may be mediated by chemical bonding, such as covalent bonding, H bonds, or van der Waals forces. Some specific chelating agents may be used to develop stronger cell-surface interactions. Among the support materials used for cell adsorption are porous glass, porous silica, alumina, ceramics, gelatin, chitosan, activated carbon, wood chips, polypropylene ion-exchange resins (DEAE–Sephadex, CMC-), and Sepharose.

Adsorption is a simple, inexpensive method of cell immobilization. However, limited cell loadings and rather weak binding forces reduce the attractiveness of this method. Hydrodynamic shear around adsorbed cells should be very mild to avoid the removal of cells from support surfaces.

Covalent binding is the most widely used method for enzyme immobilization. However, it is not as widely used for cell immobilization. Functional groups on cell and support material surfaces are not usually suitable for covalent binding. Binding surfaces need to be specially treated with coupling agents (e.g., glutaraldehyde or carbodiimide) or reactive groups for covalent binding. These reactive groups may be toxic to cells. A number of inorganic carriers (metal oxides such as titanium and zirconium oxide) have been developed that provide satisfactory functional groups for covalent binding.

Covalent binding forces are stronger than adsorption forces, resulting in more stable binding. However, with growing cells, large numbers of cell progeny must be lost. Support materials with desired functional groups are rather limited. Among the support materials used for covalent binding are CMC plus carbodiimide; carriers with aldehyde, amine, epoxy, or halocarbonyl groups; Zr(IV) oxide; Ti(IV) oxide; and cellulose plus cyanuric chloride. Support materials with —OH groups are treated with CNBr, materials with $—NH_2$ are treated with glutaraldehyde, and supports with COOH groups are treated with carbodiimide for covalent binding with protein groups on cell surfaces.

The direct cross-linking of cells by glutaraldehyde to form an insoluble aggregate is more like cell entrapment than binding. However, some cells may be cross-linked after adsorption onto support surfaces. Cross-linking by glutaraldehyde may adversely affect the cell's metabolic activity and may also cause severe diffusion limitations. Physical cross-linking may also be provided by using polyelectrolytes, polymers such as chitosan, and salts [$CaCl_2$,$Al(OH)_3$,$FeCl_3$]. Direct cross-linking is not widely used because of the aforementioned disadvantages.

A good support material should be rigid and chemically inert, should bind cells firmly, and should have high loading capacity. In the case of gel entrapment, gels should be porous enough and particle size should be small enough to avoid intraparticle diffusion limitations.

Some examples of cell immobilization by entrapment and by surface attachment (binding) are summarized in Tables 9.1 and 9.2, respectively.

9.4.3. Passive Immobilization: Biological Films

Biological films are the multilayer growth of cells on solid support surfaces. The support material can be inert or biologically active. Biofilm formation is common in natural and industrial fermentation systems, such as biological waste-water treatment and mold fermentations. The interaction among cells and the binding forces between the cell and support material may be very complicated.