

depend on both the quantity of not-freezing water as well as the interstitial water and on the types of interactions occurring among them and the solid network. Obviously, the proportion of free water becomes preponderant as the swelling ratio increases but it is not influential on the properties of hydrogel. For instance, the main fraction of water in macropores corresponds to non-bound, practically bulk water, and bound water (<1% of total amount of water in initial hydrogel) is weakly bound by the polymer. The latter is due to the absence of narrow nanopores in the macropore structures. Thus the main portion of water in macroporous hydrogels can be attributed to bulk water located in macropores.

Furthermore, other factors known as kosmotropic (structure-makers)/chaotropic (water-structure breakers) effects, dependent on the structure of polymeric groups (Wiggins 2008) and lead to changes in the water structure. On this regard, the chaotropic cations such as  $N(CH_3)_4^+ > NH_4^+ > Cs^+ > Rb^+ > K^+$  and anions  $ClO_4^- > NO_3^- > I^- > Br^- > Cl^-$  are accumulated in LDW and kosmotropic cations such as  $Al^{3+} > Mg^{2+} > Ca^{2+} > H^+ > Na^+$  and anions  $C_6H_5O_7^- > SO_4^{2-} > PO_4^{3-}$  accumulated in HDW (Chaplin 2015). In fact according to NMR studies, water is described in terms of a two-state mixture model including high-density water (HDW with collapsed (condensed) structure, under standard conditions) and low-density water (LDW with expanded structure) being in the dynamic equilibrium. However, this equilibrium shifts toward a certain state due to the effects of chaotropic and kosmotropic solutes or surface functionalities, also ionic charges or contra-ions, of hydrogel.

In view of this organization of water molecules in the hydrogel, divided into three layers, bound water, interstitial and free water, the experiments and Pollack's hypothesis, i.e., the EZ's ordered structure (Pollack 2013), could participate in the first two layers since these water molecules being closest to the polymer surface and strictly organized, are those that can remove almost anything suspended or dissolved in the water. Water dipoles would stack one upon another, forming a honeycomb layer projecting farther and farther from the surface until the disruptive forces of "thermal" (Brownian) motion limit further ordered growth. The lattice is extremely tight and therefore highly exclusive of solutes.

This brief review reveals the complex structure and dynamics of interstitial and bound water, which exhibits strongly modified properties when compared to bulk water. Part of the difficulty arises from the fact that no current theory is capable of precisely predicting water interaction with a surface, even when the surface structure is well characterized.

## The Presence and Functionality of Pores within the Hydrogels

A hydrogel is composed of statistically distributed microchannels or fluctuating pores created by the mobility of the polymer segments within an interpenetrating network, in the presence of a solvent (Fig. 10).

At a given site in the network, these pores are formed and removed as a result of thermal motion of the chain. The presence of pores in the hydrogels is particular relevant for one of the hydrogel applications: tissue regeneration (Migliaresi and Motta 2014; Pollack 2001) because the pore dimension strongly affects the capability of cells to adhere and proliferate (Fig. 11).