$\text{CO}_3$, $\text{F}$</td>
<td>Mineral</td>
</tr>
<tr>
<td>Human enamel apatite</td>
<td>$(\text{Ca}_2\text{Mg})_x\text{(PO}_4\text{, HPO}_4\text{, CO}_3\text{)}_y\text{(OH,Cl)}$</td>
<td>$\text{Mg}$, $\text{HPO}_4$, $\text{CO}_3$, $\text{Cl}$</td>
<td>Biological apatite</td>
</tr>
<tr>
<td>Shark enameloid</td>
<td>$\text{Ca}_x\text{(PO}_4\text{, CO}_3\text{, HPO}_4\text{)}_y\text{(OH, F)}$</td>
<td>$\text{F}$, $\text{CO}_3$, and $\text{HPO}_4$</td>
<td>Biological apatite</td>
</tr>
</tbody>
</table>

The united cell of apatite is $\text{Ca}_{10}\text{(PO}_4\text{)}_6\text{(OH)}_2$, which is why solid solutions in Table 2.1 can be described as $(\text{Ca}$, $\text{Mg})_{10}\text{(PO}_4$, $\text{CO}_3$, $\text{HPO}_4)_6\text{(OH, Cl, F)}_2$. Other substituents in low concentrations are also possible, especially other metals such as $\text{Sr}$, $\text{Ba}$, $\text{Na}$, $\text{Li}$, $\text{Mn}$, and $\text{Zn}$. Thus three main positions—one for cations and two for anions—are found within the apatite structure. In many chemically bonded bioceramics (CBBCs) apatite structures are formed. In several other CBBCs two of these three positions are the same as in apatite. As an example for hydrated Ca-aluminate the phase $\text{Ca}_3[\text{Al(OH)}_4]_2\text{(OH)}_4$ is shown.

The amount of apatite in enamel is very high, approximately 96 wt.%. In dentine and bone tissues the apatite content is approximately 60% and 35%, respectively. The soft tissue part in hard structures is different types of collagen, intracellular matrix, and water.

The structures of apatite in hard tissue are designed to meet requirements on the macro-, micro-, and nanosize levels with regard to the formation and mechanical properties developed. All structures are based on nanosize crystals and nanosize inter- and intralayers [1, 3]. See Table 2.2.
Table 2.2  Tooth structure sizes

<table>
<thead>
<tr>
<th>Tooth structure</th>
<th>Size in mm</th>
<th>Size in mm</th>
<th>Size in nm</th>
<th>Size in nm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole tooth</td>
<td>10</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Individual plates</td>
<td>–</td>
<td>0.2</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Nanocrystals</td>
<td>–</td>
<td>–</td>
<td>15</td>
<td>–</td>
</tr>
<tr>
<td>Single crystal within a nanocrystal</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>1.5</td>
</tr>
</tbody>
</table>

The importance of the nanostructure of biological apatite material and the nanostructure of CBBCs will be dealt within section 2.2.1 in this chapter and further in Chapters 6–8.

2.2 Interaction between Chemically Bonded Ceramics and Hard Tissue

All hard tissue structures are sensitive to temperature changes. Artificial materials such as biomaterials can practically only be placed in vivo and formed in situ if the temperature and temperature increase can be controlled at low levels.

Biomaterials which can be formed at body temperatures belong to some of the following material groups: solid solutions of soft or fluid metals (e.g., gold and mercury, amalgams), organic polymers formed by condensation (e.g., resins) or cross-linking (e.g., glass ionomer cement), and chemically bonded ceramics (e.g., Ca-aluminate- and Ca-silicate-based materials, Ca- and Zn-phosphates, and Ca-sulphates). All the CBBC materials have a similarity in chemistry to that of apatite, and these biomaterials can be injected into the hard tissue structure and formed in situ, in vivo, mainly due to the reaction pattern involving hydration mechanisms. Water reacts with the original phase(s), and hydrate(s) are formed.

The material when introduced in the body as a dental or as an orthopaedic material is in most cases a paste.

2.2.1 Contact Zone Reaction between Chemically Bonded Bioceramics and Hard Tissue

The chemistry, including the phases formed, and the structures obtained with CBBCs in contact with hard tissue facilitate and
improve the connection between the biomaterial and the biological tissue. In many cases a nanostructural integration occurs. Five or six reaction mechanisms have been identified, which all contribute to a safe contact zone, chemically and physically [4]. These reactions are summarised in Table 2.3. More details concerning the mechanisms are dealt with in Chapters 3 and 6–8.

**Table 2.3** Summary of chemical reactions facilitating integration between chemically bonded ceramics and hard tissue

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanism 1</td>
<td>Main hydration reactions (aluminates, silicates, phosphates, or sulphates)</td>
</tr>
<tr>
<td>Mechanism 2</td>
<td>Apatite formation in the presence of phosphate ions in the biomaterial (aluminates and silicates)</td>
</tr>
<tr>
<td>Mechanism 3</td>
<td>Apatite formation in the contact zone in the presence of body liquid (aluminates, silicates)</td>
</tr>
<tr>
<td>Mechanism 4</td>
<td>Transformation of hydrated phases into apatite</td>
</tr>
<tr>
<td>Mechanism 5</td>
<td>Biologically induced integration and ingrowth</td>
</tr>
<tr>
<td>Mechanism 6</td>
<td>Mass increase reaction when unhydrated Ca-aluminate or Ca-silicate is present</td>
</tr>
</tbody>
</table>

The main reaction involves precipitation of nanocrystals on contact areas and within the injected material. Repeated precipitation occurs until the original powder or the water is consumed, resulting in closing of cavities, gaps, and voids. This opens up for multipurpose use as a biomaterial in many different applications, depending on the selection of the chemically bonded ceramic system. This is presented in detail in Chapters 9–11.

Complementary reactions occur when the Ca-aluminate or Ca-silicate is in contact with tissue containing body liquid. Several mechanisms have been identified which control how the material is integrated into tissue. These mechanisms affect the integration differently depending on what type of tissue the biomaterial is in contact with and in what state (unhydrated or hydrated) the biomaterial is introduced. These complementary reactions are described in more detail in Chapters 3 and 6–8.

The contact zone developed depends on a combination of the above-mentioned mechanisms and the actual tissue. The latter varies from a cellular-free high-content apatite tissue in the case of
dental enamel via dentine to a bone structure with cellular and body liquid contact. In contact with body liquid apatite is precipitated due to the alkaline systems Ca-aluminate and Ca-silicate. The hydrogen phosphates of the body liquid—HPO$_4^{2-}$ and H$_2$PO$_4^-$—are reduced to pure phosphate ions, PO$_4^{3-}$. Due to the extremely low solubility product of apatite ($pK_s = 10^{-58}$) precipitation of apatite occurs upon the originally precipitated nanocrystal of the main system [5].

The material can also be in contact with other implant materials such as dental crowns, dental screws, or coatings on implants. Mechanisms 1 and 2 and mechanism 6 occur at all contact areas, between the paste and other biomaterials and between the paste and tissue. Mechanisms 3–5 occur mainly at interfaces with body liquid and tissue. The CBBC material will be in contact with different tissues—enamel, dentine, and hard bone tissue and soft tissue—as well as other biomaterials’ contact surfaces. The six mechanisms affect the integration differently depending on (a) what type of tissue the biomaterial is in contact with, (b) in what state (unhydrated or hydrated) the material is introduced, and (c) what type of application is aimed for (cementation, dental fillings, endodontic fillings, sealants, coatings, or augmentation products). Both pure, nanostructural, mechanically controlled integration and chemically induced integration seem plausible. This will be discussed further in Chapters 6 and 8.

When apatite is formed at the interface according to any of the reaction mechanisms 2–4 above, at the periphery of the bulk biomaterial, biological integration may start. Bone ingrowth towards the apatite allows the new bone structure to come in integrated contact with the biomaterial. The transition from tissue to biomaterial is smooth and intricate [4]. For an experimental Ca-aluminate-based system the ingrowth is shown in Fig. 2.1.

**Figure 2.1** TEM image of the ceramic–bone contact zone in a sheep vertebra. Black particles are zirconia (a), STEM image of the hydrated area (b), and HRTEM image of the hydrated crystals (c). Abbreviations: TEM, transmission electron microscopy; STEM, scanning transmission electron microscopy; HRTEM, high-resolution transmission electron microscopy.
2.3 Conclusion and Summary

Chemically bonded ceramics have advantages related to many other biomaterials with respect to:

- the possibility of in situ–, in vivo–formed biomaterials;
- reaction temperatures close to those of tissues;
- similarity in chemistry and physics to hard tissue;
- bone and dental void–filling possibilities;
- closure of contact zones; and
- nanostructural integration.

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References

Chapter 3

Overview of Chemical Reactions, Processing, and Properties

This chapter gives an overview of chemical reactions involved in the curing of chemically bonded bioceramics (CBBCs), and how these materials are processed, and the typical property features of these biomaterials in relation to other biomaterials. A detailed description of the property profile of CBBCs will be presented in Chapters 7 and 8.

3.1 Chemical Reactions during Setting and Hardening: An Overview

Six mechanisms have been identified [1] that control how chemically bonded bioceramic (CBBC) materials are integrated onto tissue: (i) the main reaction, which includes hydration; (ii) apatite formation in the presence of phosphate ions in the biomaterial; (iii) apatite formation in the contact zone in the presence of body liquid; (iv) transformation of hydrates into apatite and other biomaterials; (v) biologically induced integration and ingrowth, that is, bone formation at the contact zone; and (vi) a mass increase reaction, especially important when unhydrated phases are used as coatings or as augmentation pastes. These mechanisms are described in next chapters.

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