simulated body fluid in vitro (Clark et al., 1976; Hench, 1991). These are as follows:

(i) Formation of silanol groups on the surface of the glass particles via a cation exchange process:

$$-Si-O^{-}Na^{+} + H^{+} \rightarrow -Si-OH + Na^{+}$$

As a result of the removal of protons from solution in this way, the surrounding pH increases.

(ii) This high local pH leads to an excess of OH^{-} ions in the solution around the glass particles. These ions attack the −Si−O−Si− units in the surface of the glass, forming $Si(OH)_4$, which is lost into the solution.

(iii) The −Si−OH groups at the surface undergo a condensation process to create −Si−O−Si− units in a prepolymerization reaction.

(iv) Ca^{2+} and PO_4^{3-} groups within the glass migrate to the surface and contribute an amorphous calcium phosphate component at the surface layer, nucleating onto the −Si−OH groups on the glass surface (Li and Zhang, 1990; Doostmohammadi et al., 2011).

(v) Hydroxide and carbonate ions present in solution become incorporated into the surface layer, and these interact with the calcium and phosphate ions to form HCA (Fitzgerald et al., 2009).

Having formed HCA by this well-defined process, there are further steps that lead to the attachment of bone. These steps are less well understood, but some aspects are known (Jones, 2013). Specifically, these are:

(i) Proteins adsorb on the HCA surface.

(ii) Cells are able to attach to the resulting deposited protein layer, and they do so, going on to differentiate.

(iii) Differentiated cells produce a bone matrix and eventually fully formed bone, bonded strongly to the glass surface.

These glass surfaces can thus be seen to have substantial biological activity. Human osteoblasts grown on bioactive glass have been found to produce an extracellular matrix, ECM, which mineralizes to form nodules of bone (Gough et al., 2004; Kaufmann et al., 2006; Bosetti and Cannas, 2005). The calcium ions and the soluble silica species dissolved from the surface of the bioactive glass stimulate cell division in osteoblasts, and also cause these cells to produce growth factors and ECM proteins (Jones, 2013).

The rate of dissolution of the various species from the bioactive glass surface is critical for these processes to occur. Dissolution must be fast enough to create concentrations able to stimulate osteoblasts cells but not so fast that toxic levels build up (Jones, 2013). This dissolution behavior is controlled by the composition and structure of the glass, and in turn its dissolution behavior controls the bioactivity of the glass and its ability to stimulate cellular level