evaporate until a defined weight loss is produced. A 10-12% final protein concentration gives good results. Once the desired protein concentration has been reached, the fibroin sol is then gelled.

[0116] A number of methods can be used for inducing gelation of a fibroin sol. For example, these include immersion in acidic buffers at a pH between 3.5 and 6.4, treatment with vapour from a mildly acidic volatile buffer such as ammonium acetate or immersion/vapour treatment with aqueous alcoholic solutions.

[0117] A porous structure with a high density of intercommunicating pores with fairly uniform diameter distribution can be readily be produced by rapid freezing. Intercommunicating pores with mean pore sizes from 50-300 μm may be produced by varying protein concentration and length of exposure to acid.

[0118] An anisotropic porous structure may be produced by controlling the direction of movement of a freezing zone across the material.

[0119] Even without a fibre lay, the porous hydrogel formed by acid gelation of fibroin followed by freezing has a compressive stiffness of between 1-2 MPa—in the range of articular cartilage (1-20 MPa).

[0120] Other methods can be used for rendering the hydrogel matrix porous. These include, for example, thermally induced phase separation, solvent casting and particle leaching, superciritical gas foaming, salt leaching with particulate sodium chloride, freeze drying, mixing the fibroin with a water-miscible polymer capable of inducing the microphase separation, partially dissolving silk fibres with formic acid and sticking them together in a porous felt, incorporating additional soluble fibres into the silk fibres of the fibre lay that can be extracted after polymerising the hydrogel and applying insufficient protein to the fibre lay to completely fill the interstices.

[0121] A pore size of 70-120 μm is to be preferred for the porous hydrogel. This value is a compromise between the optimum value to allow for cell infiltration (approximately 150-300 μm) and the need for a low pore density to optimize the compressive properties of the hydrogel.

[0122] Once the porous hydrogel has been prepared it may be advantageous to add a cross-linking agent to stabilize it and bind it firmly to the silk fiber lay.

[0123] A range of cross-linking agents may be used to cross-link hydrogels of different compositions. For example, these include members of the aliphatic aldehyde series, dialdehydes, carbodiimides, succinimides, succinamides, peroxidases in the presence of hydrogen peroxide, transglutaminases, phenoloxidases, phenolases, tyrosinases, ruthenium (II) tris-bipyridyl in the presence of ammonium persulfate followed by light treatment, Fenton reaction catalysts, 10-60% w/v methanol or ethanol and 10-40% formic acid.

[0124] In the case of alginates, stable hydrogels may be prepared by the addition of moderate concentrations of calcium ions.

[0125] More than one cross-linking agent applied consecutively or together. Alternatively or additionally, the implantable devices may be cross-linked and/or sterilized by gamma irradiation, neutron irradiation, or high voltage discharge.

[0126] Porous fibroin hydrogel may be treated with 50% ethanol for 1 hour at room temperature to increase the formation of intermolecular beta sheet hydrogen bonds.

[0127] Porous hydrogel may also be treated with 10-50% glutaraldehyde to covalently cross-link the porous gel.

[0128] After exhaustive washing in water the hydrogel may be treated with freshly prepared aqueous 0.1% sodium borodhydride at 4 degrees C. until no more hydrogen is evolved. This stabilizes the resulting aldimine cross-links formed by reaction with the arginine and lysine groups of fibroin. It also reduces any remaining unreacted aldehyde groups to non-toxic alcoholic ones. These two mechanisms greatly reduce the toxicity produced by glutaraldehyde cross-linking.

[0129] Aqueous formic acid solutions have two effects on dry silk fibroin: making it sticky by swelling or partially dissolving it and cross-linking it by inducing the formation of intra- and inter-molecular β-sheet hydrogen bonds. Due to this, a porous cross-linked fibre lay may be prepared by adding formic acid to a silk fibre lay which is then allowed to dry. Using this method, pore size may then be varied by stretching, compressing or bending the fibre lay. Powdered fibroin may be introduced to partially or substantially fill the interstices of the fibre lay before treatment with formic acid.

[0130] Cross-linking both the fibre lay and hydrogel components of the implantable device has the additional advantage of increasing the resorption time of these components of a device. Thus the extent of covalent cross-linking can be used as a method of tuning the resorption rates of these components. Addition of an acylating agent capable of substituting a hydrophobic group into a hydrophilic side chain provides an additional method of tuning the resorption rate of both fibre lay and hydrogel. Hydrophilic carboxyl, hydroxyl, amine and sulphydryl side chains of amino acids within silk proteins may be used as sites for acylation. A wide range of monofunctional, bifunctional or polyfunctional acylating agents may be used to increase the hydrophobicity of proteins. In the case of bi- or polyfunctional acylating agents these have the additional effect of cross-linking the protein components. Acylating agents that can be used to increase the hydrophobicity of the proteins include, for example, acylating and alkylating agents. Acylating agents suitable for increasing the hydrophobicity of proteins include, for example, perfluorobutanoyl chloride, lauroyl chloride, myristoyl chloride, benzophenonetetracarboxylic acid, diaminodiphenyloxide, aliphatic and bifunctional isocyanates, dodecyl ioscyanate, hexamethylene diisocyanate, aliphatic anhydrides, octadecenyl succinic anhydride.

[0131] The relatively high compressive modulus of the device and hence its resistance to compression is dependent in part on the swelling pressure of the hydrogel constrained within the fibre lay. This is because the swelling of the hydrogel pre-stresses the fibre lay so that even a slight bending or compression of the device results in an immediate marked increase in stress of the fibres. The stiffness and strength of the composite material arises in part because an application of a bending or compressive force increases the hydrostatic pressure in the hydrogel matrix and this force per unit area is immediately transferred to the pre-stressed fibres. It is accordingly desirable that the hydrogel within the fibre lay is treated with a cross-linking agent in a state in which it is incompletely swollen and in such a way that it will tend to hydrate further and swell after cross-linking or when implanted into the patient. This can be achieved, for example, using one or a combination of the following methods: partially removing the water from the hydrogel before and during cross-linking by adding a colloid such as polyvinylpyrolidone or polyethyleneglycol to sequester some of the water, partially removing some or all of the water before and during