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THE MECHANICAL PROPERTIES OF HYDROGEL POLYMERS

ADRIAN SIMON TREVETT

Doctor of Philosophy

THE UNIVERSITY OF ASTON IN BIRMINGHAM

October 1991

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Hydrogel polymers have been used in a range of biomedical applications, particularly as soft contact lenses. Although such polymers are relatively well tolerated by the body, their further use as biomaterials has been restricted because the mechanical properties of these materials are rather poor. The mechanical properties of hydrogels have been the subject of a number of studies, but because there are no standard procedures to test hydrogels, comparison of mechanical property data is often difficult.

The characterisation of the mechanical properties of hydrogel polymers forms an integral part of this work. Methodologies are developed that enable more meaningful data for the tensile properties of hydrogels to be obtained, both in the form of thin membranes, and as finished devices.

A methodology was developed to test soft contact lenses in tension which may be of interest to manufacturers as an aid in quality assurance. In addition, clinicians may find this method a useful aid in lens selection, the techniques sensitivity making it a convenient way to distinguish between different lens materials.

The adoption of a suitable "standard" technique for testing hydrogel polymers in tension is also valuable in terms of the development of new materials, since new polymers can then be compared, both with one another and with existing materials. An appropriate test method has been applied to a range of hydrogel copolymers, and substantial improvements in strength and stiffness have been achieved.

The copolymers produced formed the basis for further development, and by using other synthetic strategies, a new range of hydrogels of improved mechanical properties have been developed. The tensile properties of some interpenetrating network polymers approach those that are found for articular cartilage. Further development may enable the production of a synthetic cartilage material, that is based on a hydrogel polymer.

Keywords: **Hydrogels, Mechanical Properties, Characterisation, Synthetic Cartilage**

To all those I love.......

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List of Abbreviations

Å	Angstrom
AIBN	Azo bis isobutyronitrile
AllylMA	Allyl methacrylate
BMA	Benzyl methacrylate
°C	Degrees Centigrade
CHexMA	Cyclohexyl methacrylate
E	Modulus
EGDM	Ethylene glycol dimethacrylate
EOEMA	2-Ethoxyethyl methacrylate
EWC	Equilibrium water content
gl	Gauge length
HEMA	2-Hydroxyethyl methacrylate
IPN	Interpenetrating polymer network
MMA	Methyl methacrylate
MPa	Mega Pascal(s)
HexMA	n-Hexyl methacrylate
NVP	N-vinyl 2 pyrrolidone
PhEMA	Phenylethyl methacrylate
PhOEMA	Phenoxyethyl methacrylate
PMMA	Poly (methyl methacrylate)
PVA	Poly (vinyl alcohol)

t	Thickness
TBMA	Tertiarybutyl methacrylate
ε_b	Elongation to break
σ_f	Failure stress

Chapter 1 Introduction

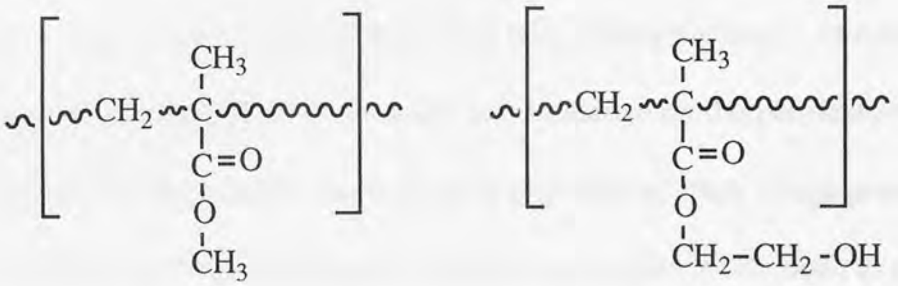
1.1 General introduction

Hydrogels are an important class of polymeric materials. In this chapter the nature of these fascinating materials is briefly described, with reference to the water which is so fundamental to their behaviour. The main strengths and weaknesses of hydrogel polymers are outlined, and the reasons behind their successful exploitation as soft contact lens materials will be discussed. These factors having been established, some aspects of the future potential for these materials are investigated, specifically with regard to the their more widespread adoption in the area of biomaterials, as possible prosthetic implant devices. In order to assess the potential for hydrogels in this matter, the structure and properties of two of the body's "hydrogel" structures, those of the cornea and articular cartilage, are examined in some detail to see what can be learnt from nature's own materials, and also to ascertain what property requirements might be needed in order to develop a synthetic cartilage material. Having thus introduced hydrogel materials, the remainder of this thesis is devoted firstly to the characterisation of the mechanical properties of these materials, and secondly to the problem of optimisation, where in the attempt to "design" improved hydrogel materials, some of their potential weaknesses might be overcome, whilst hopefully still retaining their more desirable properties.

1.2 Hydrogels - a Unique Family of Materials

Hydrogel polymers were first developed in the 1960's by the Czechoslovakian workers Wichterle and Lim,(1) who produced the simplest and perhaps the most widely known hydrogel, poly (2-hydroxyethyl methacrylate) or poly HEMA. This material is structurally very similar to that of poly (methyl methacrylate) (PMMA or Perspex). In the absence of water, both materials are quite similar, being hard, brittle, and glassy in nature. A striking change occurs when these polymers are exposed to water however. Whereas PMMA remains relatively inert in the presence of water, poly HEMA absorbs an appreciable quantity of water, and swells noticeably if left in water for any length of time. The properties of this "new" polymer are demonstrably different - the material behaves more like a gel, and becomes soft and pliant (although maintaining its transparency).

The structures of poly HEMA and PMMA are shown in Figure 1.1 below, from which it is apparent that the most significant structural difference between these two polymers is that poly HEMA contains the presence of a hydroxyl group in every unit of the polymer chain.



Poly MMA

Poly HEMA

Figure 1.1 The structures of poly MMA and poly HEMA

This pendant hydroxyl group interacts appreciably with water molecules, so that the net effect is one of plasticisation, where the water acts rather in the manner of an "internal lubricant", facilitating chain mobility. Hydrogels then, can be considered to be a class of water swollen polymers, where the water acts as a plasticiser, rather than as a solvent for the system.

1.2.1 Water - The Giver of Life

The presence of water in hydrogel systems is fundamental to their behaviour. Water plays a major part in determining the mechanical properties of these polymers, generally making them soft and compliant and not dissimilar in feel to those of some natural body tissues such as skin. This similarity to body tissue, both in the physical nature, and chemically in terms of the presence of water, suggests that such hydrogel materials will find applications as biomaterials. In terms of the biological interface between the body's own tissues and those of a potential implant material, hydrogels offer distinct advantages over many currently used prosthetic materials. The imbibed water contained within the hydrogel matrix, makes for a less severe change in chemical nature across the interface between natural and synthetic material, meaning that hydrogels are relatively well tolerated by the body. In addition the water in the hydrogel structure also has an important influence on the permeability of the material. In relation to a biomaterial, this is of great importance, since a high permeability will permit the diffusion of molecular species vital to the processes of life, such as dissolved oxygen.

Because the presence of water has such a profound influence on the properties of these materials, it is not too surprising that much attention has been focused on the nature and structuring of this water.(2-5) Although the precise form that this water exists in is still a matter of some debate, it seems likely that in most hydrogel systems the water is structured in two ways. The total water uptake of the gel is composed partly of water that is "bound" within the polymer matrix, and partly that which is "free", or the "plasticising" water. Because the technique of differential scanning calorimetry has often been used to characterise the nature of water in hydrogels, the terms "freezing" and "non-freezing" water, have sometimes been adopted to describe the two different states that this water is felt to exist in. The ratio of freezing to non-freezing water may be the main influence on the polymers properties, rather than the total water content, or more precisely the equilibrium water content (EWC) of the gel.

1.2.2 The Soft Contact Lens - a Case Study in Biomaterials Design ?

To date, the main commercial success of hydrogel materials has been in the area of soft contact lens materials, an area that has been reviewed by Tighe,(6) and and also by Refojo.(7) The development of hydrogels as contact lens materials has been outlined by Tighe, who has shown why hydrogels are so suitable for this particular application. It is the unique combination of optical transmittance, oxygen permeability, and surface and mechanical properties,(8) that make hydrogels an almost automatic choice for soft contact lens materials.

This particular instance of polymer design has implications for the further development of biomaterials,(9) and several lessons can be learnt by treating the development of the soft contact lens almost as a case study in materials design. The eye is a particularly accessible body site, and as such is quite favoured for the design of implant materials. Although the eye does not have quite the same complexity as applications involving blood contact, the fundamental design criteria remain the same. A successful interface must be formed *i.e.*the material needs to be well tolerated by the body site involved, thus the surface properties of the implant material are of particular importance. The mechanical properties of the prosthesis are also important in order for the implant to fulfil its desired function, especially with respect to the materials long term durability. Although the mechanical strength of a contact lens might not immediately be considered important, the lens still has to resist the deforming forces caused by the eyelid every time a blink occurs. In addition the material must be resilient enough to withstand normal handling when outside the usual environment of the eye. There are almost certainly going to be other requirements that are specific to the particular application in mind. For a soft contact lens material, these include oxygen permeability, (since the cornea is living tissue and needs to "breathe") and light transmittance, as well as the factors related to fabrication and handling.

It is finding the overall balance of the appropriate property requirements, that forms the basis of biomaterials design. To achieve optimum function, the contact lens can best be considered as an extension of the cornea, so that the overall design goal should be to match the properties of the cornea as closely as possible. These sorts of design criteria will form the basis behind the initial development of a synthetic cartilage material, as discussed later in this thesis. In the case of the soft contact lens, it so happens that the properties of the cornea are quite similar to those of a typical soft contact lens material, so that only minimal development has so far been necessary, although this does not mean to say that contact lenses cannot be made significantly better by further improvements in materials design.

Since contact lenses have such a potentially huge market, it is important to be able to produce these optical devices on a large scale. There are currently three main methods of contact lens production, and these are lathe cutting, spin casting, and cast polymerisation. The most widely adopted of these techniques is lathe cutting, where the polymer is cast in the form of buttons (or rods), and is then turned to the desired shape, using a lathe. The material is finally "finished" by polishing with an alumina/oil based paste. In spin casting, the liquid reagents, often including a diluent such as ethylene glycol, are poured into a rotating mould, where the centrifugal forces allow the development of the required concave form, whilst the mixture is undergoing polymerisation. Cast polymerisation is potentially the most convenient way to mass produce lenses, since in this case the monomer mix is cast directly into moulds having the exact form that is required for the finished lens. There are problems encountered with this particular method of production however, in that it is particularly difficult to produce lenses having the desired edge quality. Yet again we see that the ultimate success of hydrogels as soft contact lenses, is due in a great part to their unique intrinsic properties - it would be impossible for instance, to lathe cut a swollen hydrogel, but the dehydrated xerogel is relatively easily machined.

Hydrogels have been so successful as soft contact lenses, that there are a plethora of different materials now on the market, sold under a variety of trade names, and many hundreds of patents have been filed. The most important commercial aspects of contact lens materials have been summarised in the review by Tighe.(6)

1.2.3 Further Development of Hydrogels as Biomaterials

It is relatively straightforward to produce hydrogels, either by free radical polymerisation or by radiation polymerisation, and as such the properties of hydrogels can be conveniently altered, by means of copolymerisation for example. The fundamental aspects of hydrogel synthesis and structure have been described by Peppas and Mikos.(10) Because of their ease of preparation, their facility for improvement by chemical means, and their great potential as biomaterials, hydrogels have won widespread use in medical areas outside that of the soft contact lens. For instance, hydrogels have been used in drug delivery systems,(11) as artificial muscles and tendons,(12, 13) and as wound or burn dressing materials.(14) There are also a whole host of other biomedical applications where hydrogel materials have either been tried, or are still being developed, the most important of which have been summarised by Peppas.(15) One of the main stumbling blocks hindering the development of hydrogels as potential biomaterials is their lack of mechanical strength/durability (again a consequence of the water held within the structures). To illustrate this the mechanical properties of poly HEMA are compared to those of a variety of different engineering and natural materials in

Table 1.1.

	Tensile Strength / MPa	Tensile Modulus / GPa	Elongation to Break / %
Glass Reinforced Plastic (GRP)	1200	40	10
Mild Steel	460	210	35
Wood	190	12	45
Bone	140	28	15
Epoxy Resin	50	4.5	5
Perspex (PMMA)	50	3	5
Poly HEMA	0.6	0.0006	150

Table 1.1 Mechanical property comparisons for a variety of different materials

Although the mechanical properties of hydrogels have received much attention for this reason (see chapter 3), they are still relatively poorly characterised, and the structural factors responsible for these mechanical properties are not particularly well understood. It is the intention of this work to provide further insights into the structure/property relationships of hydrogels, and to characterise more completely their mechanical behaviour. Ultimately, through the production of hydrogels of improved mechanical integrity, it may be possible to develop hydrogel biomaterials that are suitable for more physically demanding applications, such as might be required in the development of an artificial cartilage material for example.

Before a synthetic articular cartilage material can be designed, it is important to understand the properties of the natural material. Equally important, is an understanding of the underlying structural factors that govern the behaviour of the natural material. Thus the following section describes the structure of articular cartilage. Also included here is a brief description of the cornea, as there are several structural similarities between these two tissues. It is interesting to note that the mechanical properties of the cornea have been approximately matched in the design of soft contact lens materials, and yet those of articular cartilage are far superior to any existing homogeneous hydrogel. The subsequent sections in this chapter deal with some of the mechanical and other important properties of cartilage. Finally a short resume of previous work on the development of synthetic cartilage materials is included.

1.3 Nature's Composites: Structure

1.3.1 The Structure of the Cornea

Like many of the body's structures, the cornea is a composite material. Articular cartilage and the cornea have a very similar bulk composition (Table 1.2), the main constituents being water and collagen. Essentially the collagen acts as reinforcement for the matrix - in this case a proteoglycan gel. It is in the arrangement of these collagen fibres, that the main structural differences between the cornea and cartilage exist.

	Cornea	Cartilage
Water	78.0 %	70-75 %
Collagen	15.0 %	15-20 %
Other Proteins	5.0 %	2-10 %
Keratin Sulphates	0.7 %	
Chondroitin Sulphates	0.3 %	
Salts	1.0 %	

Table 1.2 The compositions of collagen and cartilage

The cornea is composed of five separate layers.(16) These are the epithelium, the stroma, Bowmans layer, Descemets layer and the endothelium (Fig 1.2). The epithelium and endothelium are cell layers, and as such, play little part in determining the mechanical properties of the cornea. Bowmans layer provides a transition between the epithelium and the stroma and is composed of a random dispersion of collagen fibrils. These are both thinner and more densely packed than those of the stroma. The stroma itself comprises the bulk of the cornea, and it is this section that gives the cornea its rigidity. The stroma consists of a large number of collagen lamellae (approximately 250) which run parallel to the surface of the cornea. The lamellae themselves consist of fibrils approximately 360 Å in width, with a spacing of between 120 and 180 Å. Each fibril has a periodicity of 620 Å, and is further divided, with striations appearing every 60 Å. Descemets layer is somewhat similar to Bowmans layer and is also composed of fine collagen fibrils, though in this case the fibrils are of a much more uniform distribution.

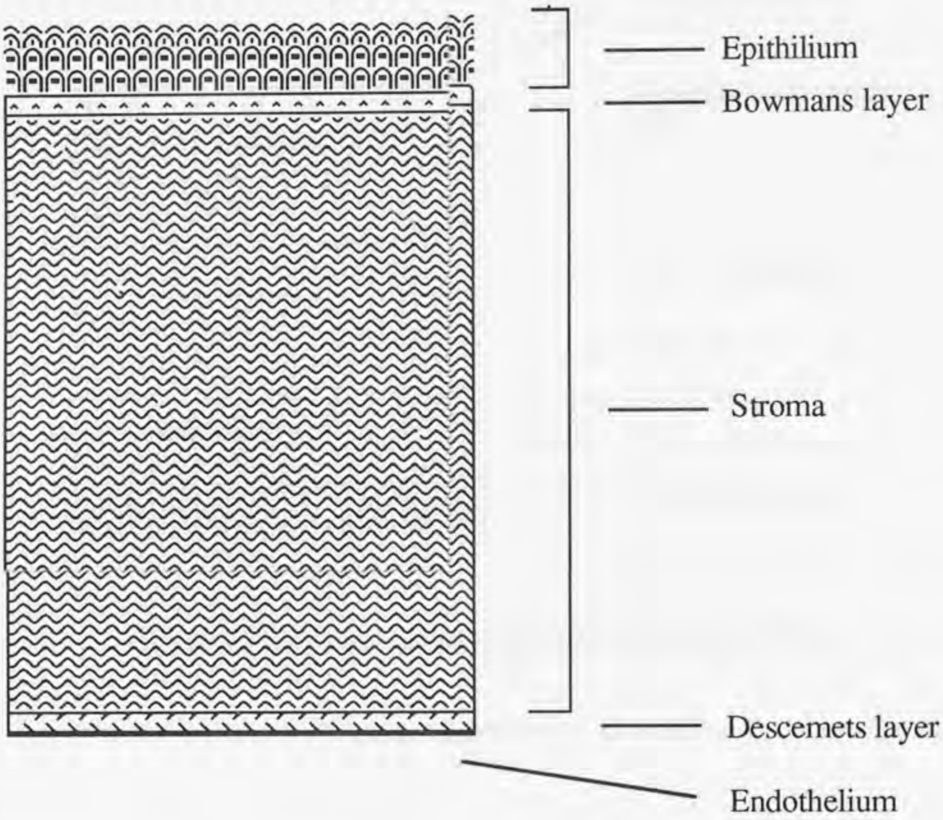


Figure 1.2 Schematic section through the cornea

1.3.2 The Structure of Articular Cartilage

The structure of articular cartilage can also be divided into layers or zones, for example, Akizuki *et al.*(17) Here the four layers are described as the surface, the subsurface, the middle layer, and the deep layer. Where the cartilage attaches to the sub-chondral bone, a calcified layer exists. A characteristic of the division between these two lower zones is the so called tide mark. Figure 1.3 above, illustrates a simplified section through articular cartilage.

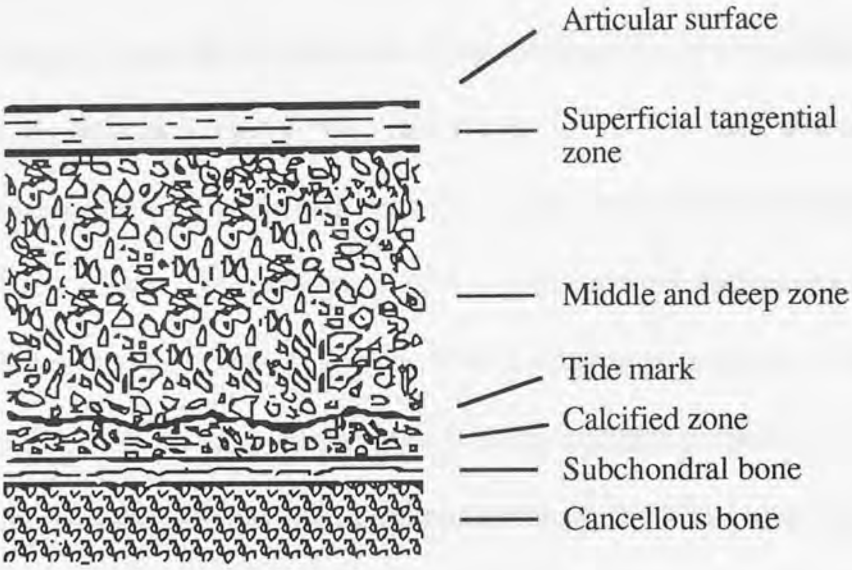


Figure 1.3 Schematic section through articular cartilage

A more simplified description of the variation of cartilage structure with depth is used by Hiltner *et al.*(18) Three zones are described. The first zone (Zone I) is the region closest to the articulating surface. In this section the collagen fibrils lie parallel to the articulating surface, similar to those of the corneal stroma. The fibrils are both thinner and more closely packed than those in the other two layers. In addition the actual proportion of collagen is greatest in this region. Zone III is the area adjacent to the sub-chondral bone. Here the fibrils lie perpendicular to the surface of the bone, and are also orientated in a very regular fashion. The middle zone, or Zone II can be thought of as a transition between the first two layers. In this region the collagen fibrils are thought to be randomly arranged, although this is still a point of some controversy. For example, some workers have reported a bimodal distribution of the fibres, whilst others have described the existence of a structure resembling that of a Gothic arch, for this particular section.

Apart from the usual microscopic techniques there are several other methods that have been used in order to study the arrangement of the collagen fibrils in cartilage. One such technique is X-ray diffraction, as used by Aspden and Hukins.(19) Indeed, the information found by these workers was important evidence for the somewhat idealised three layer structure described above. The technique of X-ray diffraction has the major advantage that the tissues do not need to be dried out, as is the case in electron microscopy. The orientation of the collagen fibrils, as found by Aspden and Hukins, is shown graphically in Figure 1.4. A somewhat similar approach has been used more recently by Vidal and Vilarta,(20) who have used optical birefringence to study the arrangement of collagen fibres. No support for the "Gothic arch" was found, although variations in the proteoglycan content with depth from the articular surface were noted.

In contrast a micro-mechanical approach has been utilised by Broom,(21, 22) to study cartilage structure. Essentially a fracture mechanics test was employed and this illustrated a difference in tear resistance parallel and perpendicular to the articular surface, the perpendicular direction being the most resistant. Evidence from optical microscopy enabled the author to postulate that a meshwork of collagen fibres existed. This meshwork would interact to produce a strain locking effect in the radial direction (perpendicular to the articular surface), but not in the transverse direction. The author also goes on to suggest that the breakdown of this mesh, may be an important factor in the degeneration of articular cartilage that is associated with arthritis.

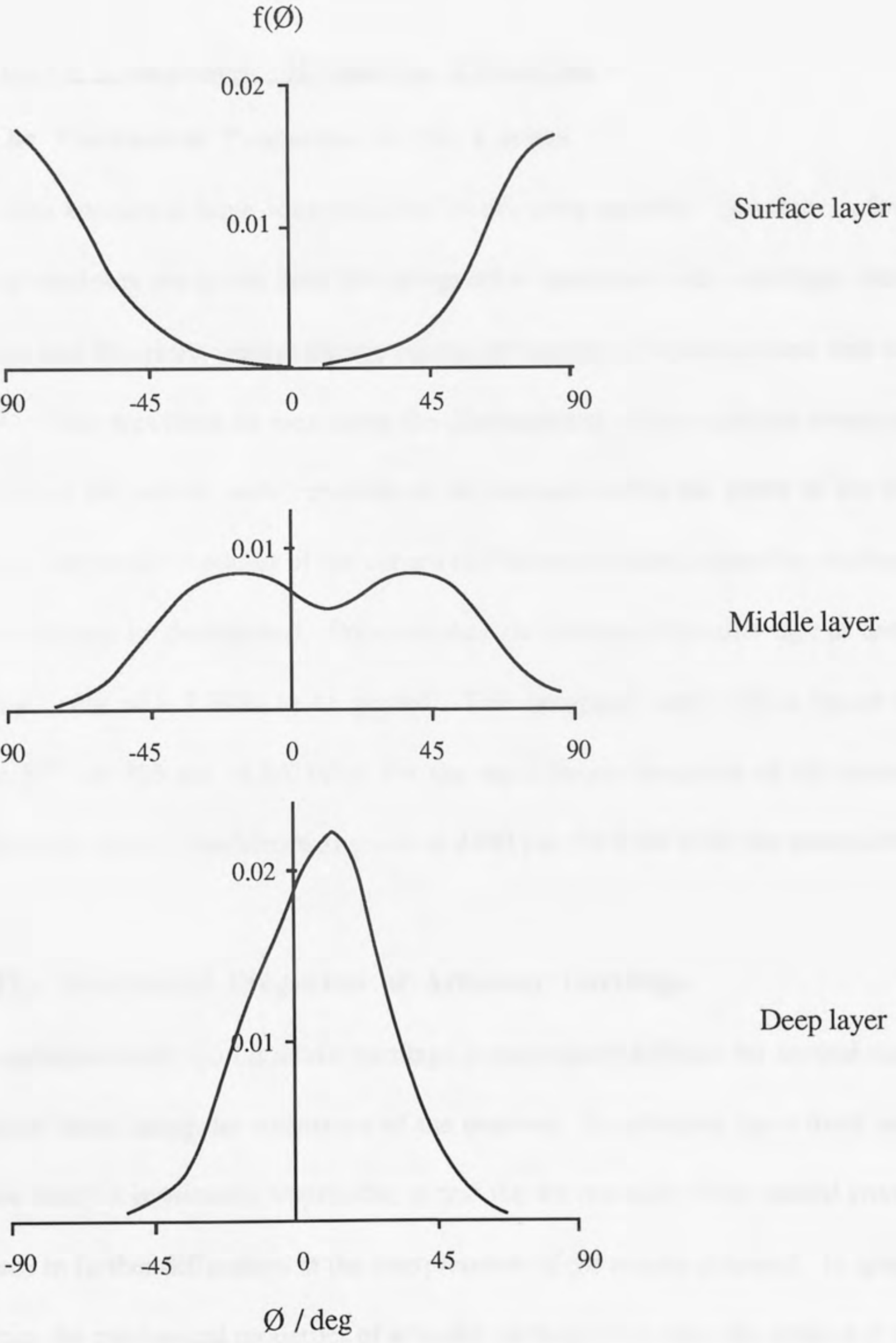


Figure 1.4 The orientation of collagen fibrils in the different layers of articular cartilage, as determined by X-ray diffraction. (Aspden and Hukins 1981)

1.4 Nature's Composites: Mechanical Properties

1.4.1 The Mechanical Properties of the Cornea

Little data appears to have been produced in this area recently. However, a few typical values of modulus are given here for comparative purposes with cartilage. (see section 1.4.2) Jue and Maurice compare the mechanical properties of human cornea with that of the rabbit.(23) This was done by measuring the displacement of two mercury drops placed on the surface of the cornea, with variations in the pressure within the globe of the intact eye. A value of the tensile modulus of the cornea had to be estimated, since the thickness of the cornea could not be determined. Previous data on corneas of similar age to those tested enabled a value of ~ 5 MPa to be quoted. This compares well with a figure found by Nyquist (24) of 705 psi (4.86 MPa) for the equilibrium modulus of the cornea. The instantaneous value of modulus was given as 2400 psi (16.6 MPa) by the same author.

1.4.2 The Mechanical Properties of Articular Cartilage

The mechanical testing of articular cartilage is particularly difficult for several reasons, not the least of these being the anisotropy of the material. In addition, apart from indentation tests (see later) it is virtually impossible to test the the material in its natural environment. This leads to further difficulties in the interpretation of the results obtained. In spite of these difficulties the mechanical properties of articular cartilage have been the subject of numerous investigations. One of the reasons for this interest has been that it may be possible to explain the factors influencing the breakdown of cartilage during arthritis, by examining changes in mechanical properties with, for example, age. Here, the tensile and compressive properties of cartilage are discussed separately, since the structural factors governing the two are quite different.

1.4.2.1 Tensile properties

The very fact that collagen appears as a major constituent of cartilage suggests the presence of tensile forces in the joint. (Collagen, like any other fibre reinforcement, is only really effective at transmitting tensile loads). Thus the tensile properties of articular cartilage might be expected to vary with both the collagen content and the orientation of these fibres. In a comprehensive review, Kempson,(25) has discussed early work on the mechanical properties of cartilage, some of the main features of which, will be outlined briefly here. The tensile strength of the material does indeed vary with fibre orientation. By testing parallel and perpendicular to the split line direction (*i.e.* that pattern shown up when the surface of the cartilage is punctured and then stained with ink), it was shown that the tensile strength was greatest in the direction parallel to the said pattern, (figure 1.5) the relevance of this being that the split line pattern is felt to be a consequence of the fibre orientation in the superficial zone (or Zone I). Similarly, a variation of strength with depth has been found. In this case the region of greatest strength is to be found at the articular surface, with a subsequent decrease in strength towards the sub-chondral bone (figure 1.6).

In terms of actual values of the tensile strength, Kempson in his review, quotes the following ranges for cartilage tested from the superficial zone and parallel to the split pattern. Tensile strength - 10-40 MPa, tensile modulus - 150-500 MPa.

Research by Kempson and co-workers (26) has suggested a reasonably good correlation between the tensile strength and the collagen content, whereas no such relationship with the total proteoglycan content could be established.

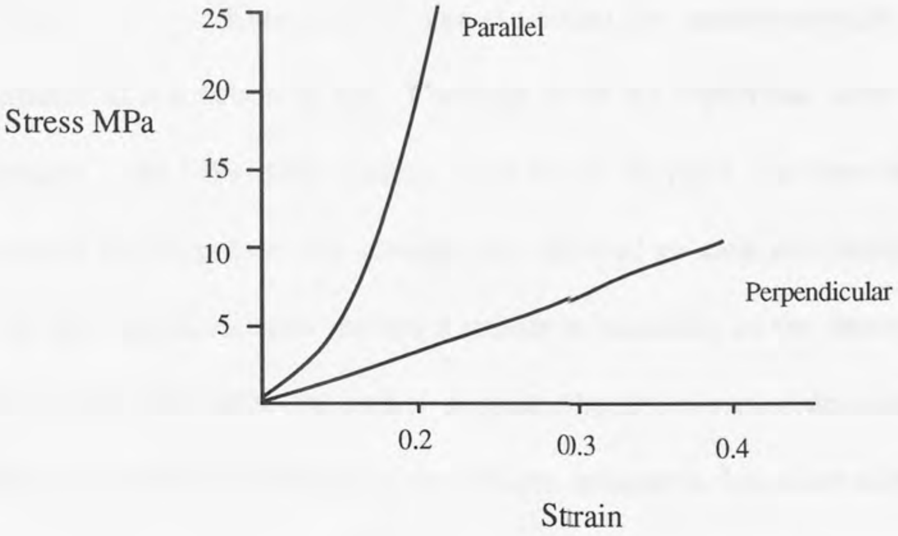


Figure 1.5 The variation in the tensile behaviour of articular cartilage, parallel and perpendicular to the split line pattern (redrawn from Kempson 1980)

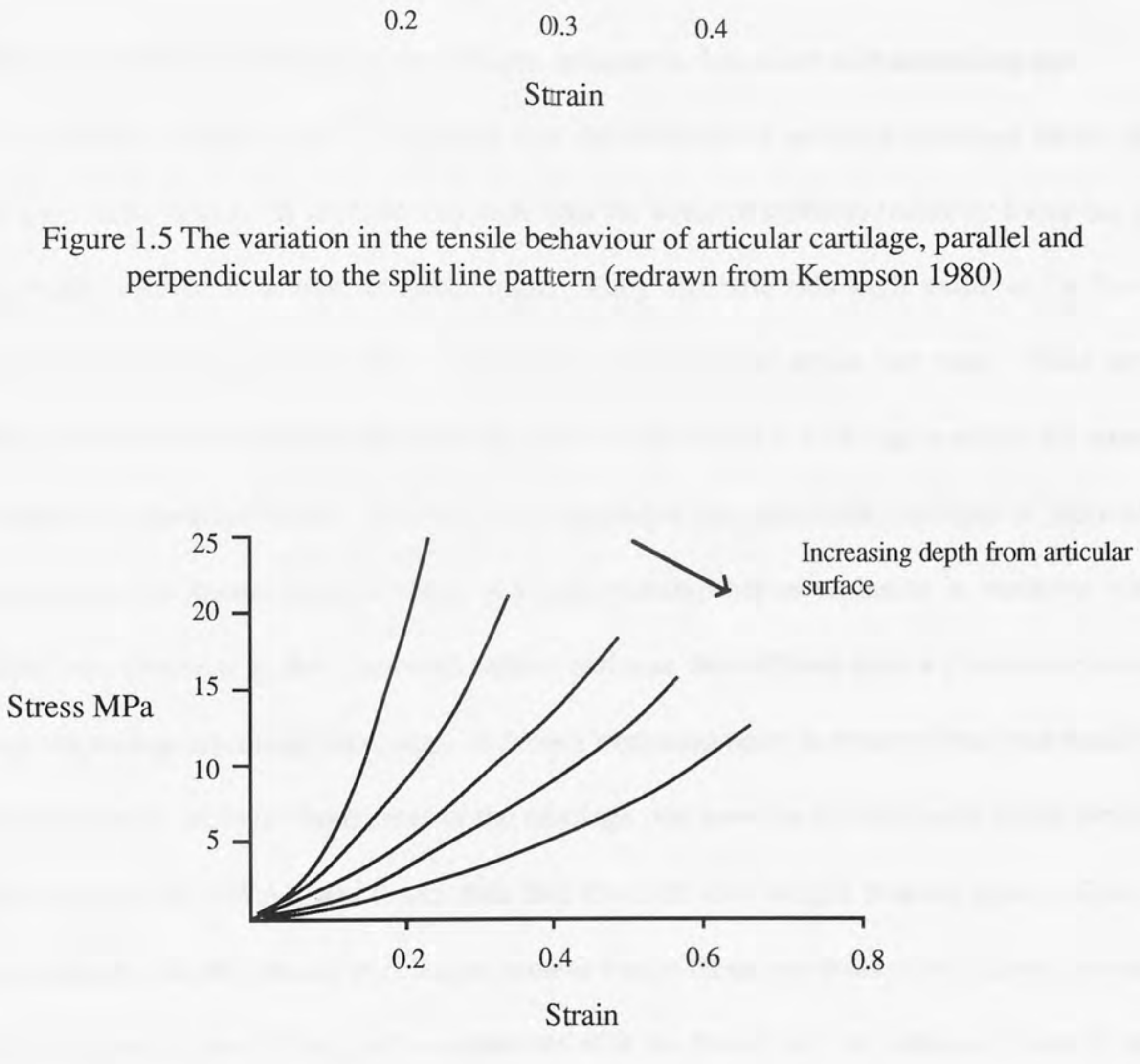


Figure 1.6 The variation in the tensile behaviour of articular cartilage, as a function of depth from the articular surface (Kempson 1980)

More recently, Kempson,(27) has examined the tensile strength of human knee joint cartilage as a function of age. Cartilage from the superficial layer reached a maximum strength (~40 MPa) from patients aged about 30 years, and then decreased steadily. In terms of the deep zone, the strength here showed no such maximum. Values of stiffness from the superficial zone showed a similar relationship as the strength, the peak modulus being about 150 MPa. The author suggests that the observed deterioration in properties is due to organisational changes in the collagen meshwork that occur with advancing age.

In contrast, Akizuki *et al.* (17) believe that the modulus of articular cartilage shows no such age dependence. In addition they state that the value of stiffness found by Kempson in the work referred to above, is rather high. They attribute this high value to "a flow-generated stiffening effect", that is associated with constant strain rate tests. Thus they measured a flow independent modulus by using small strains (~15%) up to which the stress strain curve remained linear. This led to the conclusion that the tensile modulus of "normal" cartilage is not greater than 30 MPa. A similar relationship of variation in modulus with depth was observed as that discussed earlier, and also the stiffness bore a good correlation with the collagen/proteoglycan ratio. A further important point to emerge from this work is that the tensile stiffness from areas of the cartilage that bore the highest loads (high weight bearing areas or HWA), was lower than that from the low weight bearing areas. This is explained by the differences in collagen content within these two areas (the collagen content being highest in the LWA), and is consistent with the belief that the collagen controls the tensile properties of cartilage, and the proteoglycan gel, the compressive properties.

Other work on bovine articular cartilage (28) has suggested that the mechanical response of immature tissue is superior to that of the mature tissue, and that in cartilage, it is the surface layers that play the most important part in protecting the rest of the tissue from any damage caused by tensile forces. Although bovine cartilage is less stiff than human cartilage, the variation in tensile properties parallel and perpendicular to the split line pattern was very similar to that observed by other workers on human articular cartilage.

The mechanical properties of cartilage also vary depending on where in the joint it is tested. Silyn-Roberts and Broom, have adopted a micromechanical testing approach to measure the variation in mechanical properties of bovine cartilage across the patellar groove.(29) The tensile stiffness of cartilage from the deep zone was found to decrease sharply from the medial margin, pass through a minimum approximately half way across (corresponding to the trough of the patellar groove), and then rise again, although the stiffness of the lateral margin was always less than that of the medial margin. A similar trend was observed for the compressive stiffness, and it was shown that the more compliant material had a less dense arrangement of collagen fibrils, and that these fibrils were aligned preferentially in a radial direction. Interestingly some of these observations are in disagreement with the work of Akizuki,(17) where high weight bearing areas were found to have a low tensile stiffness, although the reason for this may be due in part, to the different methods used to determine tensile stiffness.

1.4.2.2 Compressive properties

In terms of measuring the compressive properties of articular cartilage there are essentially two basic approaches. These are to use either indentation measurements, or to use uniaxial compression tests. In both cases similar problems in obtaining meaningful results arise as those found for the tensile properties. Indentation tests have the advantage that they are relatively straightforward and quick to perform. In addition the properties of the cartilage can be determined whilst it is still attached to the bone, and the small size of the needle means it is possible to determine topographical variations across the surface of the material.

Unfortunately, the results are difficult to interpret, since they rely on the assumptions of Hertzian theory, and are also dependent on the specimen thickness, which in the case of cartilage is rarely uniform. Uniaxial compression tests are to be preferred where the rheological properties of the material are to be determined. Rheological properties are particularly important because a large proportion of the water in cartilage is free to move through the matrix, and this movement helps to explain the viscoelastic response of this interesting material.

Cameron and co-workers have used microhardness measurements to evaluate the properties of femoral cartilage in compression.(30) They found that the hardest part of the femoral cartilage is the surface layer, and that the plane at right angles to the direction of motion, was stiffer than the plane parallel to the direction of motion. No absolute values were given for the compression stiffness since the data was purely qualitative, and was performed on a comparative basis, using the cartilage from the stiffest area as a reference point.

The review by Kempson (25) also considers the properties of cartilage in compression. Typical values for the compression modulus of the material were in the range 1-10 MPa as determined by both indentation and uniaxial tests. As in the case of tension, attempts have been made to relate the mechanical properties to the various chemical constituents of the material. In the case of compression a reasonable correlation has been established between the modulus and the total proteoglycan content, although nothing could be determined by relating the modulus to the collagen content. Kempson himself has attempted to illustrate the variation of properties across the cartilage surface by using indentation tests. By this means it was possible to estimate where the high load bearing areas were. It was also shown that cartilage from osteoarthritic joints had a significantly lower stiffness than "normal" cartilage.

Another paper concerned with the variation in cartilage properties factors such as age, is that of Armstrong and Mow.(31) Here a confined compression creep test was used to measure the properties of human articular cartilage. The authors concluded that the mechanical properties did not change significantly with age. Not unexpectedly however, there was a marked dependence of the compression properties with the water content, the equilibrium modulus falling from about 1.2 MPa at a water content of ~70 % to less than 0.5 MPa for a water content of approximately 85 %. The permeability was also found to be dependent on the water content of the material. The permeability is an important property of cartilage because it determines the flow behaviour of the interstitial water.

A more recent review (32) has concentrated on fluid flow in articular cartilage, and on the various attempts at modelling the mechanical properties of the material. It appears that the best models for cartilage are those which consider the material as being biphasic, and poroviscoelastic. One such model is that of Mak (33), where it was concluded that both the interstitial fluid flow and the intrinsic matrix viscoelasticity made a significant contribution to the overall compressive properties of the material.

Compressive loads have also been used to study cartilage from other mammals, such as dogs.(34) Similar findings were made as regards the properties of the cartilage with depth from the articular surface, and also in that the areas found to be stiffest in compression are closely correlated with lower overall fiber contents, but greater proteoglycan concentrations. Information such as this from smaller mammals, may be of importance, since the preliminary response of a potential replacement cartilage material will probably have to be evaluated using some form of animal trials.

1.4.2.3 Other mechanical properties

Due to the nature of the loading of the joint, significant shear forces may occur during normal articulation. A synthetic cartilage material will therefore need to be able to resist these forces. Studies have been made on bovine articular cartilage in shear, in order to try and isolate the properties of the matrix from those of the interstitial water, and a value of the shear modulus of articular cartilage has been quoted as 0.37 MPa.(35) Other research has been directed at determining the shear properties of bovine cartilage in fatigue.(36) Because of the presence of these shear stresses, Peppas (37) has suggested that a synthetic cartilage material will therefore require a degree of tear resistance, in order that it will be able to withstand these forces.

1.4.2.4 Other design considerations for a synthetic cartilage material

An important consideration in the design of a cartilage replacement is the effect of fatigue. Weightman *et al.*,(38) have suggested that a fatigue mechanism may account for the fibrillation of cartilage that is observed in the early stages of osteoarthritis. Simon and co-workers have shown that in shear fatigue, there is a rapid irreversible drop in the modulus of bovine cartilage of about one third after 10^5 cycles, but that after this little change in stiffness was observed.(36) The sensitivity of the fatigue resistance of cartilage to applied load, has been demonstrated by Zimmerman *et al.* At loads of about 7 MPa, cartilage from the human patellar showed signs of damage after about 1000 cycles, whilst at stresses of 3.5 MPa (which is similar to the peak loads transmitted during normal articulation), no sign of damage was observed, even after 1.2×10^5 cycles.(39)

Apart from its load bearing capacity, one of the major functions of articular cartilage is to provide an almost frictionless bearing surface. Thus an important consideration in the design of a synthetic cartilage, is the candidate materials tribological characteristics. The low friction of the synovial joint system has puzzled engineers and scientists for many years. One of the earliest investigations into the frictional properties of cartilage was performed by McCutchen (40) in the early 1960's. The instrument used to determine friction, meant that he could not measure the friction of cartilage on cartilage. Instead, flat samples of glass had to be used as the other bearing surface. Even so, low values of friction were found - a coefficient of friction of less than 0.1 was achieved when synovial fluid was used as the lubricant, although a slightly higher value was found if water was used as the lubricant. McCutchen then went on to suggest that this low value of friction arose because the cartilage acted as a "weeping bearing". Such is the complexity of the loading patterns experienced in the joint, that even today, the exact mode of lubrication is little understood. Armstrong and Mow have outlined some of the tribological factors associated with synovial joints in a short review (41), from which it could be seen that generally, the coefficient of friction of the articulating surfaces has been found to lie between 0.01 and 0.04 for joints lubricated with synovial fluid.

One of the parameters that may also be of importance in the lubrication of synovial joints is the roughness of the cartilage surface. This has been measured by Thomas *et al.*(42) By using a small stylus and a fast tracking speed, it was possible to make a direct measurement of the roughness of the femoral head. No significant anisotropy was found, and the height distribution was approximately Gaussian, leading to an estimate for the effective roughness of the surface as 20 μm. In addition a value for the hardness of the material was derived as 412 MPa, and for the modulus a value of 367 MPa was found. The authors explain this very high value of stiffness by saying that it was probably due to the small size and duration of the test.

The swelling properties of cartilage are worth mentioning briefly here, since they are relevant to the mechanical properties of the material.(43) Essentially, an equilibrium exists between the highly charged proteoglycans, and the collagen mesh, the tendency for the proteoglycans to swell, being balanced by the tension in the collagen fibres. Recently the swelling properties of cartilage have been modelled mathematically and compared to those of the corneal stroma.(44)

So far most of the above discussion has been concerned with physical property measurements taken from the cartilage itself. Design data can also be obtained from other sources however. For instance, the type of loading that articular cartilage experiences is very similar to that experienced in artificial joints such as the hip. Thus some of the lessons learnt from the design of the artificial hip may bear some relevance to the case of the synthetic cartilage material. For instance Murakami,(45) has compared the lubrication in the natural state, with that of typical hip joint prosthesis. In a series of papers, Davidson *et al.*(46, 47) have made the observation that frictional heat generated during articulation may be quite significant for some polymers, since it may be enough to cause the polymer to creep, with a subsequent effect on the wear resistance and long term performance of the system. In their experiments on conventional artificial hip materials, temperature rises of up to 20°C after 30 minutes, were found for some systems.

More recently in an attempt to produce a lower coefficient of friction in the artificial hip, softer more compliant layers have been incorporated to promote fluid film lubrication.(48) The materials used in this case were various grades of polyurethane, and it was found that the optimum hardness to obtain low coefficients of friction was ~6 MPa. The fact that such low values of friction have been obtained with soft materials, lends one to hope that hydrogel materials may be equally successful in this respect.

In summary then, cartilage can be considered as a two phase viscoelastic material, swollen by water. An equilibrium exists between a charged proteoglycan gel and a meshwork of collagen fibres, whereby the collagen fibres resist the tensile and shear forces, and flow of interstitial water, governs the compressive and time dependent properties.

Finally in this section some of the more important properties of cartilage, from a design point of view are summarised in Table 1.3.

Property	Articular Cartilage	Poly HEMA
Tensile Strength / MPa	10-30	0.6
Tensile Modulus / MPa	100-200	0.6
Elongation / %	80-100	150
Compression Modulus / MPa	1-5	1
Water Content / %	75	40
Coefficient of Friction	0.02	0.05 *
Tear Resistance / J/m^2		1000 *

Table 1.3 Comparison of some properties of articular cartilage with those of a typical hydrogel

* = PVA based hydrogel

Where possible these are compared to those of a typical hydrogel, which unless otherwise stated will be poly HEMA. Due to the difficulties associated with testing cartilage, the figures are only approximate. For a general introduction to the mechanical properties and function of human articular cartilage, the reader is referred to the review by Swanson.(49)

1.5 Previous Work on Synthetic Articular Cartilage Materials

It will be apparent that the properties of cartilage and hydrogels are quite similar in some respects, especially when one considers that hydrogels are actually quite a broad class of materials. Thus for instance hydrogels can be prepared with water contents of >80 %, though naturally with a subsequent decrease in mechanical properties.

It is not surprising then, to find that there have been several previous attempts to make synthetic cartilage materials - some of which gave been based on hydrogels. One of the earliest of these is that of Bray and Merril,(50) who made a preliminary assessment of crystallized poly (vinylalcohol) hydrogels for this particular application. Interestingly, these workers believed that not only must the physical properties of the material be correct, but that also the material must act as an ultrafiltration membrane. It was felt that cationic groups should be present, or capable of being introduced. They went on to explain that this was necessary in order to achieve the required lubrication regime. Essentially they envisaged a three stage lubrication viz: The water swollen polymer would exude water under load to provide the initial lubrication (stage 1). The polymer would then also act to filter out hyaluronic acid under greater pressures, to produce trapped pools of synovial fluid (stage 2). Under still greater pressures the lubrication would be achieved via shear of a hyaluronic acid film (caused by ionic adsorption to the charged hydrogel surface) (stage 3). Preliminary investigations indicated that PVA hydrogels might meet these requirements. Unfortunately, although strengths of ~1 MPa were achieved, further research is not forthcoming.

In a similar vein, Peppas (51) also suggested the use of crystallized PVA hydrogels. Good properties were achieved in this instance by a "drying reinforcement process". Essentially this consisted of an anneal at ~180°C followed by swelling in water at 30°C. This induced greater crystallinity to the material. It was reported that such hydrogels had a tensile modulus of about 5 MPA and ultimate tensile strengths of about 10 MPa. Tear resistance and coefficient of friction were said to be satisfactory, the latter having a value of 0.05.

Research in Japan has also centred on the use of PVA hydrogels as potential synthetic cartilage materials. For example Sasada *et al* (52) have evaluated the frictional properties of a PVA gel, where the hydrogel was used as a lining in the acetabular cup of a conventional hip prosthesis. For the combination of Al_2O_3/PVA the damping characteristics (as measured using an oscillating pendulum technique) were found to be quite similar to those found in healthy dogs. Potassium hyaluronate was also noted to be an effective lubricant for this type of prosthesis.

Another group of Japanese researchers developed a similar PVA hydrogel, which was evaluated for its biological response by implantation into the knees of young rabbits.(53) The results from this study were felt to be quite promising and only slight inflammation, during the early stages of implantation, occurred. Comparison with controls of ultra-high molecular weight polyethylene (a material that is commonly used to form the acetabular cup in Charnley style hip prosthesis), suggested that the hydrogel offered improved biocompatibility over the polyethylene. The authors conceded that although the strength of their material was felt to be adequate, further development was required on both the tribological properties, and the longer term durability of this hydrogel.

A review of the development of an artificial cartilage, using this type of PVA hydrogel, has been published recently by the same group of workers.(54) In this paper the authors list the main requirements that would be needed in order to develop a successful artificial cartilage material. These were: 1) good lubrication, 2) sufficient shock absorbing ability, 3) high wear resistance, 4) good biocompatibility, and 5) firm attachment to the underlying bone. Some more details about the hydrogel itself were given, atactic PVA with a relative molecular weight of approximately 300,000 was made semicrystalline by cooling below room temperature and then subsequently annealing at 140°C. This material had a water content of about 20 %, although unfortunately no mechanical property data were quoted.

Overall the material does not sound dissimilar to that produced by Peppas in the mid 1970's. The biocompatibility of this material has already been mentioned (53) and in terms of the material's wear resistance, pin on disk experiments using a stress of 3 MPa showed that the wear factor was 5 times greater than that of polyethylene. Problems were still encountered with the fixation of the device however. In order to address this problem the authors have been attempting to use porous alumina or a fine titanium mesh, which would form a composite with the hydrogel, and facilitate bone growth into the structure, so providing a degree of anchorage.

On a slightly different tack, HEMA sponges have also been investigated for synthetic repair/replacement cartilage materials.(55) Several sponges of different pore size were evaluated, both histologically after implantation in the knees of rabbits, and in terms of their mechanical properties. The advantage of poly HEMA sponges is that they are felt to induce calcification and subsequent bone ingrowth, provided that the pore size exceeds 40μm. It was said that sponges of large pore size could be prepared by a salt extraction method. In one sponge, similar mechanical properties were observed, as to those made in the normal manner but with 40 times smaller pore size. The main conclusion of the work was that only those sponges with pore sizes of less than 50μm were suitable, since histological examination showed that those of greater pore size disintegrated under the service conditions.

A similar attempt to use poly HEMA as an artificial cartilage replacement material, has been made in Czechoslovakia.(56) In this work, Pavlansky *et al.* fitted a 3 mm thick cup to the femoral head of dogs. Although the initial response appeared quite satisfactory, after 3 to 5 months implantation the hydrogel crumbled, and again, it would appear that insufficient attention was given to the material property requirements for this application.

In a further attempt to resurface the hip, a biodegradable polymer has been utilised, and again evaluated in dogs. Here, a poly L lactide acetabular cup was used, the rationale being that the polymer would protect the undamaged cartilage, whilst allowing the natural processes of regeneration to repair slightly damaged tissue.(57) Again the initial response was very satisfactory, and a considerable improvement over controls without the device. Ultimately though, the prosthesis was not successful, although the authors believe that longer degradation times (*i.e.* greater than the 60 days used in these preliminary trials) may be necessary to allow more complete recovery of the damaged cartilage.

It was hinted in the above sections that one of the problems of a synthetic material might be attachment to the sub-chondral bone. In a recent patent application (58), this problem is believed to have been overcome. The approach adopted here was to use demineralized bone as a replacement/repair material. Demineralized bone is stated to have a spongy texture which serves as the cartilage material, whilst a non demineralized portion of the implant acts so as to anchor the substitute to the normal healthy tissue. The demineralization is produced by dissolving in a suitable organic acid, coupled with a chelating agent *e.g.* EDTA. Subsequent tanning via a glutaraldehyde mixture is used to render the material "non-antigenic and biocompatible". Unfortunately, no mechanical property data were provided, making an assessment of the success or otherwise of the material on this basis impossible.

A current method of repairing partial cartilage lesions, is the use of a carbon fibre mesh or pad.(59) This method has been adopted quite successfully, although the reasons behind its success are poorly understood. It would seem that the carbon fibres act primarily as a mesh or framework around which further collagen is allowed to develop, and that the carbon acts as an irritant, speeding up this process of regeneration. It may be significant however, that the collagen that is produced, is not of the same type as that which is found predominately in articular cartilage.

In a further attempt to find a satisfactory way to repair damaged cartilage, Shagaldi *et al.* (60) have evaluated the response of various biological implants, to implantation in the knees of goats. The three materials used were a glutaraldehyde-fixed bovine meniscal xenograft, a similarly fixed bovine costal cartilage xenograft, and a viable osteochondral allograft. It was discovered that the meniscal xenografts performed adequately over the trial period of one year, whilst the costal cartilage implant broke down after about 6 months. The response of the viable allografts was somewhat mixed, with some failures and some successes by the end of the implantation period. An important point to arise from this study was that the positioning of the implant was critical to its success or failure, with minor changes in level above or below the articulating surface, producing profound changes in the tissue reaction of the surrounding undamaged cartilage.

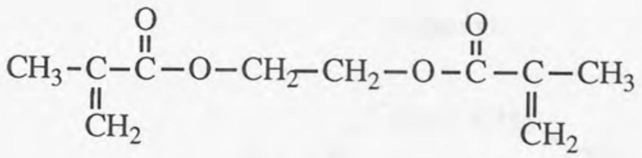
Chapter 2 Experimental Methods

2.1 Reagents Used

Optical grade 2 hydroxyethyl methacrylate was supplied by Ubichem Ltd., and optical grade N-vinyl pyrrolidone by Vickers laboratories. Ethylene glycol dimethacrylate (BDH), and azo bis isobutyronitrile (Aldrich) were also used, all the above being used as supplied. The other methacrylate monomers were obtained from Rohm GMBH, and were distilled in order to remove any inhibitors and/or stabilizers. Further details can be found in the literature. (2,91) The structures of the main monomers used in this work are given in figures 2.1 and 2.2.

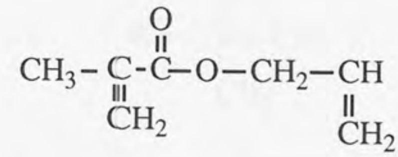
2.2 Preparation of Hydrogel Membranes

Hydrogel membranes were prepared in the following manner. First suitable moulds were made. Typically these consisted of two glass plates approximately 150 mm x 75 mm which were separated by polythene gaskets to the required thickness (usually 0.4 mm). The glass plates were backed with sheets of melinex in order to prevent adhesion of finished membrane to the mould. The whole assembly was then held together by means of several bulldog clips. A total of 4 g of the appropriate monomer (or monomers) was weighed out. To this was added 1 wt % of the crosslinking agent EGDM (ethylene glycol dimethacrylate), and 0.5 wt % of the initiator AIBN (azo bis isobutyronitrile). In order to reduce the porosity of the finished membrane, and also to displace any oxygen which may act as an inhibitor, dry nitrogen was bubbled through the mixture for about 5 minutes. Finally the solution was carefully injected into the moulds via a syringe. The filled moulds were then placed in an oven for curing, which consisted of three days at 60°C and a postcure of two hours at 90°C. After curing, the xerogel was removed and allowed to hydrate in distilled water for a period



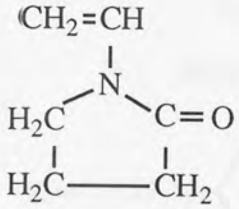
$$CH_3-\underset{\underset{CH_2}{||}}{C}-\overset{\overset{O}{||}}{C}-O-CH_2-CH_2-O-\overset{\overset{O}{||}}{C}-\underset{\underset{CH_2}{||}}{C}-CH_3$$

Ethylene glycol dimethacrylate

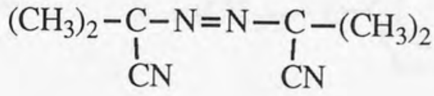


$$CH_3-\underset{\underset{CH_2}{|||}}{C}-\overset{\overset{O}{||}}{C}-O-CH_2-\underset{\underset{CH_2}{||}}{CH}$$

Allyl methacrylate



N-vinyl 2 pyrrolidone



$$(CH_3)_2-\underset{\underset{CN}{|}}{C}-N=N-\underset{\underset{CN}{|}}{C}-(CH_3)_2$$

Azo bis isobutyronitrile

Figure 2.1 Structures of some of the reagents used in this work

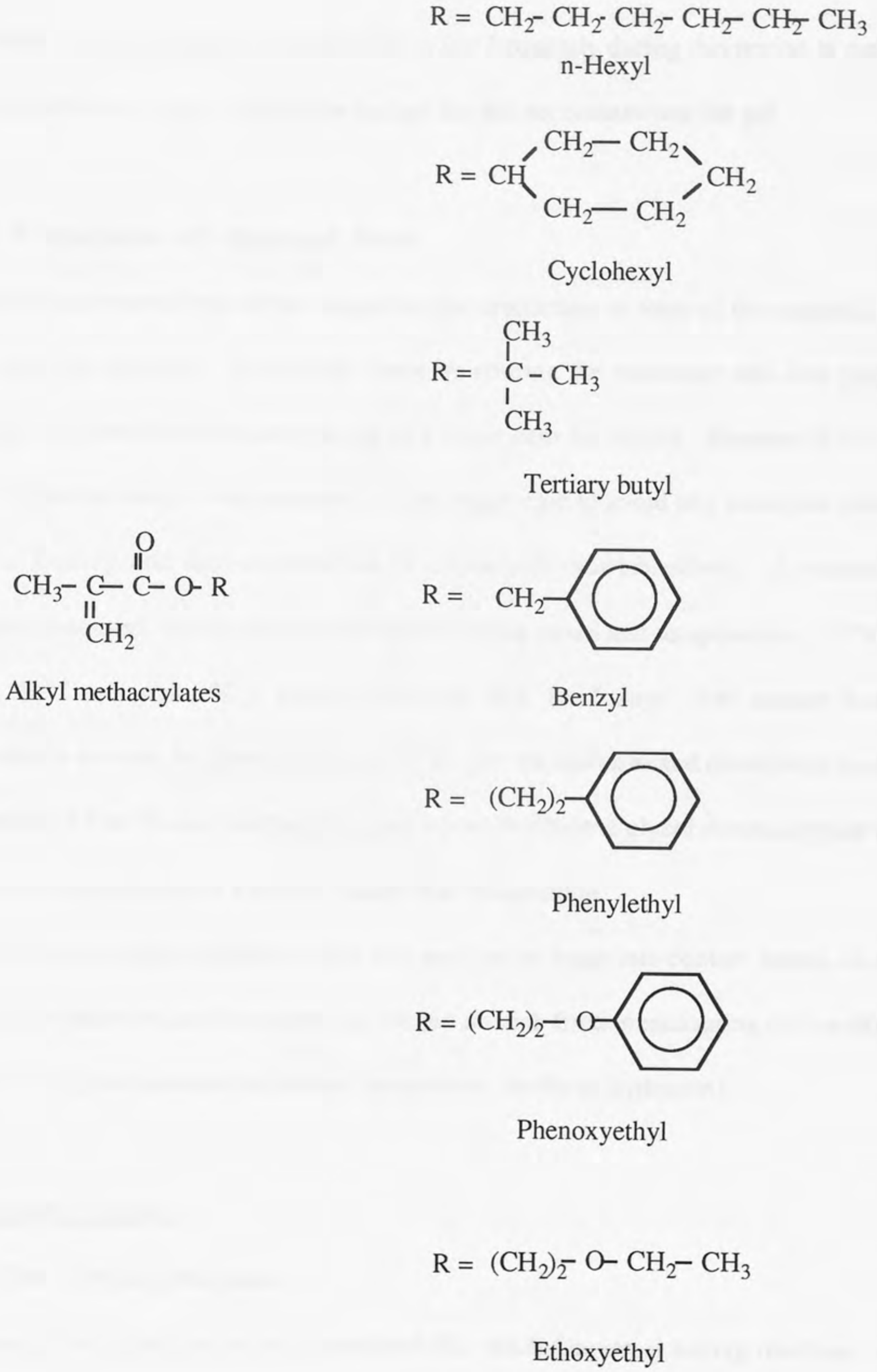


Figure 2.2 Structures of some of the methacrylate monomers used in this work

of a week. It was necessary to change the water frequently during this period in order that any unreacted monomers that may be leached out did not contaminate the gel.

2.2.1 Preparation of Hydrogel Rods

A more convenient form of the xerogel for the production of some of the materials in this work was that of a rod. These were made by pouring the monomer mix into polythene tubes of 12.5 mm diameter and placing in a water bath for curing. Because of the larger bulk of material used it was necessary to use longer cure to avoid any problems caused by internal heating and auto-acceleration (Trommsdorff Norrish effect). A ramped cure schedule was used, which consisted of the following times and temperatures : 30°C for 4 hours, 40°C overnight, 50°C for 12 hours and 60°C for 6 days. The sample was then postcured in an oven for about 3 hours at 90°C. For the rods a mixed crosslinker was used, comprising 0.5 wt % allyl methacrylate and 0.5 wt % ethylene glycol dimethacrylate as this was more representative of a typical contact lens composition.

The completed rods were then either sent away to be made into contact lenses, or turned down to the appropriate dimensions for the pin on disk friction measuring device that was used. (Taking into account the amount the polymer swells on hydration).

2.3 Tensile Testing

2.3.1 The Testing Machine

Testing was carried out on an Hounsfield HK 10KN Universal testing machine, which was linked to an IBM 55sx personal computer via an RS232 interface. Generally speaking a 10 N load cell was suitable for most of the hydrogels tested.

The grips used were custom designed to the sample configuration that was finally adopted (see later). A light spring provided just enough pressure to grip the more fragile samples (particularly those of higher water content), and a sensitive thumbscrew allowed fine adjustments of pressure for the stiffer materials. The top set of the grips needed to be lightweight (due to the sensitivity of the load cell) and weighed only 60.4 g. This was then freely suspended from a light chain to ensure axial alignment during the test. Further experimental details regarding the tensile testing of the polymers are given in sections 3.2 and 4.2, where appropriate methodologies are developed.

2.4 Compression Properties

In order to measure the compression modulus of the hydrogels, a micro hardness indentor was used. This instrument was first developed by ICI to study paint films.(61, 62) The instrument operates on the principle that an applied gas pressure (dependent on the depth of indentation of a small needle into the sample) is amplified via a series of nozzles, flappers, and bellows to be subsequently indicated on a chart recorder. This enables changes in indentation depth with time to be monitored, both during the application of a small applied load, and during the subsequent recovery of the material after the removal of the said load. A value for the modulus of the material can then be estimated by applying the Hertzian theory of elastic contact, or a modification thereof.

2.5 Friction Measurements

In order to asses the frictional properties of the hydrogels, a modified pin on disc friction measuring machine was used. Tiny hydrogel samples were stuck onto small brass pins using a cyanoacrylate adhesive. The coefficient of friction was then measured as a function of the speed of rotation of a steel counterface which had a diameter of approximately 3 cm.

The frictional load was indicated by means of a galvanometer which was calibrated against a series of applied loads. Water was dripped onto this rotating surface, to act as lubricant and to prevent dehydration of the hydrogel.

2.6 Measurement of Tear Resistance

Tear resistance was determined in accordance with British Standard 903 part A3, "tear resistance by the trouser tear method", although the specimen configuration was altered

Figure 2.3 Specimen configuration for trouser tear tests

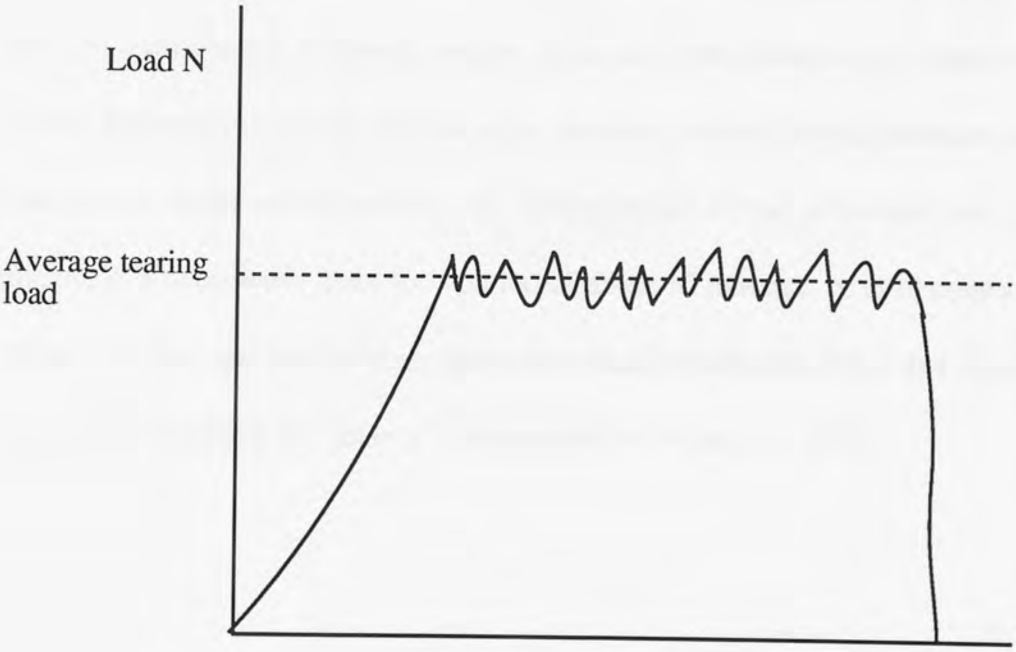


Figure 2.4 Idealised load/time curve for the tear resistance of a "brittle" polymer film

slightly in order to accommodate more samples from each membrane. A total length of 40 mm was used, with width 15 mm (see figure 2.3), and an initial tear was cut to a length of 15 mm using a sharp scalpel. Because a smaller size had been used, the crosshead speed for testing these samples was suitably adjusted, so that a speed of 50 mm/min was generally used. This gave failure in a reasonable length time (approximately 30 seconds). The value of tearing load was taken to be the average (peak to trough) height once tearing had been initiated (figure 2.4). The tear resistance of the material is then given by dividing this load by the specimen thickness.

2.7 Determination of Equilibrium Water Contents

Equilibrium water contents were measured by determining the weight difference between the fully hydrated polymer, and the dehydrated xerogel. This difference is then expressed as a percentage of the hydrated weight in order to obtain the equilibrium water content of the gel. To measure the hydrated weight, discs cut from the hydrogel sheet were carefully "dried" between two pieces of filter paper, so as to remove surface moisture, but not so hard that excess water was squeezed out. Dehydration of the polymers was carried out by placing in a microwave oven for a period of about 10 minutes, or until constant weight was achieved. Previous work in these laboratories had demonstrated that this length of time was equivalent to placing the gel in a vacuum oven for 24 hours at 90°C.

Chapter 3
The Mechanical Properties of Hydrogel Polymers - a General Overview

3.1 Introduction

Hydrogel materials have found widespread use as biomaterials, particularly in the area of soft contact lenses. The presence of a significant proportion of water incorporated in these polymers, enhances their general biocompatibility with body tissues, but also serves to make such polymers rather weak. Several authors have attempted to re-address this shortfall by various means, including copolymerisation,(63-66) introduction of crystallinity,(67) semi-interpenetrating networks,(68) and the production of hydrogel composites,(69, 70) in order to produce a hydrogel that is suitable for more demanding prosthetic applications.

Mechanical testing, particularly in tension, is an extremely useful technique for the evaluation of materials, since it is relatively straightforward to perform, and, for this class of materials, is sensitive to small changes in composition and/or sample preparation. Hence static tensile testing is frequently used to examine structure property relationships.(63-72) This was also the method chosen by Lee *et al*, in their investigation of the influence of tacticity on poly HEMA.(73) Tensile testing is not the only method suitable for investigations concerning structure property relationships however. For instance, Huglin *et al*. (74-77) have used compression testing in order to evaluate various hydrogel networks, particularly with respect to their swelling behaviour, relating this to the resultant crosslink density of the polymers so formed.

The use of mechanical property testing to investigate fundamental structure property relationships is clearly very important, but it is by no means the only reason for performing such tests. The evaluation of a material to determine its suitability for a particular application is also of paramount importance. It is obvious that a full mechanical characterisation of a material cannot be done just by using one particular test, since other properties of the material may well be important, depending on the envisaged application. For example the viscoelastic nature of polymers means that their mechanical response is a function of time, temperature and previous loading history. Hydrogel materials are no exception to this rule, and viscoelastic behaviour has been the subject of two studies, one by Janacek,(78) and more recently by Migliaresi.(79) By using tensile tests at different strain rates and temperatures, and by altering the crosslink density of the gels, Raab and Janacek (80) attempted to characterise the properties of poly HEMA more fully, and developed a universal failure envelope for this particular hydrogel. A further property that is important for some applications is a measure of the tear resistance, or the fracture toughness, of the material. Peppas (37) recognised this in his early attempts to develop a synthetic articular cartilage material. A fracture toughness approach was also used by Jackson, where he measured this particular property in order to compare a number of different commercial soft contact lenses.(81)

Considering that soft contact lenses are by far the most important application of hydrogels to date, it is perhaps surprising that there are relatively few references that deal with the mechanical strength of these particular devices. Presumably this is because the loads generally experienced by the lens, are small enough for the limitations of the given material not to be exceeded during normal wear. Where data does exist it is usually of a comparative nature, and frequently poly HEMA is used for the basis for this comparison, for no better reason than that it has already become a very successful soft contact lens material. Hosaka and co-workers (82) used this principle to assess MMA/NVP copolymers as possible lens materials. Testing was carried out on discs of hydrogel prepared under laboratory conditions, and therefore may not be equivalent to the same polymer in its fully fabricated state, *i.e.* in the form of a fully finished contact lens (due to differences in the polymerisation conditions for example). On the other hand Jackson, in his work, used the finished article for his toughness tests. Tighe and Trevett,(83) have suggested the use of the initial modulus of the lens as an indication of clinical performance. They developed a method to test a contact lens in tension, and so also obtain information regarding the lens's strength and elasticity, as well as modulus.

The rationale behind mechanical property testing lies not so much in the absolute value obtained for the strength, modulus *etc*, but rather in the manner in which it is measured. Thus, whether testing is done in a research laboratory to study effects of say, copolymer composition, or whether in a more conventional engineering sense to assess whether a particular polymer will be mechanically suitable for a given application - it is next to useless, unless suitable comparisons can be drawn between different materials. Because of this, various standards for the testing of materials now exist, for example ASTM D638 and BS 903. At the present time, no such standards exist for the mechanical testing of hydrogel materials, which leads to a rather unsatisfactory state of affairs.

Take for example the case of one particular hydrogel, poly HEMA, and its static tensile properties (*i.e.* strength, modulus and elongation to break). The findings of various authors who have attempted to measure these properties for poly HEMA are summarised in Table 3.1. From this it will be seen that quite a range of values have been quoted for these particular properties. This is not all that surprising when one considers all the variables that exist in such tests, even though they are relatively simple and straightforward to perform. For instance some workers have conducted their tests at room temperature (20-25°C), whilst others, because they are dealing with potential biomaterials, have naturally enough used body temperature (37°C). Similarly a whole range of strain rates have been utilised. Commendably one of the few things these authors do agree on is that an appropriately shaped dumbbell specimen should be used, though ideas on what its size should be, differ.

	Tensile Strength / MPa	Tensile Modulus / MPa	Elongation to Break / %	Conditions of Test	Strain Rate / % / min	Sample Geometry / mm	Composition wt %	Cure Schedule
Kolarik and Migliaresi (63)	0.32 ± 20%	0.39 ± 10%	181 ± 20%	22°C ± 2	89	dumbell gl 22.5	0.5 EGDM 0.4 AIBN	65°C, 8 hrs
Migliaresi *et al.* (64)	0.25	0.7	40	37°C immersed	66	dumbell gl 7.6	0.5 EGDM 0.1 AIBN	90°C, 1hr 100°C, 4hrs
Raab and Janacek (80)	0.33 ± 0.01	-	196 ± 6	25°C immersed	267	dumbell gl 22.5	1.0 EGDM IPPC	60°C,4 hrs
Lopour *et al.* (70)	0.23	-	250	room temp	X-head 1.7 mm/s	dumbell	0.3 EGDM	-
Nagaoka (69)	0.7	0.27	200	37°C in saline	X-head 10 cm/min	-	EGDM BEE	10°C, 24 hrs, UV 90°C, 24 hrs
Lee *et al.* (73)	0.75	6.0 -	47	25°C	16.7	dumbell gl 30	2.5 HMDIC	-
Hosaka *et al.* (82)	1.22 ± 0.34	1.48 ± 0.33	208 ± 26	23°C immer / 50%RH	1000	parallel length 10	-	-

IPPC = Isopropyl percarbonate, BEE = Benzoin ethylether, HMDIC = Hexamethylene diisocyanate

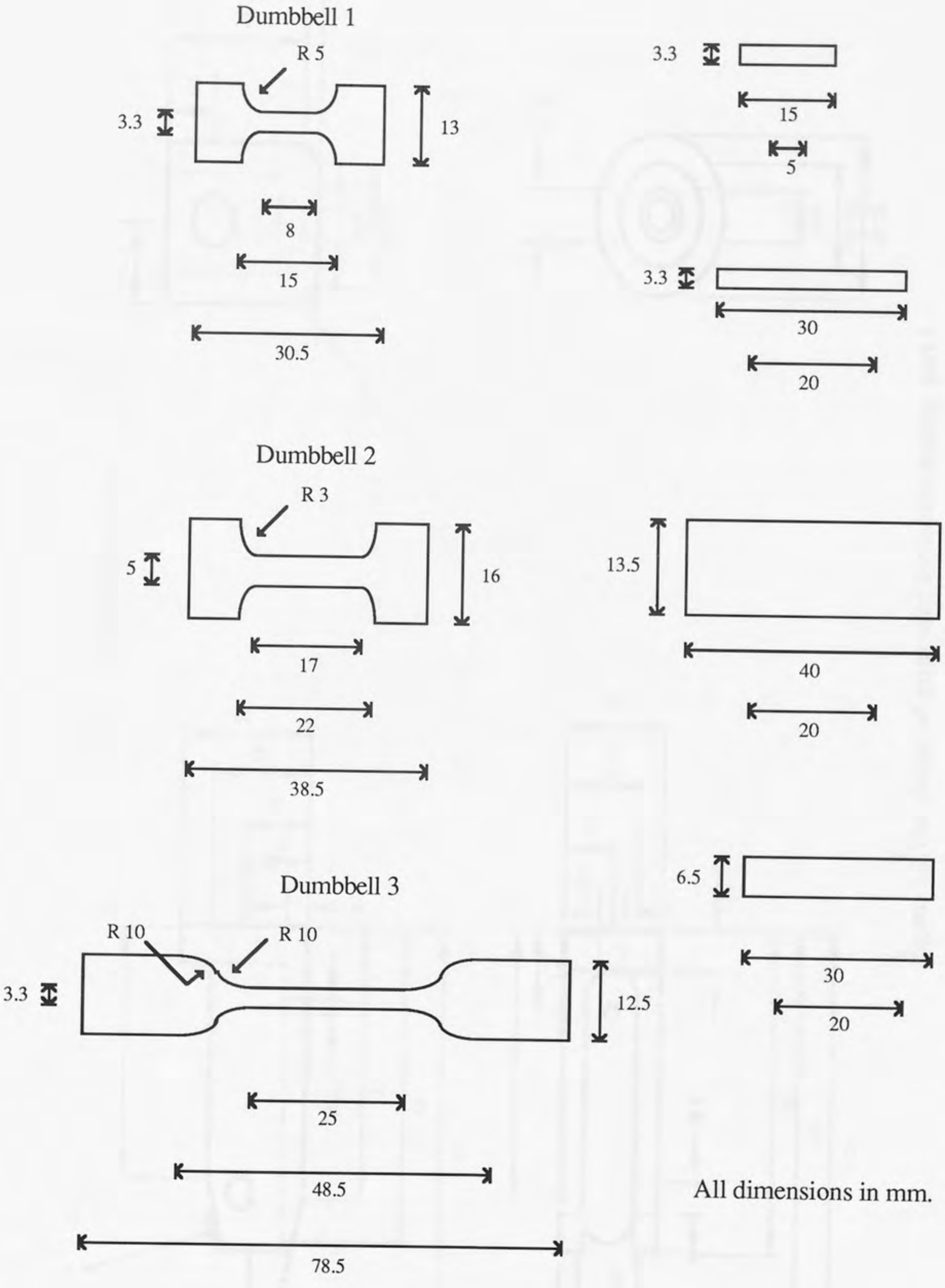
Table 3.1 Tensile properties of poly HEMA as determined by various authors

(In the one case where a dumbbell specimen was not used, this was because of size restrictions of the available material). Further disagreement over whether or not there is a need to keep such materials fully hydrated during testing is also apparent. Surprisingly, little reference is made as to how such fragile and slippery materials should be gripped, an important and often overlooked variable. Finally, a wide range of preparation techniques and slight compositional differences (for example the nature and amount of crosslinking agent) occur, even for this one simple hydrogel.

It is not the aim of this thesis to propose such standards, rather it is to highlight some of the difficulties associated with the testing of these unique materials. Furthermore, by means of some limited tests, it is hoped to be able to place these factors on a scale of relative importance, and by this means introduce some order into what at times, can be a somewhat confusing situation. In addition the development of a suitable methodology to determine the tensile strength of these polymers will be of particular value in future work on hydrogels within the Speciality Materials group at Aston.

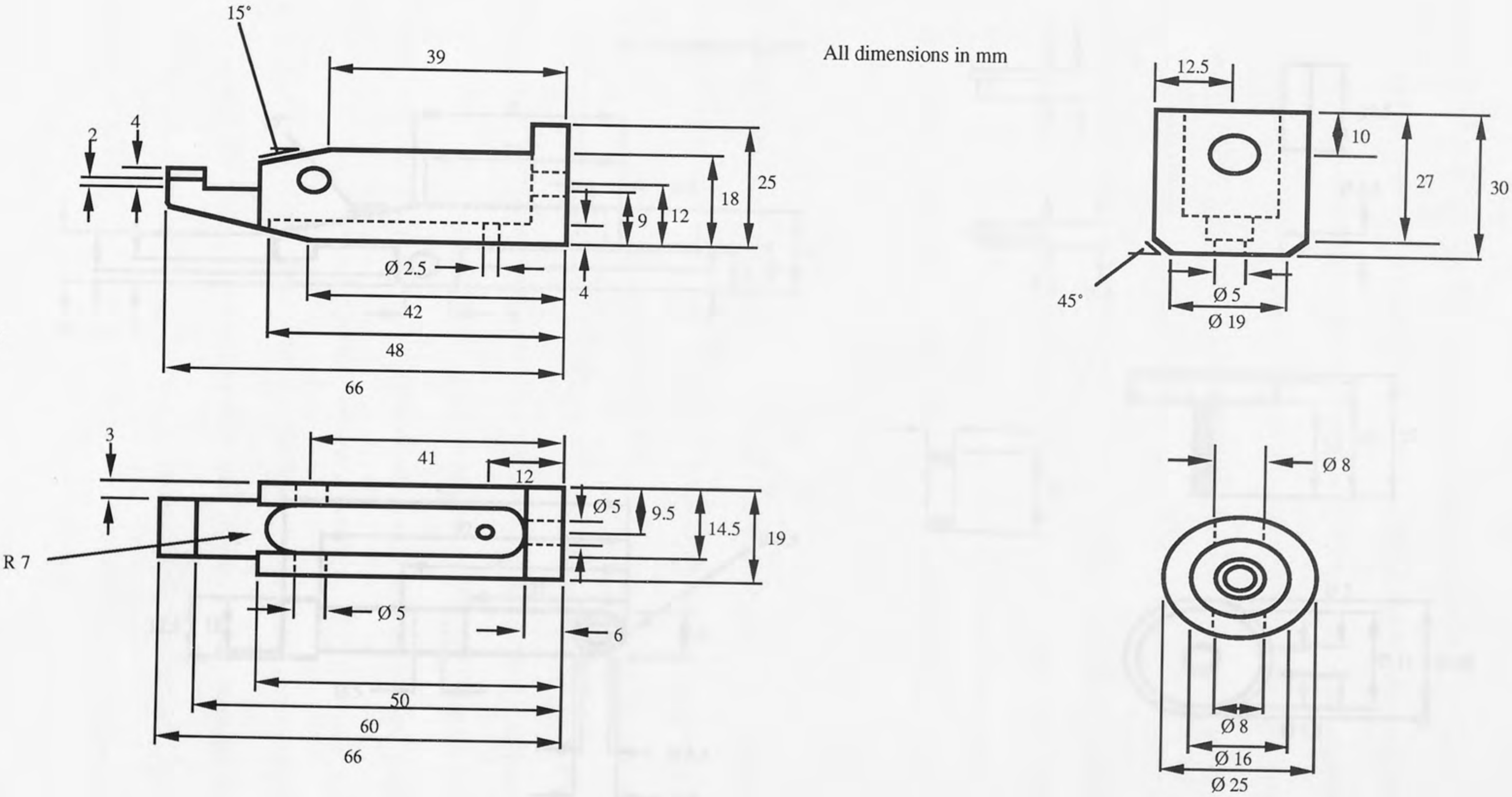
3.2 Methodology

Membranes of poly HEMA were prepared by polymerisation of the monomer mix between two glass plates, as has been described previously. The HEMA membranes were then tested in uniaxial tension using variety of strain rates and sample geometries. Figure 3.1 illustrates some of the various sample configurations used. Tensile testing was carried for the most part using an Hounsfield HK 10KN universal testing machine coupled to an IBM P.C. Some of the early work was performed on an old Instron 1085 machine. In this case, Instron grips operated by means of compressed air were used. The majority of the work was done using some lighter weight grips that were custom built by Hounsfield to our own



All dimensions in mm.

Figure 3.1 Specimen configurations used for tensile testing



All dimensions in mm

Figure 3.2 The design of grips used for tensile testing: part 1

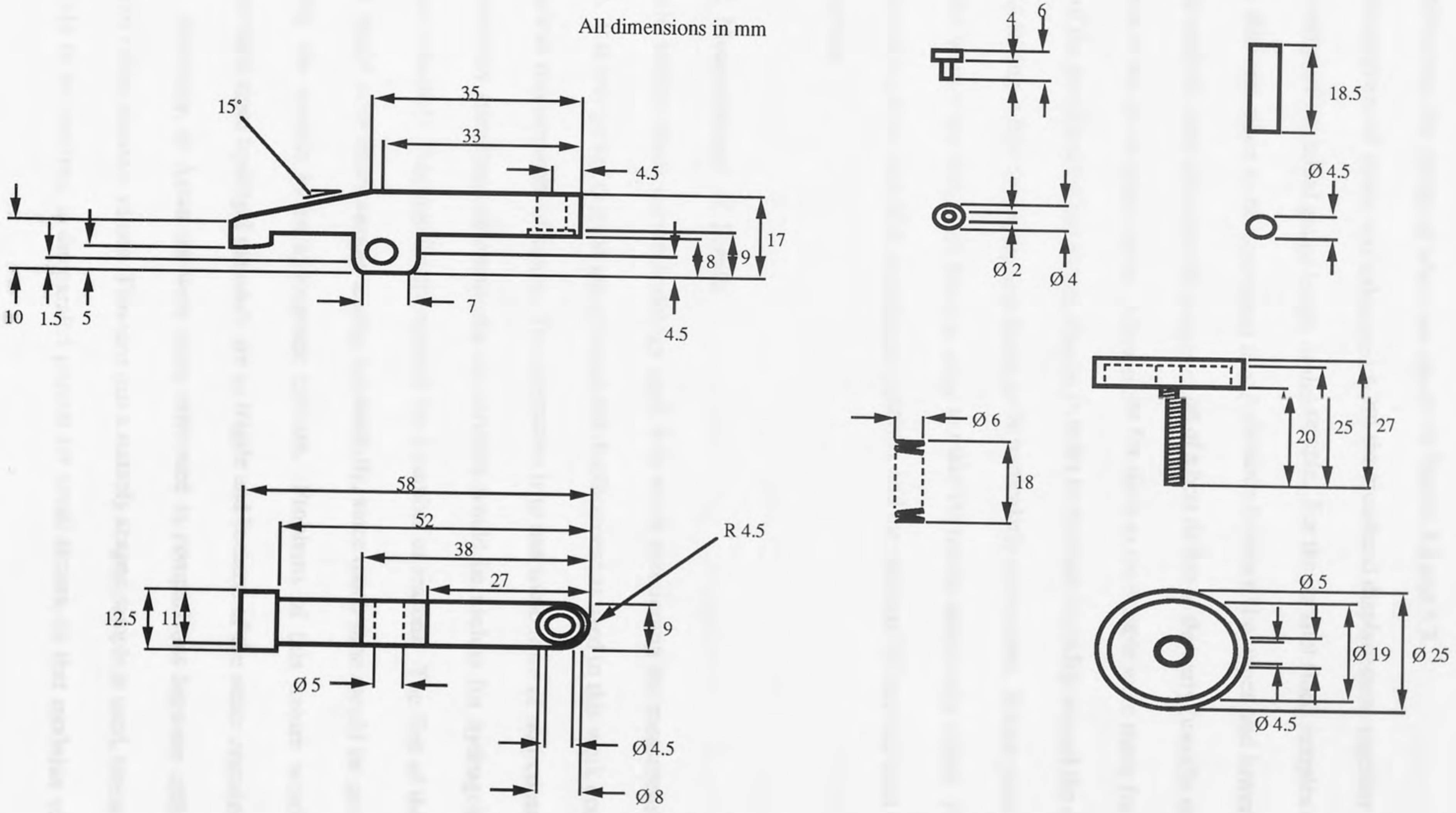

All dimensions in mm

Figure 3.3 The design of grips used for tensile testing: part 2 specifications, the design of which are shown in figures 3.2 and 3.3.

Measurement of strain was calculated from the crosshead displacement together with a knowledge of the initial gauge length of the sample. For the parallel sided samples (figure 3.1), this was taken to be equivalent to the distance between the upper and lower grips. Initial modulii were calculated by construction of a best fit line to the early (usually straight) portion of the stress strain curve. Allowances for slack in the sample were made for in the case of the parallel sided test pieces. Finally in order to maintain humidity around the sample during testing, a fine mist spray was found to be particularly convenient. Where possible 10 samples were tested from each batch in order to make the results statistically viable. Figures are quoted together with 95% confidence intervals, and the students "t" test was used where appropriate.

3.2.1 Measurement of Strain

Whilst talking about the methodology used, it is worth mentioning the measurement of strain. It is recognised that the use of crosshead displacement as used in this work does not give a true measurement of strain. The alternative is to use some form of non-contacting extensometry (the more common clip on varieties would be useless for hydrogels, for obvious reasons). This was finally rejected for a number of reasons. The first of these is that it would slow down sample testing substantially, since much time would be spent on marking the sample in an appropriate fashion. Problems of this nature would be compounded since hydrogel materials are so fragile and because of the water contained in them. Secondly, at Aston we were more interested in comparisons between different materials rather absolute values. Provided that a suitably shaped sample is used, extensions are likely to be confined to the parallel portion for small strains, so that modulus values should not be greatly affected. It is only in terms of the actual elongation to break that errors are more likely to be significant, where at high values of strain it is inevitable that some extension of the tabbed region will occur and be included in the value of elongation to break. Raab and Janacek however, (80) have estimated that this type of error in their work on poly HEMA did not exceed 10%. The final reason for not making use of extensometry is that much of our work here is confined to samples of such a size that it would be impossible to use a non-contacting extensometer. Even for the specimen configuration finally chosen, it would only be possible to use such a system with a certain degree of modification because of its relatively small size.

3.3 Testing Conditions

3.3.1 Influence of Different Testing Machines

Since the work was performed on two different testing machines and using two different types of grips, it was first necessary to ascertain if there were any significant differences between the two. Results from a series of tests carried out on parallel sided samples are shown in Table 3.2. From this it will be seen that there are no major differences between samples tested on the different machines. Thus it is reasonable to conclude that the effect of changing the testing machine has had little influence on the results so obtained. Moreover, the manner in which the specimen is gripped also appears to be of relatively little significance to the results. The Hounsfield grips were the ones adopted by choice for several reasons: they were not only lighter than the corresponding Instron grips, (an advantage when dealing with small loads, as it improves the sensitivity of load measurement), they were also less cumbersome to operate, since the use of a gas cylinder was obviated. Finally they offered a more sensitive adjustment of pressure than the air pressure grips. The Instron grips were being operated at the limit of their of capability in that it required a certain amount of pressure in order for the grips to close fully - any more than this and there was a danger that the sample would become crushed. This was particularly the case for the thicker parallel sided samples. On the other hand, with the Hounsfield jaws, pressure could be adjusted with a large thumbscrew to an appropriate degree of 'bite'. In addition the Hounsfield grips had been designed with the short specimen configuration, that was finally adopted, in mind.

3.3.2 Influence of Specimen Geometry

Before any further work could be carried out, a suitable test piece design had to be selected, which should ideally have the basic dumbbell form. Three dumbbells were evaluated on three different materials, (in order that any differences could be attributed to geometry, rather than a material characteristic). The specification of the dumbbells used has already been given (figure 3.1). The materials tested were poly HEMA, polyethylene, and a hydrogel copolymer (NVP/CHexMA). These three materials were chosen because it was known that they exhibited very different stress/strain behaviours. This is shown schematically in Figure 3.4. As can be seen from this figure, the polythene sheet gives a very high elongation to break, and undergoes considerable necking, whereas poly HEMA extends rather in the manner of an elastomer, and the NVP/CHexMA material is somewhat brittle. The hydrogels were tested at a strain rate of 250% / min where possible, although the limitations of the Instron machine meant that a strain rate 200% / min had to be used for the larger dumbbell (dumbbell 3). A different batch of poly HEMA (HEMA 2) was later tested to confirm the results. Tests were carried out at room temperature ~ 21°C, and the hydrogel materials were kept moist by means of the atomiser described earlier. The

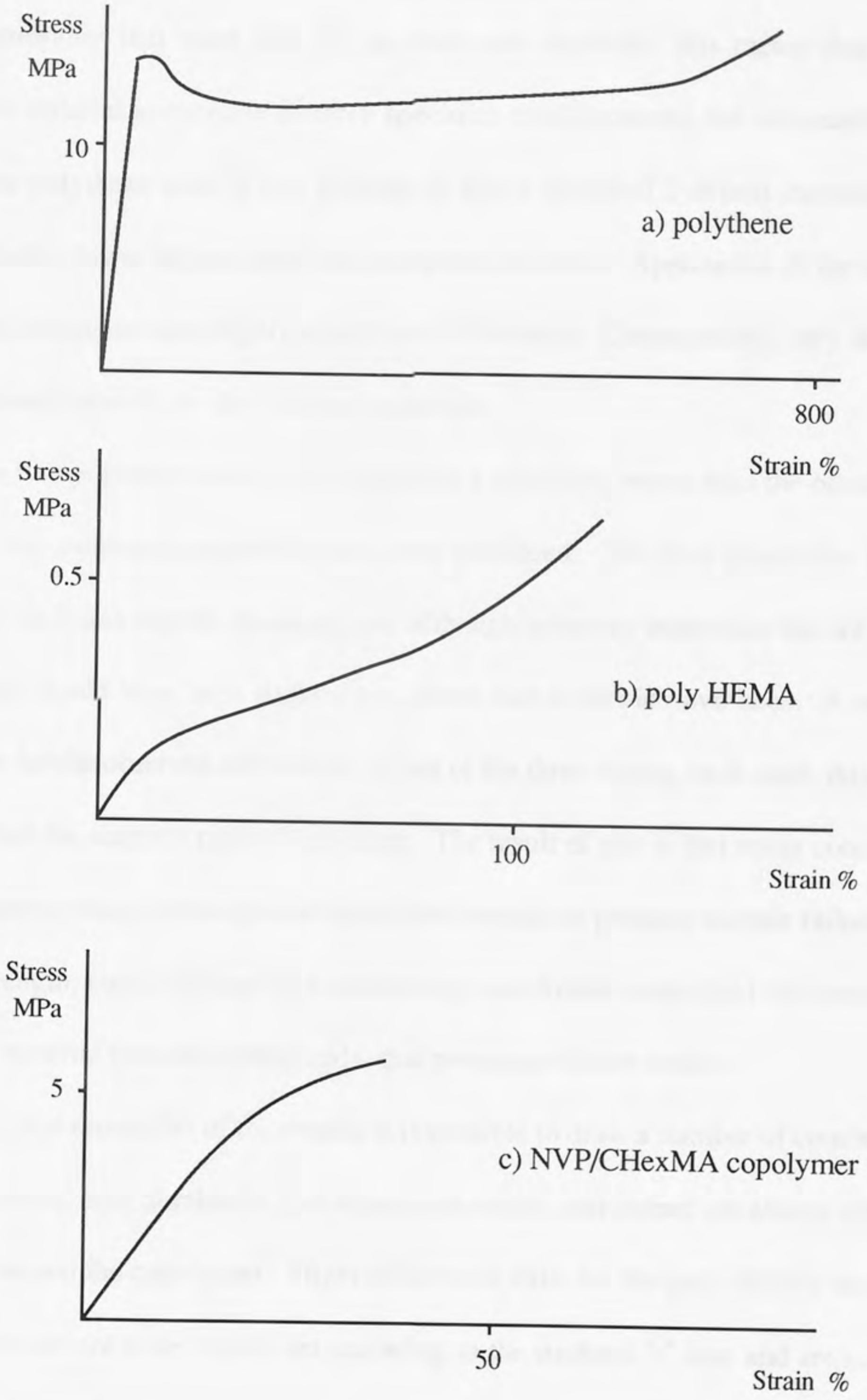


Figure 3.4 Schematic stress/strain curves for a) polythene b) an "elastomeric" hydrogel and c) a "brittle" hydrogel

polythene sheet was tested at a higher strain rate of 400% / min because of its anticipated higher elongation to break. Table 3.3 summarises the results obtained. Because of the size of the membranes that were cast for the hydrogel materials, this meant that there was insufficient material to evaluate all three specimen configurations, but fortunately from the work on the polythene sheet it was possible to reject dumbbell 2 almost immediately, as it produced both a lower failure stress and elongation to break. Application of the students "t" test showed that these were highly significant differences. Consequently, only dumbbells 1 and 3 were used to evaluate the hydrogel materials.

There are two possible reasons why dumbbell 2 should be worse than the others tested in respect of the measured properties that were produced. The first possibility is that the cutting tool itself was slightly damaged, and although a cursory inspection did not reveal any flaws, the die could have been slightly less sharp than it should have been. A more likely explanation for the observed differences, is that of the three cutting tools used, this particular dumbbell had the sharpest radii of curvature. The result of this is that stress concentrations may be present, which, although not significant enough to produce sample failures outside the gauge length, could still set up a sufficiently non-linear stress field (by restricting the flow of the material from the tabbed ends) that premature failure results.

Examining the remainder of the results, it is possible to draw a number of conclusions. In terms of strength, both dumbbells give equivalent results, and indeed are almost identical for the polythene and the copolymer. Slight differences exist for the poly HEMA samples, but these were found not to be significant according to the students "t" test, and are more likely due to the fact that these samples may have been taken from different membranes (see later). As a general rule, the shorter dumbbell (1), tended to give slightly higher elongations to

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Dimensions	Property	**Instron**	**Hounsfield**
Width 3.3 mm Gauge Length 5 mm	Stress / MPa	0.72 ± 0.11	0.55 ± 0.15
	Modulus / MPa	0.82 ± 0.03	0.68 ± 0.02
	Elongation / %	152 ± 32	117 ± 39
Width 3.3 mm Gauge Length 20 mm	Stress / MPa	0.53 ± 0.05	0.69 ± 0.07
	Modulus / MPa	0.98 ± 0.05	0.98 ± 0.11
	Elongation / %	78 ± 9	109 ± 6
Width 6.3 mm Gauge Length 20 mm	Stress / MPa	0.50 ± 0.05	0.54 ± 0.05
	Modulus / MPa	0.85 ± 0.03	0.85 ± 0.03
	Elongation / %	95 ± 10	94 ± 9
Width 13.5 mm Gauge Length 20mm	Stress / MPa	0.38 ± 0.05	0.53 ± 0.10
	Modulus / MPa	0.69 ± 0.04	0.87 ± 0.01
	Elongation / %	82 ± 13	90 ± 20

Table 3.2 Influence of testing machine and effect of size for parallel sided samples

Material	Property	**Dumbbell 1** (gl 8 mm)	**Dumbbell 2** (gl 17 mm)	**Dumbbell 3** (gl 25 mm)
Polythene Sheet	Stress / MPa	19.0 ± 0.75	17.0 ± 0.87	19.3 ± 0.67
	Elongation / %	733 ± 34	596 ± 31	660 ± 24
NVP/CHexMa	Stress / MPa	7.6 ± 0.6		8.0 ± 0.8
	Modulus / MPa	90.1 ± 3.8		131.6 ± 7.7
	Elongation / %	41 ± 36		26 ± 7
Poly HEMA (Batch 1: Instron)	Stress / MPa	0.62 ± 0.04		0.51 ± 0.09
	Modulus / MPa	0.61 ± 0.03		0.65 ± 0.04
	Elongation / %	147 ± 10		106 ± 23
Poly HEMA (Batch 2) (Hounsfield)	Stress / MPa	0.55 ± 0.05		0.61 ± 0.05
	Modulus / MPa	0.57 ± 0.01		0.69 ± 0.04
	Elongation / %	131 ± 12		128 ± 15

Table 3.3 The effect of different test piece geometries on the tensile properties of various materials

break, although this is not conclusive for the poly HEMA samples. It is very probable that these differences are caused by the effect of the geometry, but it also likely that had extensometry been used to measure strain, a much less significant difference would have been observed, for the reasons outlined earlier. Differences obtained for the initial moduli are less clear cut, but appear to follow a similar trend to the elongations with, in this case the longer gauge length giving an apparently stiffer material. Again part of the explanation for this could lie in the technique used to measure strain.

Thus despite some reservations about the values of modulus, dumbbell 1 was adopted as a standard for this work. It appears to give identical strength values as the larger dumbbell, and in addition gives a consistently higher value of elongation to break. Part of the reason for its final choice however, lies in that its smaller size makes it more convenient for the size of membrane usually made in these labs, whilst still leaving the option for extensometry if desired.

3.3.3 Influence of Humidity

Having chosen a suitable test piece, and machine, all that remained was to derive the testing conditions. Since hydrogels are elastomeric in nature, it seemed appropriate to use a fairly fast strain rate. A strain rate of approximately 250% / min was found adequate for this combination of material and geometry, in that samples failed in a reasonable length of time (round about 2 minutes) and it also seemed fast enough to prevent any significant dehydration. The effects of dehydration (at this particular strain rate) were studied for samples that were continuously sprayed with the mister described earlier, and some that were not wetted at all during the test, but had remained in water until immediately before the test was started. Experiments with samples completely immersed in water were not conducted because of the extra complications involved.

	Tensile Strength / MPa	Initial Modulus / MPa	Elongation to Break / %
Poly HEMA (atomised) (H 3)	0.53 ± 0.06	0.66 ± 0.02	118 ± 17
Poly HEMA (not atomised)	0.61 ± 0.05	0.64 ± 0.03	144 ± 14

Table 3.4 Effect of atomisation (humidity) on the tensile properties of poly HEMA

From Table 3.4 it can be seen that there are slight differences between the two batches, the atomised samples appearing to be slightly stronger and more elastic than those of the initially wet samples. Application of the students "t" test, however, showed that none of these differences were statistically significant. Not surprisingly the initial moduli are almost identical, since this was determined before any significant dehydration could occur. As dehydration occurs, hydrogel materials in general become stiffer, stronger, and more brittle. Although the atomised samples are rather weaker, they are also less elastic which suggests that no embrittlement is happening within the time scale of the test. Also examination of the stress strain curves showed that the two batches were almost identical in behaviour, which again tends to confirm that for this set of conditions no significant dehydration takes place. It is important to note that the use of the atomiser was not rejected at this point since materials other than poly HEMA may well be more sensitive to the effects of dehydration. The results also tend to confirm that provided a suitably fast strain rate is used, the elaboration needed to conduct such tests fully immersed in fluid is not strictly necessary, provided only comparative data is being sought.

3.3.4 Strain Rate Sensitivity

The effect of strain rate is shown in figure 3.5 and table 3.5 for dumbbell samples of the geometry adopted, and using our technique of atomisation to maintain humidity round the samples during testing. The results show that within experimental error, there is a small increase in strength the faster the samples are tested, which is typical of materials in general. The trend in terms of elongation to break is almost identical. It is difficult to draw any definite conclusions about the effect of strain rate on modulus, however because of the relatively small number of strain rates that were tested, (The limitations of the Instron machine was the reason behind this) and because of the scatter in the data. Thus the tensile modulus appears to be almost independent of strain rate under these circumstances.

The influence of temperature on this material was not studied here, due to the extra complications that would be necessary - specifically the need for a temperature controlled water bath in which to immerse the samples. Suffice it to say, that the temperature of the test will have a significant bearing on the results obtained. Predictions as to the influence of temperature, can be made for instance, on the basis of modulus changes found by various workers who have studied the dynamic mechanical response of these polymers.(78, 79)

From what has already been said, the complex nature of the testing protocol should now be apparent. Most of the variables that have been discussed so far, are interrelated in some fashion, and hence a necessary degree of judgement had to be exercised in the choice of such variables. This was based on a number of years experience that we have had at Aston in making and testing these interesting materials.

3.3.5 Influence of Specimen Size

A variety of different geometries were investigated - the effect of different dumbbell configurations has already been discussed. There are occasions when it may not be possible to use a standard dumbbell - a good case in point is the soft contact lens, where size

Strain Rate / % / min	Tensile Strength / MPa	Initial Modulus / MPa	Elongation to Break / %
62.5	0.52 ± 0.05	0.65 ± 0.02	117 ± 15
125	0.46 ± 0.07	0.64 ± 0.02	97 ± 19
250	0.55 ± 0.06	0.63 ± 0.03	122 ± 16
625	0.52 ± 0.04	0.63 ± 0.02	118 ± 14
1250	0.68 ± 0.08	0.66 ± 0.03	154 ± 22
2500	0.68 ± 0.12	0.66 ± 0.02	156 ± 39

Table 3.5 Influence of strain rate on the tensile properties of poly HEMA

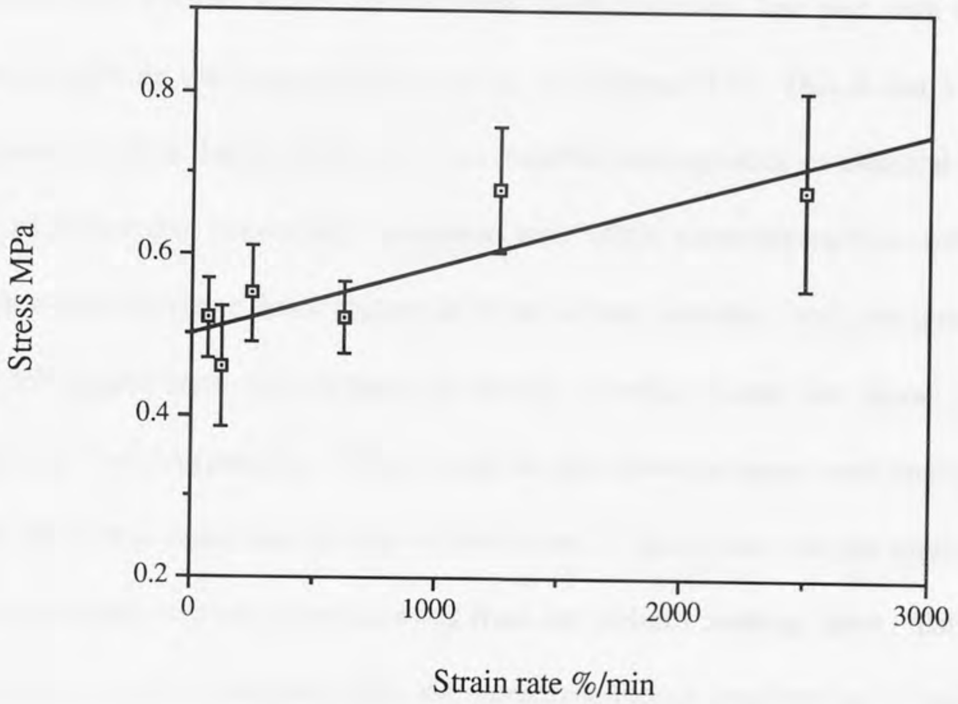


Figure 3.5 Influence of strain rate on the failure stress of a simple hydrogel polymer

restrictions make this impossible. Thus this section of the work was performed firstly to see if the results from the dumbbell specimen matched those of a similar sized parallel sided sample. Secondly it was necessary to know if the actual sample size has any significant affect on the results so obtained. The results for this section of the work have been shown earlier (Table 3.2). An interesting trend was observed for the samples tested on the Instron machine. When the results from the dumbbell shaped specimens are included, the effect of specimen volume becomes apparent. (for the dumbbell samples, volume was taken to be the dimensions of the parallel portion of the design, and an average thickness for that particular batch of samples was taken. Similarly for the parallel sided samples, where in this case, the volume taken was assumed to be the whole of the ungripped region).

A plot of log volume verses failure stress gives a straight line plot with the smallest volume producing the highest failure stress. (see figure 3.6) This is not a completely unexpected result in that it can be predicted from Weibull statistics - a classical "weak link" theory of failure that is normally associated with brittle materials such as ceramics. It is perhaps a little surprising that it appears to relate to these materials, until one remembers that in the dehydrated state, the polymer, or xerogel, is rather brittle and glassy - somewhat analogous to PMMA (perspex). Thus it could be that flaws are being unwittingly introduced into the polymer at some stage during its fabrication. A likely time that this might occur is as the newly formed polymer is peeled away from the melinex backing sheet. This procedure is normally carried immediately after the membrane/mould combination comes out of the oven, and whilst the polymer remains hot enough to be in a soft rubbery state. Experience has indeed shown that if this step is performed too slowly, the polymer becomes brittle and cracks easily. This further emphasises the need for care at this stage of polymer preparation.

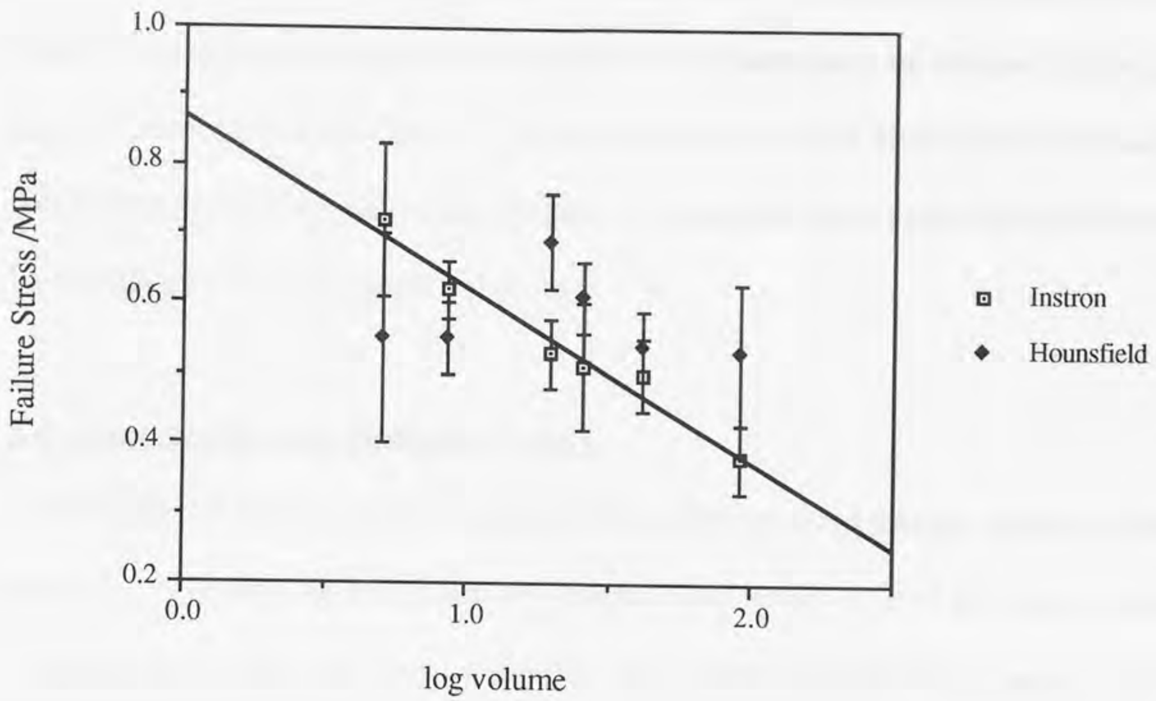


Figure 3.6 Log volume versus failure stress for poly HEMA

This downward trend of failure stress with increasing volume is not so evident for the poly HEMA tested at a later date using the newer Hounsfield machine, unless one discounts the two results for the smallest volume. It is possible that these particular sets of results were tested from a different membrane that may not have had exactly the same composition as previously, and hence do not fit the trend exactly. In addition for the work done on the Hounsfield machine a smaller number of samples were tested (five), making the results less statistically valid. As it may have been noticed previously, there is generally quite a strong correlation between the tensile strength and the elongation to break, so that as the volume increasing, the sample tends to become more brittle. Again this is consistent with Weibull statistics. From the results obtained for strength and elongation, it is worth mentioning that the smallest geometry tended to produce an apparently wider scatter in results. The explanation for this lies in the fact that jaw breaks were not discounted from sets of results. Thus it is possible that this particular geometry is not particularly satisfactory in that there may be stress concentration effects. These could extend into the whole body of the sample (because of its relatively short gauge length). Consequently these particular results should be considered as a 'lower bound' value only.

3.4 Composition and Monomer Purity

From table 3.1 we have seen that poly HEMA can be produced that has slightly different properties, depending on how it has been prepared and tested. One of the most important compositional factors that can be varied is the choice of crosslinking agent, and the concentration in which it is added. Raab and Janacek (80), have already shown the effect of increasing the crosslink content on the resultant properties of the gels produced. The choice of which crosslinking agent is used, is generally governed by experience, in particular a thorough understanding of the polymerisation behaviour of the system is necessary. A brief study of the effects that two different crosslinking agents (both of which have been used commercially used in hydrogel polymers) have on the mechanical properties of these polymers was made, in order to demonstrate the importance of polymer composition.

Two membranes of poly HEMA were prepared in the usual manner (see chapter 2), one of which was made using 1 wt % of EGDM, and another that contained 1wt % of AllylMA. In both cases AIBN (0.5wt %) was used as the initiating species. Tensile tests were performed, the results of which are given in table 3.6. These results are particularly interesting, and one of the first things that will be noticed is that although the two polymers have broadly the same tensile failure strength, there are considerable differences in terms of the modulus and elongation to break values. These are considered to be significant in terms of the students "t" test, even though only 8 samples were tested per batch, in this case. (The results from the "t" test comparisons are shown in table 3.7) What is the reason behind these differences ? One fairly obvious explanation is that the concentration of crosslinking agent was different in each case. Generally speaking, as the crosslink density is increased, then the polymer tends to become stronger, more brittle, and less elastic, which certainly appears to be the case here. It is possible (because of the difficulties associated with weighing small volumes of liquid which are added in a dropwise manner, as is the case here) that there may have been slight concentration differences introduced. Assuming that this was not the case however, means that there must be another explanation. In terms of the actual molar concentration, there is in fact (again assuming no weighing inaccuracies) a higher concentration of crosslinker in the membrane made using AllylMA, since its formula weight is 126.2 g/mol compared to 198.2 g/mol for the EGDM. It is therefore unlikely that the differences that were shown can be explained solely on the basis of changes in concentration. The much more likely explanation is that one is a more effective crosslinking agent (when it is polymerised with HEMA) than the other, and this can be accounted for in terms of the different reactivity ratios that these particular crosslinking agents have with

Composition	Tensile Strength / MPa	Initial Modulus / MPa	Elongation to Break / %
HEMA 1 wt % EGDM (H 1)	0.87 ± 0.30	0.65 ± 0.03	172 ± 53
HEMA 1 wt % AllylMA (H 2)	0.75 ± 0.07	0.49 ± 0.03	260 ± 24

Table 3.6 The Influence of the choice of crosslinking agent on the tensile properties of poly HEMA

HEMA. Essentially if the two monomers being polymerised are equally reactive *i.e.* the reactivity ratio of each monomer is 1, then there is an equal probability that in the growing polymer chain, either reacting species will be added next. In this case since there is only 1 % of the crosslinker, then on average the polymer formed will consist of 1 crosslink for every 99 units of HEMA, and these crosslinks will be randomly distributed throughout the polymer. If as is more usually the case, the two monomers are different in terms of their reactivity, then it is probable that the more reactive species will react with itself in preference to the other monomer with the result that the polymer will become blocky, with long sequences of one type of reactant linked together. In the extreme case, this results in compound where almost none of the unreactive monomer is used in the early part of the polymerisation, and only reacts when the concentration of the more reactive species is so low that it is able to react with itself. Again translating this to the case of a lightly crosslinked polymer, although the same overall number of crosslinks would be formed, they would no longer be distributed evenly throughout the polymer.

This hypothesis does in fact fit the observed results quite well, in that AllylMA is known to have a lower reactivity ratio than EGDM. (AllylMA is sometimes used as a crosslinking agent in vinyl pyrrolidone based contact lenses because it is felt to be more compatible with the extreme low reactivity of the monomer NVP for this reason). This means that because of the difference in reactivity, some of the crosslinking agent may remain unreacted until right at the end of the polymerisation, and if the reaction does not go to complete conversion some of it may not react at all. On subsequent hydration of the gel, the unreacted monomers are leached out, and the result would be a polymer with a lower overall crosslink density, as the results from the tensile tests seem to indicate.

A further very interesting point to arise from these results is that in the case of the poly

HEMA made using 1 wt % AllylMA (H2), the resultant membrane gives significantly less variation in its properties than its EGDM counterpart. Again part of the reason for this may be because of differences in the reactivity ratios. Although there is an overall lower crosslink density for the AllylMA crosslinked material, it may well be that, those crosslinks that are present, are evenly spaced throughout the polymer, and vice versa for the other polymer. The effect of having an uneven crosslink distribution could therefore account for the wide range of tensile strengths (low 0.50 MPa, high 1.48 MPa) and elongation to break values that are observed.

Yet another important point to arise from this set of results, is that the properties that are produced seem to depend very much on how well the polymer is made, and in particular the monomer purity is of great importance. In table 3.7 "t" tests comparisons are also made between this particular batch of HEMA/EGDM (which was in fact made by another member of the group as a control experiment) and a typical batch of HEMA/EGDM (H3). Results for the tensile tests for this particular batch have already been given in Table 3.4. These

Comparison	t value	Number of Degrees of Freedom	Inference
H1 to H2 (Stress)	0.91	14	Difference not Established (<90%)
H1 to H2 (Modulus)	9.97	14	Highly Significant Diff. (>99.9%)
H2 to H1 (Elongation)	3.59	14	Significant Difference (>99%)
H1 to H3 (Stress)	3.00	17	Significant Difference (>99%)
H1 to H3 (Elongation)	2.57	17	Probable Difference (>95%)

Table 3.7 Students "t" test comparisons for poly HEMA membranes

results show that there significant differences in terms of failure stress and elongation, though the values of modulus are almost identical. The most likely explanation for this is that the monomer used in batch H3 is of lower purity than that in H1, and consequently a shorter chain length has been produced in this material, making it weaker and less extensible.

3.5 Discussion

In this chapter we have seen that the mechanical properties quoted for one particular hydrogel vary quite widely, a brief literature survey showing that there was no universally accepted manner in which to test these materials. An investigation into the effect some of these variables have on the mechanical properties of the polymer was then made. A number of important conclusions can be made from this study. Firstly, the most important factor influencing the properties is the actual preparation of the polymer, in particular the degree of monomer purity is of critical importance, otherwise a poor network will be produced.

Also of great significance is the choice of crosslinker used. This can have a profound effect on the resultant polymer because of the different reactivities they have with the bulk monomer. By controlling this factor it may be possible to "design" hydrogel materials where, by the appropriate choice of comonomers, a particular sequence distribution can be formed in the polymer, which in turn may produce a hydrogel of improved, or unique properties.

Of the other variables looked at, perhaps the next most significant is that, in the time scale of a single test (depending on the strain rate), the influence of sample dehydration is quite minimal. This means that testing does not have to be carried out completely under water, although it is recommended that the humidity is kept as high as possible by some other interesting to note that smaller samples tended to be stronger. If the explanation of this is sought in terms of a "weakest link" theory such as the Weibull model, then this has implications for the preparation of the polymer. Possible sources of a flaw distribution could be 1) imperfect network formation, 2) porosity, or 3) careless removal from the mould. Of these the first is probably most likely, and 3 the least. It has already been shown that it is possible to produce a hydrogel with a low variation in properties by appropriate choice of monomers and their purity, and the fact that a size effect seems to be present, is itself a reflection on how perfect the network formation in this particular polymer is. The design of specimen used is also quite important, although the results tend to suggest that broadly similar results are obtained between parallel, and dumbbell shaped samples. (see also chapter 4) Of the cutting tools used, the die with the sharpest radii of curvature seemed to produce inferior results, as one might have expected.

In conclusion some of the variables associated with testing hydrogel materials have been examined, and a suitable test methodology has evolved that will enable such test results to to be more readily compared and understood.

Chapter 4
Tensile Testing of Soft Contact Lenses

4.1 Introduction

It is important for contact lens manufacturers to be able to obtain data on the properties of their products, in order to provide feedback on the manufacturing process. Currently this is done by measuring the equilibrium water content and swelling behaviour of the lens, although this is perhaps not the most sensitive of methods. If good reproducible mechanical property data can be provided, both on the lens materials and the finished lenses themselves, this may be of great assistance to the manufacturer. In addition the practitioner needs to be able to compare different lenses with one another in order to be able to prescribe the best for the patient, since no one patient has exactly the same requirements. This is becoming an even more important issue because of the vast range of different contact lens materials that are now on the market.

Although there are standards for the tensile testing of plastic film and sheet, *e.g.* BS 903, ASTM D698, there are no such standards for the tensile testing of soft contact lenses, or indeed hydrogels in general, if one considers them a class of materials in their own right. Even if such standards for hydrogels did exist, there is no reason to believe that such methods would be applicable to a soft contact lens in its "finished" form. In fact, this is very unlikely to be the case due to the geometry of a lens, and the different manufacturing processes that are used to make lenses.

One of the aims of this work was to develop a satisfactory method for testing contact lenses in tension, and then ultimately to compare the new method with tests on sheets of an identical chemical composition, in order to check its validity. Ideally such a test method should be fairly simple, relatively quick to perform, and allow good reproducibility between different laboratories. The choice of tensile testing enables data to be obtained about the strength, stiffness and elasticity of the lens. Because both the strength and elongation to break of a polymer are good indications of how perfect the polymer network is, these two properties may therefore be of some benefit in quality control. The stiffness or modulus of the lens is also one convenient way in which a contact lens practitioner can distinguish between lenses, particularly those having a similar equilibrium water content.

4.2 Development of a Technique for Testing Soft Contact Lenses in Tension

There are a number of problems associated with the mechanical testing of soft contact lenses. These can essentially be divided into two basic groups, group A, those associated with the material, and group B, those associated with the geometry of the lens itself. These are briefly summarised in the table 4.1 below, (though are not necessarily in order of importance).

Group A - Material.	**Group B - Geometry**
1 Gripping ? (jaw breaks !)	1 Small Size of Lens.
2 Dehydration ?	2 Curvature of Lens.
3 Strain Rate ?	3 Test Piece Geometry ? (parallel sided vs dumbbell)
4 Temperature ?	4 Dimensions ! (thickness varies across lens - true t ?)
5 Small Loads ! (approx 100g max)	5 No. of samples per lens ?
6 Specimen Preparation ! (Great care needed)	6 Sample to be taken from which part of lens ?

Table 4.1 Summary of the most important parameters that need to be considered in the development of a tensile testing methodology suitable for soft contact lenses

Most of the factors under group A have been dealt with in the previous chapter, although there were some minor differences which will be discussed later. Perhaps the most important factor in group B is the physical size of the lens. Most standard lenses have a diameter of somewhere between 12 and 14 mm. Because of their circular shape, the final test piece will clearly be smaller than this. Since the thickness of the lens is determined by the manufacturer and is therefore not a variable that can be altered, and that the width of any test piece can only be varied between the predefined limit of the diameter of the lens, this means that a testing machine capable of measuring small forces accurately, is necessary. (Typically for the work here loads of approximately 100 g were needed to break the sample). In an ideal situation, a miniature dumbbell shaped cutting tool would be used to prepare specimens from a lens, as per B.S.903 for example. This does however have its limitations. For example, i) The cutting tool would need to be small, and would therefore be expensive (and difficult) to produce on a one off basis. ii) The dumbbell shape would almost certainly only allow one sample from each lens to be cut. This in turn means that more lenses would have to be tested in order to obtain any statistically competent data. In addition to this, any variations within an individual lens would not become apparent. iii) The curvature of the lens means that each individual sample must be cut from the same area of the lens each time - presumably the centre. This is frequently the area where the greatest changes in dimensions occur (*i.e.* the point of maximum curvature), although this does depend on the design of the particular lens being tested.

On the other hand, the advantages of using a dumbbell are that it would have a known fixed gauge length and width, and that it would permit a more uniform stress distribution in the sample, giving a "truer" reflection of the actual tensile properties. Potential stress concentrations at the gripped ends would be eliminated, thus producing fewer jaw breaks than might be the case for other sample configurations.

An alternative approach is to try and obtain three parallel sided samples from each lens as shown below in figure 4.1 By using three samples from each lens this would mean that fewer lenses would need to be tested for statistical purposes. Potential disadvantages include the possibility of jaw breakages, and the difficulty of controlling the gauge length of the sample.

Figure 4.1 Two alternative specimen configurations for samples cut from a contact lens

A brief study was undertaken to compare the two methods described in the above section. For the first case, *i.e.* those using a "dogbone" shaped test piece, the standard dumbbell cutter adopted for the hydrogel samples was found to be just small enough to go across the sample, although the tabbed ends were severely reduced in size. (see figures 3.1 and 4.1) This gave the test piece a nominal gauge length of 8 mm and a width of 3.3 mm. For the lenses used in this study, which had a diameter of 14 mm, there was just sufficient material to grip the sample at the flared ends, provided that the lens was cut carefully. Tensile tests were then carried out at a strain rate of 200 % / min, and at ambient temperature. Occasional spraying with a fine mister was used to try and minimize the effects of dehydration. Initial modulus, failure stress and elongation to break were recorded, the values of strain being taken directly from the crosshead displacement.

A slightly different set-up needed to be used for the parallel sided samples. The size of the lens meant that the gauge length had to be small-5 mm was adopted as the standard. Samples could be cut using the size of dumbbell given in figure 3.1 (dumbbell 3), where only the parallel sided portion was used. This resulted in test pieces of an identical width to those in the case already described above. After some earlier work on this method, it was found necessary to make use of a polyethylene template, which was cut using another cutting tool (dumbbell 2) which gave samples a width of exactly 5 mm. This was useful for two main reasons. Firstly it meant easier transfer of the specimen to the jaws of the machine, the surface tension of any excess water holding the sample in place whilst it was being located. Secondly, and very importantly, the gauge length of the sample was then also well defined, becoming the same as the width of the polyethylene template. Once in position, the template was then snipped in two places and the test could continue. Plates 1-4 should make the testing procedure clear. Because the grips were only rubberised on one face, the inclusion of the sheet also acted as a form of cushioning, which was felt would reduce the likelihood of jaw breakages. Testing was carried out using the same conditions as in the first case, *i.e.* a strain rate of 200 % / min, room temperature, *etc*. The lenses used in this study had a diameter of 14 mm and a power of -3.25, and the results from the study on this set of lenses are shown in table 4.2.

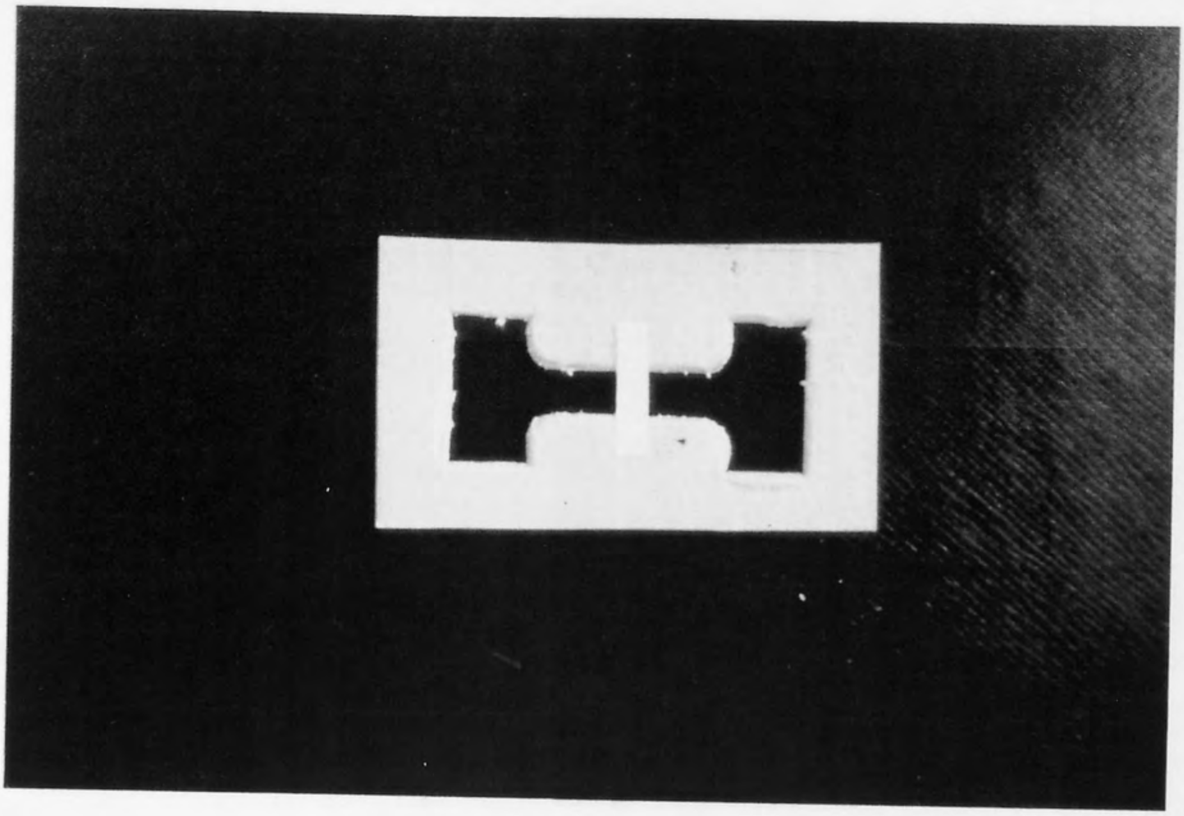


Plate 1 Tensile testing of contact lenses., Stage 1: place sample over template...

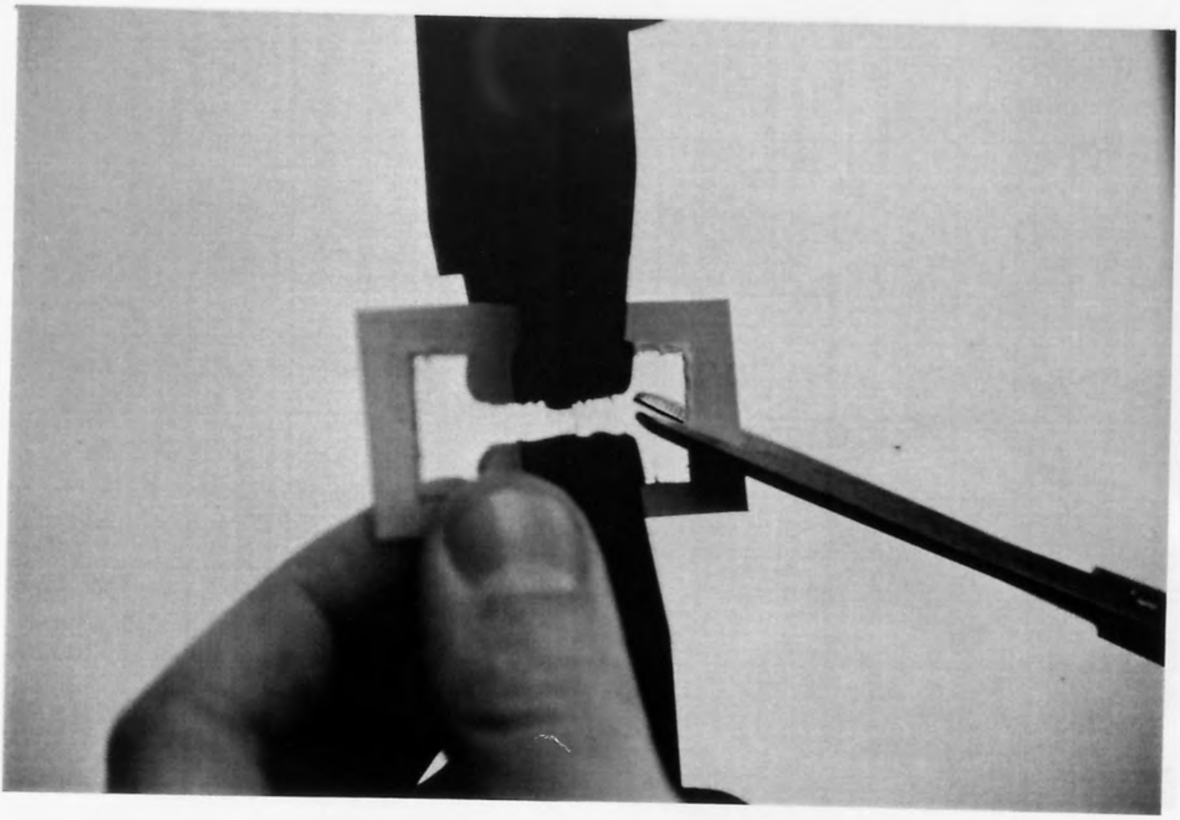


Plate 2 Tensile testing of contact lenses, Stage 2: carefully cut template...

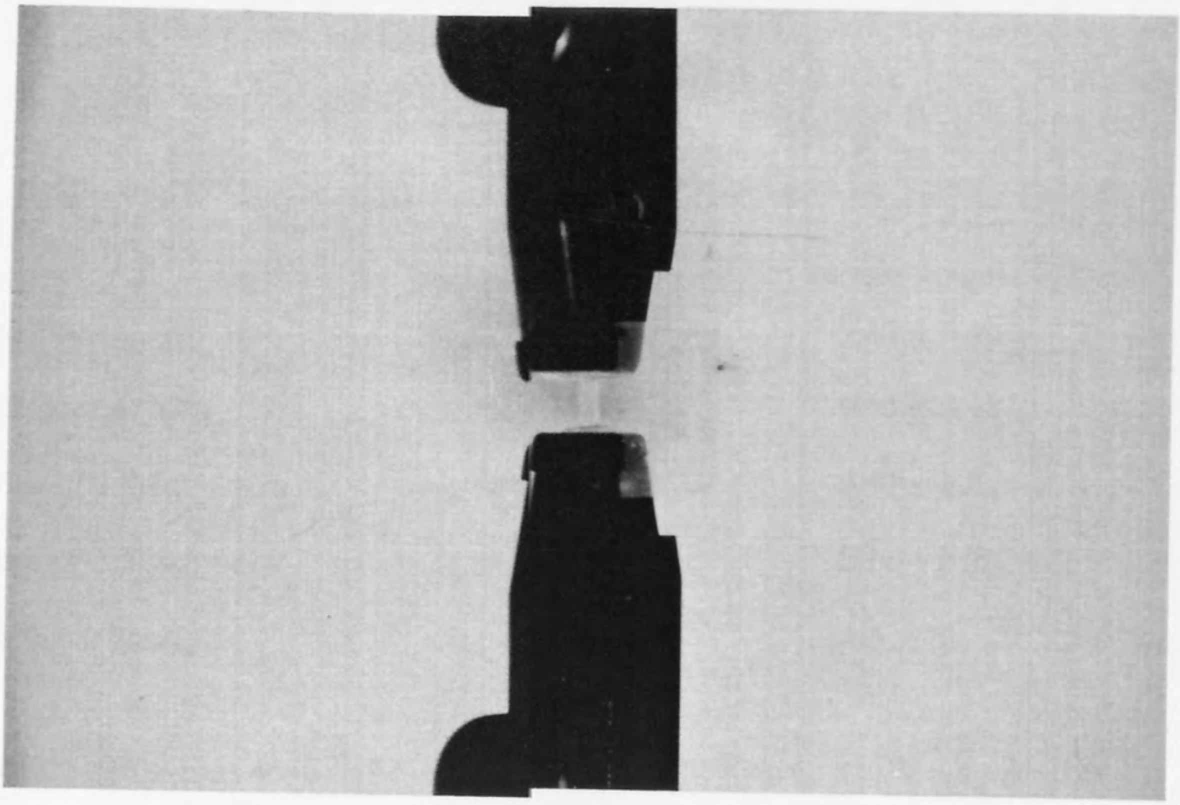


Plate 3 Tensile testing of contact lenses, Stage 3: commence testing...

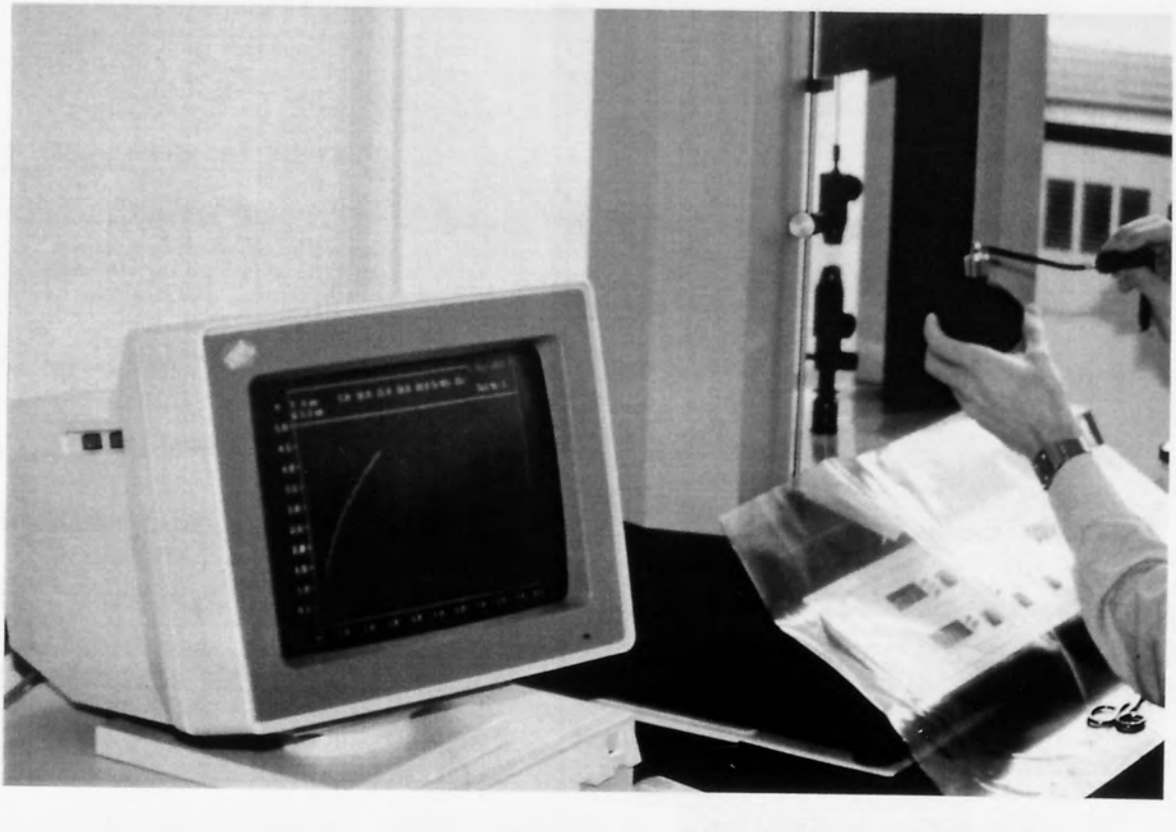


Plate 4 Tensile testing of contact lenses, Stage 4: maintain humidity around sample.

	(Column A) Dumbbell Samples	Parallel Samples
Failure Stress / MPa	1.13 ± 0.21	1.11 ± 0.19
Initial Modulus / MPa	0.40 ± 0.04	0.55 ± 0.12
Modulus (100 % ext) / MPa	0.32 ± 0.03	0.37 ± 0.05
Modulus (200 % ext) /MPa	0.29 ± 0.03	0.31 ± 0.05
Elongation to Break / %	351 ± 35	345 ± 28

Table 4.2 Comparison of two different methods for determining the tensile properties of contact lenses

N.B. Values quoted are means with associated 95 % confidence intervals, where C.I.'s are given by C.I. = t s / √n, where s is the standard deviation of the mean, and n is the number of samples. t is found from tables for n-1 degrees of freedom

4.2.1 Discussion of Methods

It will be apparent from table 4.2 that the two methods appear to give almost identical results in almost all respects, which is very encouraging, although one must qualify the following comments by saying that the sample size was relatively small (nine samples of each type were tested). It was noted that during testing, that many of the parallel sided samples failed in the gripped region (these were not discounted from the statistics), whereas none of the dumbbell samples did. Despite this, the similarity in failure stresses tends to suggest that stress concentrations have been minimized by the use of the polyethylene template. Similarly, the elongation to breaks of the two samples are not significantly different. This means that the use of the template to set the initial gauge length has also probably been successful. There is however one small area of concern, in that the initial modulus for the parallel sided samples has rather large error limits. This deserves some further investigation. Again during the testing, it was noticed that the behaviour of the centre lens pieces from the parallel sided batch, was slightly different from those cut from the outside of the lens, in that those from the centre appeared to have a lower stiffness. Table 4.3 compares these two groups.

	(Column B) Centre Pieces	Edge Pieces
Failure Stress / MPa	0.85 ± 0.60	1.24 ± 0.12
Initial Modulus / MPa	0.38 ± 0.12	0.63 ± 0.04
Modulus (100 % ext) / MPa	0.28 ± 0.06	0.42 ± 0.02
Modulus (200 % ext) /MPa	0.23 ± 0.06	0.35 ± 0.02
Elongation to Break / %	338 ± 122	348 ± 30

Table 4.3 Comparison between centre and edge samples cut from the same lens

It is then quite revealing to compare the three parallel sided samples cut from the centre of the lens (column B) with those of the dumbbell shaped batch, shown in column A in table 4.2 (which all came from the centre of the lens by necessity). In terms of modulus it is clear that the figures produced are almost identical, and it is now reasonable to assume that the position in the lens from which the sample is cut is having an influence on the measured properties. Further comparisons between column A and B also show that the elongation to break is similar in each case. The reason why there is such a large error band here is that only 3 samples were tested, and the confidence limits therefore reflect this lack of certainty in terms of a larger error limit. Similarly it is not possible to say with any degree of certainty, whether or not there is a difference in terms of failure stress between these two batches, for the same reasons. The explanation for the observed difference between modulus values from the centre and edge of the lens, lies with the determination of lens thickness, and this is discussed in the next section.

4.2.2 Measurement of Lens Thickness

The initial testing (chapter 3) was performed on hydrogel membranes, which, because of their mode of manufacture were generally of a fairly uniform thickness. This made the determination of the individual sample thicknesses relatively straightforward. This was not the case for the contact lens samples, as will shortly be seen.

Because of the nature of hydrogel materials, being as they are, soft and often fragile, particularly in the form of thin membranes, care needs to be taken when measuring the material's thickness. A dial gauge was used which had faces of approximately 5 - 6 mm in diameter. This had the advantage that, because it was measuring over a relatively large surface area, the contact pressure was lessened, making errors due to indentation less likely to occur, and meaning that the surface would not so easily be damaged or punctured as might otherwise be the case.

In actual fact this dial gauge was also used (erroneously) for the measurement of the thickness of the contact lens samples. It was not until a number of lenses had been tested, that it was realised that there was any problem. The work that was performed on the lenses that were used in the handling trial (see chapter 5) illustrated that although the specified power of the lens had no real discernible effect on the measured properties of the lens, those samples (lenses) that had a low centre thickness (say 0.03 - 0.06 mm) were giving a larger than expected spread of results in terms of their values of modulus. It now seems certain that a combination of lens design and choice of measuring instrument, led to the fact that the piece from each lens, was often thinner than the actual reading that was recorded and used in the calculation for stress. In the more severe cases, this meant that the test on the centre pieces produced an "effective" value of modulus that was roughly half that of the edge pieces cut from the same lens. To illustrate this, table 4.4 gives the results for two individual lenses of different types which are shown together with the "as measured thicknesses" and the manufacturers quoted centre thickness.

Quoted centre thickness / mm	Measured thickness / mm	Tensile Strength / MPa	Initial Modulus / Mpa	Elongation to Break / %
Hydron 04				
	0.18 (Edge)	0.49	0.98	62
0.04	0.15 (Centre)	0.47	0.41	121
	0.185 (Edge)	0.41	0.91	55
Soflens 0-3				
	0.135 (Edge)	0.50	0.32	282
0.035	0.085 (Centre)	0.41	0.16	378
	0.115 (Edge)	0.45	0.27	312

Table 4.4 Quoted and measured thickness values for two commercial lenses

This table shows that there can be a large discrepancy between our own measured thickness and that supplied by the manufacturer, because of the different ways in which this particular dimension has been determined. In terms of the derived tensile properties, in both cases the modulus of the sample cut from the centre is roughly half that of the corresponding edge pieces. For the Soflens material this factor is seen to be equivalent to the ratio of the quoted and measured thicknesses, although not in the case of the Hydron zero 4 material. Interestingly the failure stress seems to be quite consistent across the lens, and if the ratio of thicknesses is applied to the strength of the material, then an abnormally high failure stress for the centre portion would be obtained. This further illustrates the difficulty, in that the thickness measurement that would give consistent values of elastic modulus, is not necessarily the same as that that would produce similar values of tensile strength across the lens.

Part of the explanation for the similar values of failure stress that are achieved is that frequently specimens did not fail in the centre of the gauge length, but rather nearer to the gripped ends. Essentially because the adopted gauge length of the samples was very similar to the diameter of the measuring instrument, the values of thickness recorded (*i.e.*the high points of the contact lens section) occur at the opposing diameters of the measuring area of the instrument. This means that they are likely to give a better estimate of the true thickness of the sample at its observed point of failure, and therefore the values of failure stress are quite comparable. Conversely, the initial modulus value, because it is a function of the whole of the gauge length of the sample will be more in error. Even if the manufacturers value of thickness is taken, this is still not the solution, since this will tend to produce an estimate of the modulus which is artificially high, again because of the lens profile.

A further effect noticed for those contact lenses that have a low value of centre thickness, is that the values of elongation to break from centre sections of the lens were occasionally higher than the corresponding edge pieces. A possible explanation for this is that the nature of the lens design (specifically the change in lens thickness about the centre point) means that the elongation behaviour may be modified, so that extension becomes easier in those samples taken from the centre of the lens. (Essentially this particular lens section has a "built in" waisted profile). Alternatively, because samples taken from the edge of the lens possess a more uniform thickness distribution, they are more susceptible to stress concentration effects. This could lead to premature failure in the edge pieces, which would therefore account for the observed difference in elongation to break between the centre and edge of the lens. In reality, the explanation for the observed higher elongation found for the centre section, is likely to be quite complex and is probably a combination of these two factors.

4.2.3 Choice of Testing Procedure

The question now arises - how best to characterise the properties of the lens? There is no doubt that the design of the lens has an important influence on the tensile properties that are measured, because of the difficulty of assigning a value of cross-sectional area to the lens sample. The most severe difficulties seem to be encountered with those lenses that are of low centre thickness, and it should now be obvious that lenses having a more uniform thickness will produce more valid results for failure stress and modulus (in terms of absolute values). Consequently it is very important to specify the power of the lens being tested, plano lenses, or those lenses having a low minus power are likely to give the best results in terms of the reproducibility of values. Because of the difficulties associated with the determination of the thickness of the lens and the effect this has, particularly on the values of modulii, it may be misleading to try and quote an absolute value for the modulus of the lens. A better approach perhaps, is to assign a relative stiffness factor to the lens, which would be an estimate of the overall flexibility of the whole lens as suggested by Tighe and Trevett [(83)]. (See also section 4.3.2) Since the method using the dumbbell samples necessitates samples being cut from the centre of the lens, and because only one sample from each lens can be obtained, it was decided that it was preferable to adopt the method using three parallel sided samples per lens, despite some reservations about its applicability in the case of very thin lenses.

4.3 Preliminary Assessment of Technique

4.3.1 Comparison Between Membranes and Lenses of Identical Composition

In some of the earlier work a series of membranes had been prepared that had very similar equilibrium water contents. Some of the same batches of monomer mixture that were used for this, were also used in order to prepare polymer rods of exactly the same composition. After curing, the rods were sectioned and cut into individual lenses, some of which were tested at Aston, and others of which were sent to the Cornea and Contact Lens Research Unit at Sydney (C.C.L.R.U.) for their own testing and analysis to be carried out (see also section 5.5.2). Lenses were then tested in tension using the parallel sided specimen configuration that was chosen. A minor modification was necessary, in that the lenses cut from the rods had a smaller diameter than most commercially produced lenses, so that it was only possible to test two samples from each lens. Because only a small number of samples could be tested, the results, in table 4.5 are shown without error bands, and should only be considered as approximate values.

Composition / wt %	Tensile Strength / MPa	Initial Modulus / MPa	Elongation to Break / %
NVP/CHexMA 74/26	4.9	33	51
NVP/MMA 60/40	2.6	9	150
NVP/HexMA 67/33	>1	2.5	140

Table 4.5 Approximate tensile properties of lenses made of identical composition to the membranes in section 6.5 table 6.6

When these results are compared with those from the same composition, but in membrane form, (table 6.6) it is clear that there is very good agreement between the lens samples and the dumbbell samples in most cases. The elongation to break appears slightly lower in the case of the lens materials, and this may be caused by the different designs of the two samples, the parallel sided lens pieces being more susceptible to stress concentration effects since the flow of material is restricted in the regions where the sample is being gripped. Despite the fact that the elongation is lessened, the strengths of the two configurations remain very similar. The smaller volume of the specimens cut from the lens may be the major influence here, (lens pieces tested were approximately one third the thickness of the corresponding membrane) since as was suggested in the previous chapter, the smaller the volume of sample being tested, the stronger it appears. It is quite likely that the competing effects of stress concentration and smaller volume result in the similar failure strengths that are observed.

Only in one case is there any major disagreement, where the modulus of the VP/MMA lens specimen is rather higher than that of the membrane. The cause of this is difficult to explain, but it is felt that the effect of the different geometry may be particularly significant for this given material. (A similar difference in initial modulus was also observed for some of the parallel sided samples in the previous chapter). A further difficulty is caused by the non-linear extension behaviour of some of these materials at low strains, which may lead to inaccuracies in determining the initial modulus. This problem was also recognised by the group from the C.C.L.R.U., who also found it difficult to characterise the initial modulus of these materials (chapter 5). Figure 4.2 illustrates the stress/strain curves for lenses and membranes of the composition NVP/MMA 60/40, where the non-linearity is clearly shown.

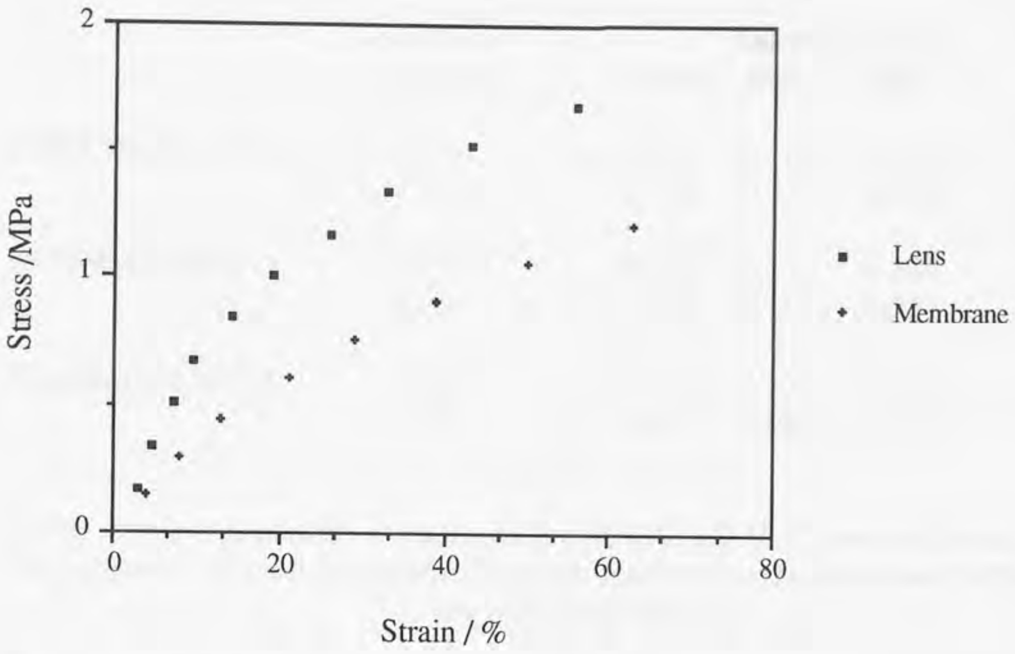


Figure 4.2 Approximate stress/strain curves for the initial extension of VP/MMA in the form of - top, a contact lens, and bottom, a membrane

This non linearity however does not explain why this particular material should be any different from the others tested, since good agreement was found in the other two cases, although it does emphasise a further difficulty in determining the modulus of these materials.

The importance of accurate characterisation of the thickness of lens samples with regard to the determination of modulus has already been demonstrated. For this particular part of the study, the dimensions of the lenses were evaluated by the C.C.L.R.U. and are given in table 4.6. This table shows that the variation of thickness across the lenses used was quite small. It also demonstrates that our own determination of thickness was relatively accurate in this case. Furthermore as has already been suggested the lower minus powered lenses tend to be of more uniform thickness and therefore more suitable for the accurate determination of the lens's properties, and the figures in table 4.6 seem to agree with this general rule.

	Lens Power (Diopters)	Thickness / mm Centre	3mm	Edge	Aston
NVP/CHexMA 74/26	-1.50	0.152	0.164	0.178	0.18
	-1.75	0.126	0.153	0.169	
NVP/MMA 60/40	-1.31	0.166	0.172	0.188	0.175
	-1.12	0.183	0.195	0.221	
NVP/HexMA 67/33	-1.21	0.170	0.176	0.186	0.17
	-0.50	0.180	0.187	0.192	

Table 4.6 Lens parameters as measured by the C.C.L.R.U. for two individual lenses from each material. Figures in parenthesis are the approximate thickness used in this work (and are from a different lens)

On balance the results of this comparison between lenses and membranes was sufficiently encouraging to allow more widespread adoption of testing protocol to be applied to a range of commercially available lenses, and this is done in the next section.

4.3.2 Tensile Properties of a Range of Commercial Lens Materials

For the testing methodology to be acceptable, it must be applicable to finished lenses, and should be sensitive enough to be able to pick up differences in material, and manufacturing technique. A small scale pilot study to test a number of commercially available lenses was set up, encompassing a range of lens materials and techniques. As anticipated, quite a range of properties were found, which can only be explained by the differences in material. From the results given in table 4.7 (See also table 5.5) it is clear that there is a general relationship between the water content of the lens, and its modulus. As one would have predicted, the higher water content lens materials tend to produce lenses that have a lower modulus, and *vice versa.* The true situation is considerably more complex than this however, since as was shown in the previous chapter, there are many different factors that can influence the mechanical properties of hydrogel materials.

Examining the results for the Etafilcon materials, it is noticed that the results are almost identical in the case of the Acuvue and of the Bausch and Lomb 58 materials. The slight differences in modulus and elongation that are observed are probably a result of the different manufacturing techniques that are used to produce these two lenses. The Vistakon material, which is based on the same constituent monomers as the Acuvue and B+L 58 is stiffer, stronger and more elastic than the aforementioned members of the Etafilcon family of lenses, and has a correspondingly lower water content. This lower water content could be caused by a higher crosslink concentration, or by more basic changes in the concentrations of the main monomers that are used.

The case for the lenses that are based on poly HEMA, (polymacon) are interesting because it can be seen that quite a range of properties can be obtained, particularly in the case of their initial modulus. At the low end of the modulus scale are the B+L materials, sold under the trade names Soflens and Optima 38, results from which are given in chapter 5 (see under effects of modulus on handling). Both these lenses give very similar results, with an initial modulus of about 0.3 MPa. This is an important observation, in that these two materials are in fact both made from the same material, and by the same manufacturing route, in this case by spin-casting. In contrast, the Hydron lenses that are based on this same important hydrogel (poly HEMA) tend to be considerably stiffer than their B+L counterparts, although there is a wider range of stiffness values found. The spin cast Zero 4 material, gives a particularly stiff lens, which has a correspondingly low elongation to break. The lathe cut materials seem to produce an improvement in properties, since both the Zero 6 series, and

Lens type	Material	Manufacturing Method	Manufacturers Water Content / %	Tensile Strength / MPa	Initial Modulus / MPa *	Elongation to Break / %
X-ten	(Amide based)	Lathe cut	72	0.21 ± 0.07	0.15 ± 0.02	159 ± 44
Permalens	Perfilcon A	Cast polymerised	72	0.19 ± 0.03	0.11 ± 0.02	273 ± 45
B+L 58	Etafilcon A	Lathe cut	58	0.15 ± 0.03	0.18 ± 0.01	104 ± 33
Acuvue	Etafilcon A	Cast polymerised	58	0.16 ± 0.06	0.22 ± 0.01	90 ± 36
Vistakon	Etafilcon A	Lathe cut	43	0.40 ± 0.09	0.26 ± 0.01	272 ± 56
Kelvin Eurothin	Polymacon	Lathe cut	38	0.65 ± 0.29	0.48 ± 0.11	189 ± 94
Titmus Hema	Polymacon	Lathe cut	38	~ 0.8	~0.6	~330
Hydron 04	Polymacon	Spin cast	38	0.50 ± 0.09	0.73 ± 0.22	84 ± 22
Hydron 06	Polymacon	Lathe cut	38	0.80 ± 0.36	0.63 ± 0.17	209 ± 91

Perfilcon = HEMA, NVP, MA, Etafilcon = HEMA, MA, Polymacon = HEMA
Mean values ± 1 standard deviation
* = "Composite" modulus

Table 4.7 Comparison of the mechanical properties of some commercially available soft contact lenses the Hydron Minilens give results showing a reduced modulus (typically 0.6-0.7 MPa) and a greatly improved elasticity. The most likely explanation for the difference between these hydron materials is that the design of the lens is influencing the measured properties to a much greater extent for the thinner Zero 4 series. Therefore the measured modulus of this particular lens, may be artificially high for the reasons associated with lens thickness outlined earlier. Other manufacturer's lenses based on poly HEMA, such as the Kelvin Eurothin material, and Titmus HEMA seem to produce lens materials with properties that lie between the two extremes produced by the Hydron and B+L polymacon lenses. Again this difference in stiffness is not entirely unexpected, due to the complex nature of hydrogel chemistry, and the variety of lens fabrication techniques.

Further material differences are encountered between the Bufilcon A (Hydrocurve II) material and the Durasoft lens (which is based on Phemfilcon), results for which are given in chapter 5, table 5.5. These two lenses have a similar equilibrium water content, and a similar value of modulus (once the thickness variations have been accounted for), and yet the Durasoft lens is both stronger and more elastic than the Hydrocurve II material.

Examining the results for lenses having similar water contents, some interesting observations can be made concerning those lenses that have a high EWC, typically in the range of 72 % water. The amide based X-ten material is very similar to the Perfilcon A composition in terms of its mechanical properties, being if anything marginally stiffer and more elastic. The two Coopervision lenses, the Permalens and the Permaflex, are worth mentioning here, since although the water content of the two materials is similar, the Permaflex material is almost twice as stiff as the Permalens. This is easily explained by the difference in materials, the Surfilcon material (*i.e.* Permaflex) is based on NVP/MMA, whilst the Perfilcon lens consists of NVP with HEMA and MA (methacrylic acid). In this case the incorporation of MMA seems to produce a stiffer and stronger lens, without compromising its elasticity.

Although a number of different properties have been observed for the commercial lenses, it is important to emphasize the fact that just because one lens has a lower elastic modulus than another, this does not necessarily mean that it is any worse (or better) for its designed purpose. Similarly an apparently weak and inelastic material can still function adequately as a lens, since *in situ*, the stresses involved are well below those needed to cause any permanent damage. Potentially the main disadvantage the weaker lenses have is that they are more likely to be susceptible to damage caused by careless handling, although some manufacturers may consider that the number of rejections that are produced through this reason is not particularly significant.

How then can the optician best be aided from this knowledge of the properties of the lens material. One way to do this is to rate the different materials based on their values of modulus. Because of the difficulties associated with the determination of the modulus of finished contact lenses, it is quite a problem to do so in a fair and meaningful manner. In order to obtain a figure for the "absolute" modulus, it may sometimes be necessary to discount the results from the tests on the centre portion of the lens. This level of sophistication may not be needed for practitioners, however, since in this case they would prefer a measure that relates to what the lens actually feels like, and for this reason it may be more appropriate to adopt a value of a "composite" modulus. If all three modulus values from each piece of the lens tested are combined, then the result is an average modulus value that also takes into account the design of the lens, particularly with respect to its centre thickness. It is suggested then, that this value of modulus be used, since it gives a fairer indication of what the lens as a whole actually behaves like, in terms of its stiffness. Since now dealing with a measure that is now no longer entirely based on the materials true properties it would be wrong to try and assign any particular units to this measurement. It is therefore more convenient to rank the lenses on a relative scale, based on an acceptable reference point, and this also has the benefit that it becomes a more readily understood value. Table 4.8 ranks a number of commercially available soft contact lenses in terms of their measured stiffness, where the "softest" material has been assigned a stiffness value of 1.

Material	Relative Stiffness
Permalens (Perfilcon A)	1
X-ten (Amide based hydrogel)	1.5
B+L 58 (Etafilcon)	2
Acuvue (Etafilcon)	2
Permaflex (Surfilcon)	2
Hydrocurve II (Bufilcon A)	2
Vistakon (Etafilcon)	2.5
B+L Soflens (Polymacon)	3
Durasoft (Phemfilcon)	3
Aquaflex (Tetrafilcon)	4.5
Kelvin Eurothin (Polymacon)	4.5
Titmus (Polymacon)	5.5
Hydron (various trade names) (Polymacon)	5.5 - 7.5
Cibasoft (Tefilcon)	7

Table 4.8 Relative stiffness values for a number of commercial soft contact lenses

The figures given in table 4.8 give a useful indication of the variations in stiffness that are encountered in soft contact lenses, and as such may be of particular value to optometrists and practitioners. However it is not intended that this sort of table be used as the sole basis for lens selection, rather, that it should be used as a guide to assist in the appropriate choice of a lens, together with other available (and equally important) measures such as the equilibrium water content of the lens.

4.4 Conclusions

In this section of the thesis, two alternative testing protocols for the determination of the tensile properties of soft contact lenses have been evaluated. Both the procedures utilised gave consistent results and were broadly comparable, the only exception being that there is difficulty in assigning a modulus value to the lens because of its non-uniform thickness. The methodology finally chosen, involves the preparation of three parallel sided samples from each lens. This was felt to be more appropriate for a number of reasons, as discussed previously. The question as to what the true modulus of a contact lens is, has still not been resolved, but by using three samples from each lens it seems to be possible to produce a value for the "composite" modulus which is a more representative measure of the stiffness of the whole device, and this particular value could be of benefit to contact lens practitioners. In terms of a material parameter, the testing of the (generally) more uniformly thick areas towards the edge of the lens, gives a more realistic value for the "true" modulus of soft contact lens materials.

The method chosen was then used to compare finished lenses with membranes that had an identical chemical composition, and good agreement was found for most of the properties measured, although unfortunately the sample size was rather small. Having established the validity of the technique, a number of commercial lenses were evaluated, and it was shown that a range of properties is obtainable, which is due in part to the many different formulations that are used to make soft contact lenses. Further comments on structure/property relationships in hydrogel polymers can be found in chapter 6, whilst in the next chapter the testing methodology used here, is extended to a number of more practical contact lens situations.

Chapter 5
Applications of the Contact Lens Testing Technique

5.1 Introduction

In the previous chapter it was shown, how, with appropriate modifications, the technique of tensile testing could be applied to the soft contact lens. The importance of being able to perform such test on the finished article (*i.e.* the contact lens itself) was emphasised. It was also demonstrated that commercial lenses made nominally from the same material showed quite a wide variation in properties. This particular variation in properties was in itself of great interest, though it is also important to recognise the fact that the method used was sensitive enough to detect these differences. It would be almost impossible to distinguish between two lenses made of the same material by a method such as determining the equilibrium water content for instance; but if tensile testing is adopted, it is a relatively straightforward procedure, and one that will enable such differences to be picked up with quite a high degree of sensitivity. The reason that tensile testing is so sensitive a technique, is that the application of a tensile stress is a particularly good way of probing network imperfections in a polymer. An imperfect network, or a polymer that is incompletely polymerised will result in a material that has a relatively low elongation to break.

It is all very well to to develop a methodology to be able to say that one lens is not the same as another, because revealing though this is, it is not in itself enough to justify the routine adoption of tensile testing as applied to contact lenses. There may be several reasons why the evaluation of the mechanical properties of finished lenses may be important. In this chapter the methodology developed earlier, is applied to a number of different situations where the the appropriate use of such a technique can be demonstrated to its full potential.

The first and most basic application, is the case of quality control or quality assurance. Many manufacturing industries use routine mechanical property testing as a means for quality control, and there is no real reason why this could not be applied in a similar fashion to the contact lens industry. The fact that it has not, is in a large part, due to the fact that at the present time there is no universally accepted method for determining the tensile properties of a contact lens.

It may be of great interest to manufacturers to know how consistent their products are in terms of the finished article. How much variation in terms of strength is to be expected from a group of lenses made from one particular run or batch or composition ? Once this is established, it leads to a method for checking the quality of the monomer mix and the polymerisation conditions. If for example an "unacceptable" number of lenses were found to have a subnormal elongation to break, then it automatically suggests that perhaps there is something wrong with the composition, or the polymerisation parameters. Thus it might be possible to evaluate different runs of material, made at different times, to check that no gross differences were occurring between batches.

Furthermore tensile testing could be a very useful guide in terms of the development of new lens materials. (For instance, slight compositional changes such as the addition of plasticisers, or an increase / change in the crosslinking content / agent). Here again, tensile testing could be used as a quality assurance tool, to check that such alterations are not having a deleterious effect on the lens.

It is very important when using tensile testing as a quality control method to adopt a statistical approach. This is because materials do not possess a strength *per se*, it is only correct to say that the strength (modulus or elongation *etc.*) lies within certain given limits for any one particular set of testing conditions. (In the early part of the century, designs for structures tended to be "over-engineered", and this in part can be said to be due to ignorance about the mechanical behaviour of the materials being used. To compensate for this lack of understanding large "safety factors" were incorporated (and indeed are still used today) leading to designs that used more material than was strictly necessary). The question for the contact lens manufacturer then, is what sort of variability can be expected from a batch of contact lenses. Any variability will be a function of two factors. The first is the inherent variability of the material itself. Typically for a hydrogel material this is of the order of ± 20% for strength and elongation, and ± 10% for modulus (63) The second factor is the manufacturing technique. *i.e.* whether the lens has been lathe cut or spin cast or moulded for instance.

5.2 Assessing Variability - the Weibull Model

In order to ascertain the sort of variability that might be expected from a batch of contact lenses, a trial of 25 lenses was performed, in which the tensile properties of the lenses were evaluated. The commercial lenses used were based on the NVP/MMA system, and had a water content of approximately 67%, being sold under the name Igel 67. The lenses tested were of a low minus power so that it would be suitable to include the centre pieces in the statistics (see chapter 4). This gave a total of 75 samples, which was felt would be suitable for the type of analysis required. The results are summarised in table 5.1 overleaf. These results are fairly typical of what might be expected for a hydrogel polymer, with both the strength and elongation having scatters of ± 20%, although the modulus seems to be relatively more consistent.

A useful way of representing these results is in the form of a cumulative probability of failure graph, where the normalised failure stress is plotted against the failure probability, and this is done in figure 5.1. Approximately 70% of the results shown in figure 5.1 lie in the range between 0.8 and 1.2 stress units (which is equivalent to the mean ± 1 standard deviation). Similarly only 4 of the results lie outside the range $x \pm 2$ sd. These values are similar to what one would expect for a normal distribution. This was confirmed

	Mean value	Standard Deviation	High	Low
Tensile Strength / MPa	0.69	0.15	1.14	0.39
Tensile Modulus / MPa (50 %)	0.45	0.02	0.48	0.40
Elongation to Break / %	192	35	278	108

Table 5.1 Results from tests on NVP/MMA lenses to assess the variability in tensile properties (n = 74)

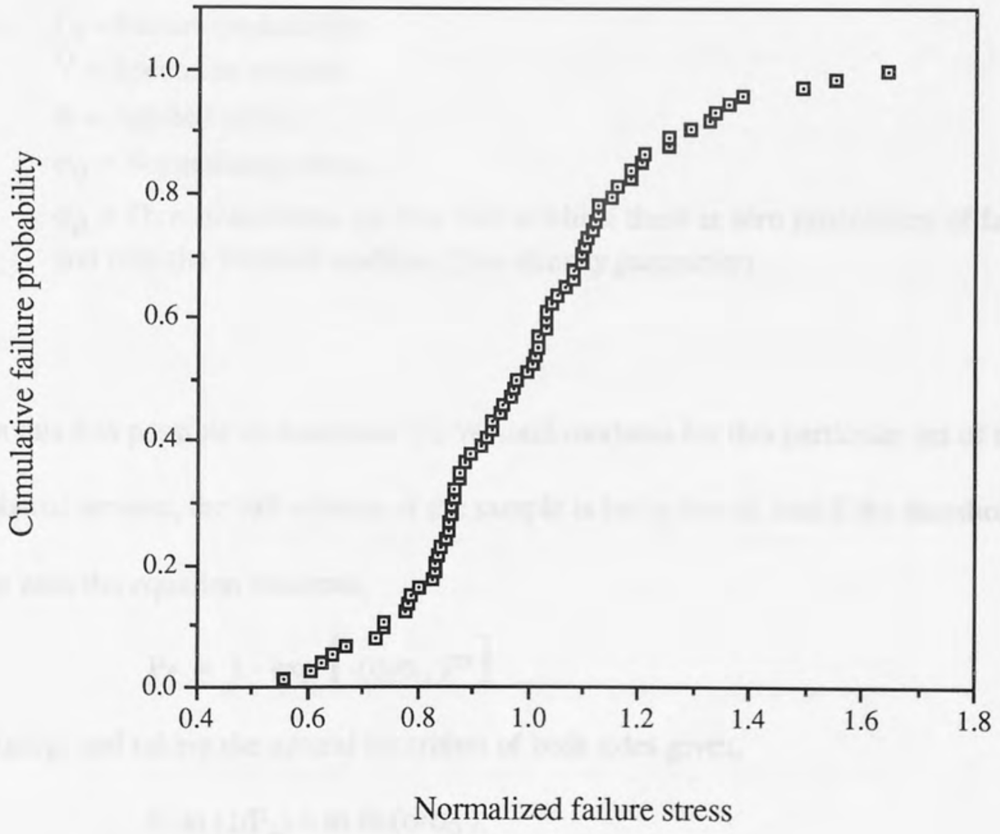


Figure 5.1 Cumulative failure probability curve for NVP/MMA lenses

by performing a normality test on the data, which gave a statistic of 0.067 and a significance of 2.82. Thus it would seem reasonable to conclude that the failure strength of this set of lenses is normally distributed about the mean.

Another way to assess the spread of tensile strength data is to estimate the Weibull modulus of the material, m, by using Weibull statistics. This approach, which is usually reserved for ceramic materials, is based on a weakest link theory, and the following relationship has been derived for ceramics (84) :

$$P_f = 1 - \exp\left[-\int_V ((\sigma - \sigma_\mu)/\sigma_0)^m\right] dV$$

Where, P_f = Failure probability,
V = Specimen volume,
σ = Applied stress,
σ_0 = Normalising stress,
σ_μ = Threshold stress. *i.e.* that below which there is zero probability of failure, and m is the Weibull modulus (flaw density parameter)

From this it is possible to determine the Weibull modulus for this particular set of samples. For uniaxial tension, the full volume of the sample is being tested, and if the threshold stress is set to zero the equation becomes,

$$P_f = 1 - \exp\left[-(\sigma/\sigma_0)^m\right]$$

rearranging, and taking the natural logarithm of both sides gives,

$$\ln \ln (1/P_s) = m \ln (\sigma/\sigma_0)$$

Where P_s = the survival probability

Hence m can be found. Figure 5.2 shows the plot to determine the Weibull modulus, from which it is seen that a value of 5.6 is obtained. Although the fit is not perfect, the regression coefficient of 0.974 suggests that the use of the Weibull model is quite appropriate in this case.

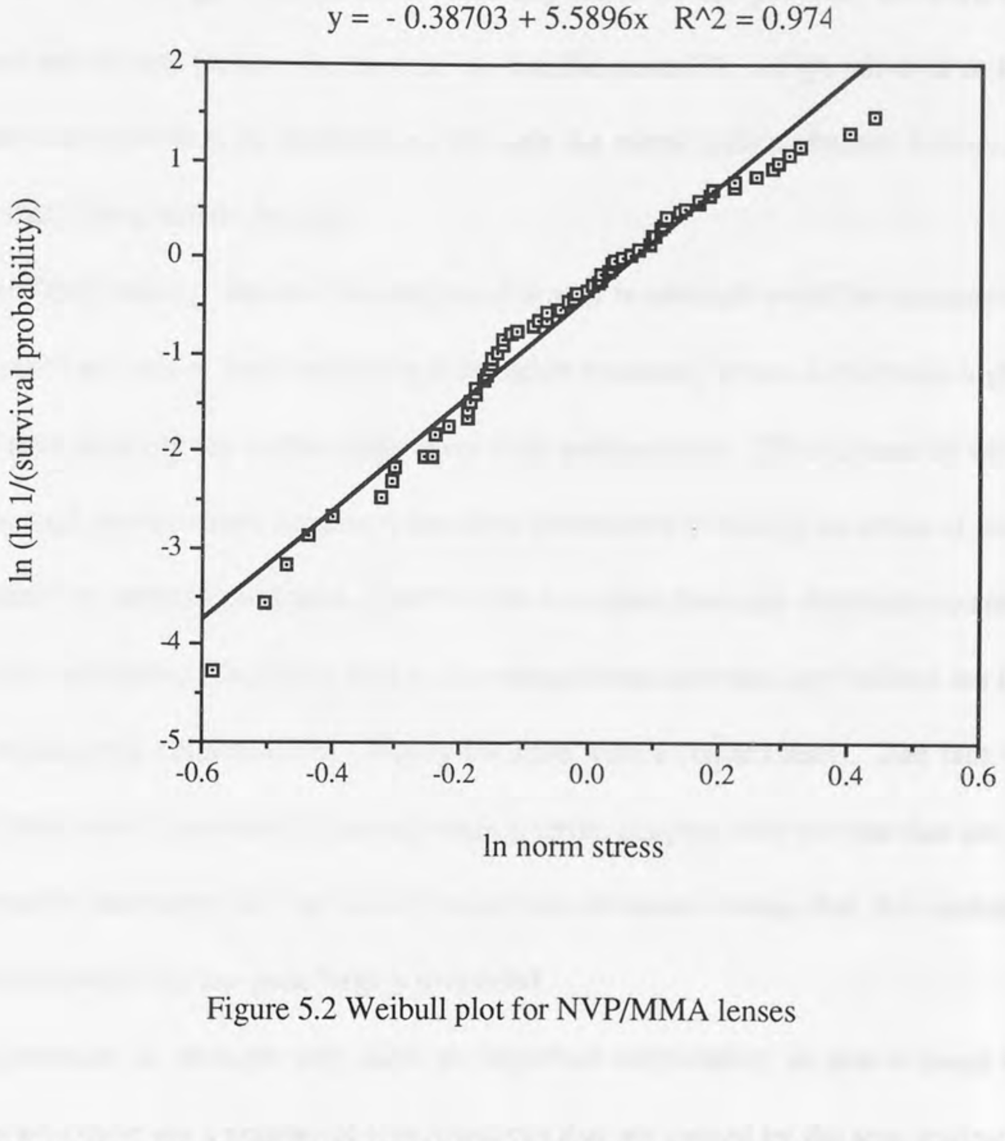


Figure 5.2 Weibull plot for NVP/MMA lenses

The value of m can also be estimated from the following rule of thumb - $m \approx 1.2 / cv$, where cv is the coefficient of variation, and this relationship seems reasonable in this case, since a value of 5.5 is obtained.

The Weibull modulus is a measure of the variability of the material, the lower the value for m, the greater the scatter. Typically steel would have a Weibull modulus of about 60 and glass fibres about 2. Thus this hydrogel lens material is on the poor side in terms of its variability, and has a value for m that is comparable to those for ceramic materials. The degree of scatter that is found for the hydrogel, is a reflection of the imperfect network formation in the polymer. Once the polymer chains become un-entangled, there is no further mechanism for energy absorption, so that any flaws in the polymer network become exposed and initiate failure. In the case of metallic materials, a high value of m is found because the movement of dislocations through the metal lattice absorbs energy, giving metals their characteristic ductility.

For an "engineering" material this degree of scatter in strength would be unacceptable, in that, to take account of such variability it would be necessary to use a relatively high safety factor, thus reducing the usable stress level quite substantially. (This is exactly the reason why for high performance ceramics, the drive in research is mainly in terms of improved fabrication, in order to produce a material with a smaller flaw size distribution, and hence reduce its variability. Clearly for high performance brittle ceramics, any failures are likely to have catastrophic consequences - hardly the case with a contact lens). The fact that the contact lens is not considered in an engineering sense, coupled with the fact that few people have tried to determine the mechanical properties of lenses, means that this variability in mechanical properties has gone largely unnoticed.

This variation in strength may have an important implication, in that it could help to explain why there are a number of lens rejections that are caused by the lens tearing during handling (since tear strength is related to network perfection and thus tensile strength). How then can this sort of variation be reduced, if at all, or indeed is it really necessary to do so? As hinted at above there is no real drive to do so, since mechanical strength is not a critical factor in terms of ultimate lens performance, and at the present time economic factors are not a strong enough driving force. Any improvements that are likely, are probably going to be found from research into the polymerisation conditions, and lens fabrication processes.

It is not sure whether the degree of variability found above is the same for all materials of this type *i.e.* lenses (hydrogels in general) or if this spread of data is unique to the particular material used, since the appropriate tests have not been performed. It would seem probable however, judging from the result for poly HEMA in chapter 3, that a Weibull modulus of about 5 is to be expected for most hydrogels. This relatively low value of m may not be important for a contact lens, but it could have a considerable influence on the design of any prostheses based on hydrogels, that are expected to be used for more stress bearing applications, such as a synthetic articular cartilage material (chapter 7).

Although this analysis has been carried out on the failure stress of the material, the values for elongation to break, ε_b, are equally sensitive to variations in polymer perfection. The values of elongation, because they are sensitive to network imperfections, and because they are not subject to the same measurement errors arising from the thickness of the lens, are probably the preferred measure for quality control purposes, although difficulties arising from any slack in the sample, and in keeping the gauge length constant, need to be recognised. (In addition to the normal sample preparation factors, such as keeping cutting tools sharp). In contrast the stiffness of the lens is probably a better parameter to use when comparing two different lenses, because of the lower variability associated with this measurement.

5.3 Effects of Polymerisation and Fabrication

Tensile tests were performed on some series of lenses which had been fabricated in slightly different ways, and which demonstrated some minor compositional differences. The results are summarised in table 5.2. Lens types A and B were known to be polymerised in the form of rods, and the subscripts t, m, and b, denote lenses cut from the top, middle, and bottom of the original rods respectively. Material A appears to be very consistent throughout the whole of the rod, since little variation in any of the properties measured occurs. This result in itself could be of significant importance to the manufacturer. Lens material B is rather different. In this case, a large difference is found between the strength and elongation of the lenses from the top of the rod, and those from the bottom of the rod. Significantly, the modulus of these particular lenses does not seem to be affected by the position in the rod.

Lens Type	Tensile Strength / MPa	Initial Modulus / MPa	Elongation to Break / %
A_t	0.70 ± 0.25	0.81 ± 0.05	117 ± 47
A_m	0.68 ± 0.38	0.74 ± 0.01	115 ± 68
A_b	0.71 ± 0.32	0.80 ± 0.06	115 ± 58
B_t	1.02 ± 0.28	0.60 ± 0.02	259 ± 47
B_m	0.69 ± 0.17	0.58 ± 0.03	180 ± 51
B_b	0.53 ± 0.22	0.58 ± 0.05	129 ± 59
C	0.68 ± 0.25	0.89 ± 0.06	96 ± 37
D	0.53 ± 0.28	0.75 ± 0.09	84 ± 47
E	0.57 ± 0.11	0.50 ± 0.03	211 ± 46

Table 5.2 Tensile properties of a series of soft contact lenses

It needs to be said at this point, that in this series of tests only a small number of samples were tested (6 samples, i.e. 2 lenses, for each particular batch). This makes any definite conclusions somewhat difficult to draw. Even so, application of the students "t" test, between the top and bottom of material B for the values of σ_f and ε_b give values of t of 3.22 and 4.23 for 9 degrees of freedom respectively, and these represent probable and significant differences. (A significant difference is indicated if the results suggest that "had testing continued there is a greater than 99% chance that this difference would have remained" ($t_{(9)}$ 99 % = 3.25). Thus even in such a small trial it was possible to ascertain significant differences between batches of lenses cut from different parts of a rod. Ideally however, it would be preferable to test more lenses than this - probably at least four lenses, as this would give a minimum of 10 samples per batch, allowing for 2 samples to be rejected either in the event of careless preparation, or through thickness-related difficulties.

Thus it would seem that the degree of polymerisation at the top of the rod is better than that at the bottom of the rod. This is illustrated by the fact that the highest values of strength and elongation for batches B_m and B_b are (almost) within the range of those from the top part of the rod, and that the modulus of these batches of lenses seems to be independent of the position in the rod. The result of this, is that a property gradient has been formed within the rod, with the "best" properties achieved at the top of the rod. The explanation for this property gradient is because of the fact that, in batch B, there has been the inclusion of a diluent (glycerol) in the polymerisation mix. The glycerol is likely to be of different density to the polymerisation mixture, so that the resulting glycerol concentration in the upper part of the rod may not be the same as that at the bottom of the rod. The effect of the diluent also helps to explain the different modulus values between batches A and B. In batch B, because the diluent was included, the resulting polymer that is formed is already at its final dimensions. In the case without the diluent however, the polymer swells on hydration, and this "pre-stresses" the polymer network, resulting in a stiffer material.

The results from batches C, D, and E are particularly significant. It is known that the only difference between batch C and batch A, was that A was polymerised in rod form, whereas C was made of the same bulk material, but was cast into buttons. There is no statistical difference between lenses A and lenses C in terms of any of the properties measured, although again, it has to be said that the sample size is small (n=6).

Lenses from the materials D and E also illustrate very interesting results. In this case the two batches were again of an identical composition, the only variable in this case, being the source of the monomer used (in this case HEMA). As was seen in the one of the previous chapters, the effect of monomer purity is extremely significant, and the degree of polymerisation is greatly affected by very small amounts of impurity. This would seem to be very much the case in this instance, as there is a highly significant difference in the values of elongation to break between the two batches, material E having almost twice the elongation to break of that of material D. It will also be noticed that the modulus for the lenses from batch E is statistically lower that those for batch D. The explanation for this lies in the nature of the impurities that are encountered in HEMA monomer. HEMA is known to be difficult to purify, and two of the main impurities encountered are methacrylic acid and ethylene glycol dimethacrylate (EGDM). This later reagent is frequently added as a cross linking agent in hydrogel materials, and thus it would appear that material D contains some residual EGDM, and that this would therefore account for the higher modulus and lower elongation to break that is observed between these two samples. Figure 5.3 illustrates typical load/extension curves from materials D and E, and shows the different behaviour in tension, of these two particular lens materials. (Note the different scales).

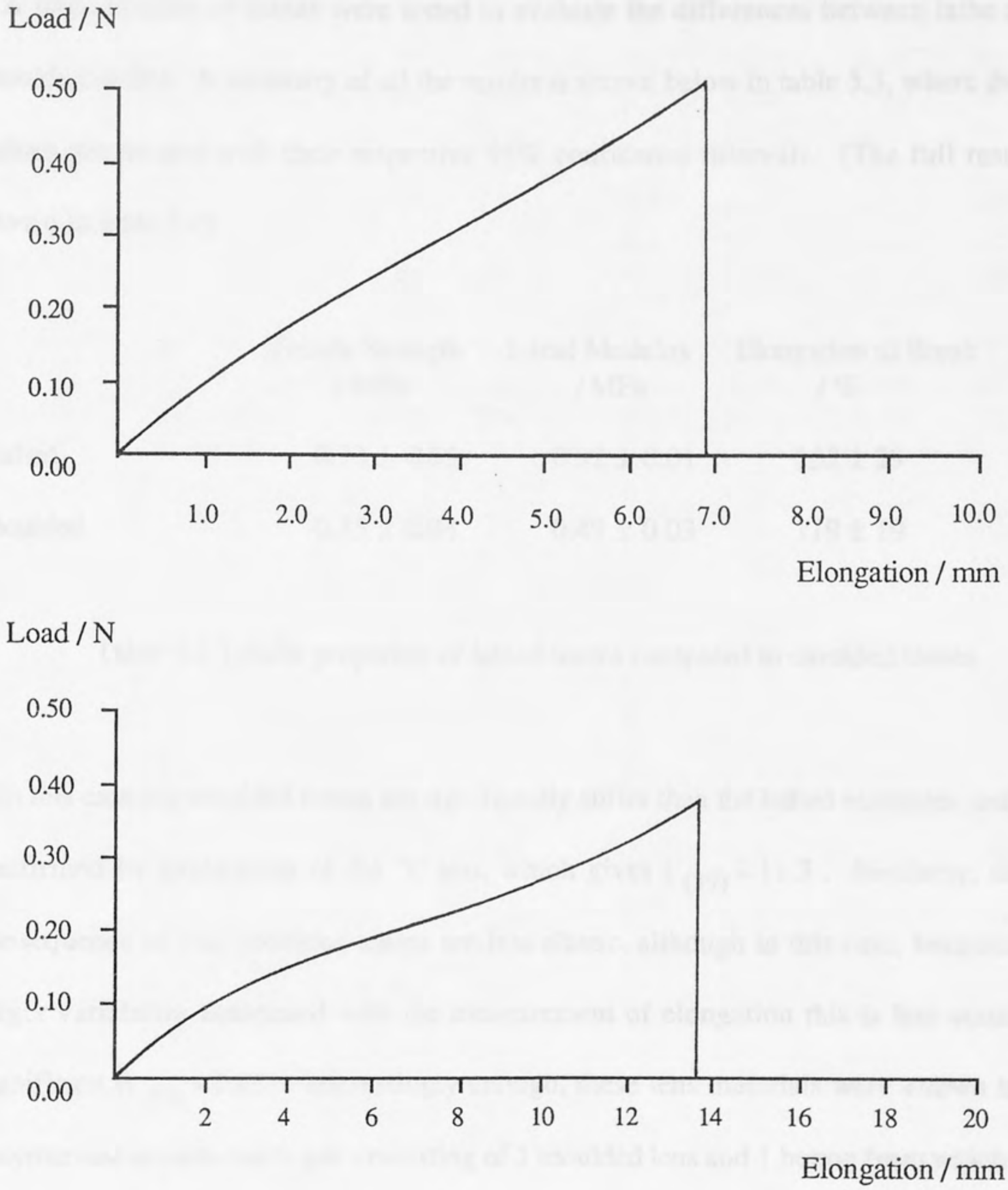


Figure 5.3 Load/elongation curves for two hydrogel lenses (of similar thickness)
(Top material D, bottom material E - see text)

5.3.1 Effects of Fabrication (continued)

A large number of lenses were tested to evaluate the differences between lathe cut and moulded lenses. A summary of all the results is shown below in table 5.3, where the mean values are quoted with their respective 95% confidence intervals. (The full results are shown in table 5.4)

	Tensile Strength / MPa	Initial Modulus / MPa	Elongation to Break / %
Lathed	0.33 ± 0.05	0.32 ± 0.01	152 ± 29
Moulded	0.35 ± 0.03	0.49 ± 0.03	119 ± 19

Table 5.3 Tensile properties of lathed lenses compared to moulded lenses

In this case the moulded lenses are significantly stiffer than the lathed examples, and this is confirmed by application of the "t" test, which gives $t_{(39)} = 11.3$. Similarly, and as a consequence of this, moulded lenses are less elastic, although in this case, because of the larger variability associated with the measurement of elongation this is less statistically significant ($t_{(39)} = 1.95$). Interestingly enough, these lens materials were known to be in polymerised in pairs (each pair consisting of 1 moulded lens and 1 button from which a lathe cut lens was subsequently taken), and had been subjected to different polymerisation conditions. Thus paired "t" tests were used in order to compare the different treatments by using the mean values of stress, modulus and elongation calculated for each individual lens. Similar results were obtained, in that modulus was significantly different, but no such differences could be proved for the failure stress and elongation to break. Trends within each type of lens (lathed and moulded) as a function of treatments 1-7 are more difficult to

	Lathed				Moulded			
	t / mm	σ_f / MPa	E / MPa	ε_b / %	t / mm	σ_f / MPa	E / MPa	ε_b / %
1	0.16	0.39	0.28	220	0.27	0.25	0.48	81
	0.15	0.30	0.34	126	0.285	0.28	0.52	78
	0.195	0.33	0.37	129	0.325	0.28	0.52	75
2	0.16	0.40	0.35	172	0.32	0.45	0.55	142
	0.20	0.26	0.32	117	0.28	0.17	0.56	38
	0.125	0.45	0.37	191	0.26	0.36	0.43	168
3	0.15	0.30	0.32	136	0.195	0.33	0.51	95
	0.175	0.43	0.36	172	0.19	0.33	0.53	90
	0.17	0.34	0.35	148	0.15	0.42	0.33	202
4	0.165	0.41	0.28	200	0.21	-	-	-
	0.19	0.43	0.30	196	0.145	0.32	0.43	118
	0.125	0.59	0.30	342	0.18	0.41	0.43	160
5	0.17	0.18	0.32	66	0.21	0.33	0.55	92
	0.17	0.20	0.32	84	0.21	0.37	0.56	103
	0.125	0.17	3.0	67	0.14	0.41	0.48	154
6	0.16	0.33	0.31	153	0.215	0.37	0.57	106
	0.12	0.37	0.35	158	0.21	0.38	0.51	123
	0.19	0.23	0.29	120	0.14	0.40	0.46	146
7	0.14	0.39	0.29	228	0.19	0.37	0.44	136
	0.195	0.25	0.28	121	0.135	0.45	0.42	173
	0.20	0.13	0.28	55	0.205	0.33	0.55	98

Table 5.4 Comparison between lathe cut and moulded lenses

see, since only one lens from each treatment was supplied. There appears to be little difference between treatments 1-3, but treatment 4 seems to be marginally better, in that a higher elongation to break, and a lower modulus result. Of the other treatments, little can be said, except that the lathe cut sample 5 is very much weaker and less elastic than any of the other lathe cut lenses, and is the only one of the paired results where the moulded lens has an improved elongation to break when compared to the lenses that were lathe cut.

Despite the fact that there are statistically significant differences in terms of the modulus, and to a lesser extent elongation, between the moulded lenses and the lathe cut ones, this difference is not necessarily entirely due to the different methods of fabrication. This is because it is not known whether the compositions of the lenses from the two types of manufacturing method are the same. In fact it seems fairly certain that the manufacturer concerned was trying to produce lenses of the same mechanical performance, but by using a different manufacturing technique. This is in fact not as easy as it at first sounds, since the polymerisation in the larger volume of the rods (which are then lathe cut) is likely to be different from that in a small mould.

5.4 The Relation Between Handling and Elastic Modulus for Soft Contact Lenses

Gavett *et al.*, at the School of Optometry, University of Missouri,(85) recently performed a fairly large scale trial of a number of commercial soft contact lenses, in order to try and establish the effects of power and lens type on the handling and inversion characteristics of lenses. They asked several experienced lens wearers to rate the lenses on a basis of a score of 1-5, 1 representing very poor handling (or inversion) and a value of 5 representing easy handling. The handling of a lens is a somewhat subjective measure, but is still very important to assess clinical performance. It was felt that it was important to see if it was possible to correlate the handling of a lens with a suitable property of the lens material. This needed to be some measurable property of the lens that, ideally would be sensitive to such differences between lenses as, the lens material, its water content, and method of fabrication. The modulus or stiffness of the lens was felt to be a relatively good indicator for this, and consequently, the same nine types of lenses that were used in the Missouri trial were evaluated at Aston using the contact lens tensile testing methodology that was outlined earlier in this thesis. Hence values of strength, modulus, and elongation to break were recorded, and are given in table 5.5.

	Tensile Strength / MPa	Initial Modulus / MPa	Elongation to Break / %
Soflens (0-3)	0.48 ± 0.05	0.31 ± 0.10	244 ± 85
Permaflex	0.49 ± 0.14	0.22 ± 0.03	229 ± 53
Hydron Zero 4	0.46 ± 0.04	0.77 ± 0.25	79 ± 29
Durasoft (D3 X4)	0.74 ± 0.27	0.34 ± 0.03	325 ± 102
Optima 38	0.41 ± 0.10	0.29 ± 0.07	279 ± 90
Aquaflex	0.28 ± 0.05	0.49 ± 0.07	68 ± 13
Hydron (Minilens)	0.85 ± 0.06	0.61 ± 0.01	265 ± 9
Cibasoft	0.81 ± 0.04	0.75 ± 0.11	135 ± 29
Hydrocurve II	0.28 ± 0.11	0.23 ± 0.08	150 ± 88

Table 5.5 Tensile properties of lenses used in handling trial

(mean value of at least one complete lens ± 1 standard deviation)

Unfortunately, some problems were encountered with the modulus determination of certain of the lenses in that there was a high degree of scatter, that one would not normally associate with the determination of modulus. The reason for this has already been expounded upon (see chapter 4 - determination of lens thickness). Thus the centre sample from each lens was subtracted from the results, and new mean values for modulus calculated. These are the values that were used for the comparisons in the following sections, and are given in table 5.6. Also shown in table 5.6, for comparative purposes, are the handling and inversion ratings as found by the group in Missouri.

	Modulus			Handling			Inversion		
	Mean	s.d.	n	Mean	s.d.	n	Mean	s.d.	n
Permaflex	0.22	0.03	7	3.898	1.051	88	3.575	1.254	87
Hydrocurve	0.31	0.04	2	3.761	1.114	88	3.489	1.356	88
Optima	0.34	0.03	4	3.500	1.104	88	3.784	1.264	88
D3 X4	0.34	0.03	2	3.384	1.180	86	2.898	1.406	88
0-3	0.35	0.07	4	1.723	0.875	65	2.492	1.336	66
Aquaflex	0.49	0.07	3	3.455	1.144	88	3.057	1.334	88
Minilens	0.61	0.01	3	3.682	1.273	88	3.227	1.311	88
Cibasoft	0.78	0.02	2	3.045	1.338	88	2.648	1.356	88
Zero 4	0.95	0.04	2	3.379	1.259	66	3.500	1.292	66

Table 5.6 Comparison between modulus and handling / inversion characteristics of a number of commercially available soft contact lenses

(Where s.d. represents 1 standard deviation, and n is the number of samples tested.)

There appears to be almost no correlation between the modulus of the lenses and the inversion statistics as found at Missouri. In the case of the handling, one lens in particular does not seem to fit any pattern, and that is the 0-3 lens which although giving an intermediate modulus value was markedly worse in terms of its rating for handling. Clearly this particular lens is very different from any of the other lenses tested in terms of its adjudged handling characteristics, and thus for the time being this result will be omitted from the more general analysis. If this is done, then there does appear to be a slight correlation between modulus and handling. This is illustrated by figure 5.4 where the handling statistic as found Gavett and and co-workers is plotted against the measured value of modulus. This graph would suggest that a lower value of modulus is associated with improved handling characteristics. Unfortunately this is not a particularly significant relationship, since the correlation coefficient is only approximately 0.4.

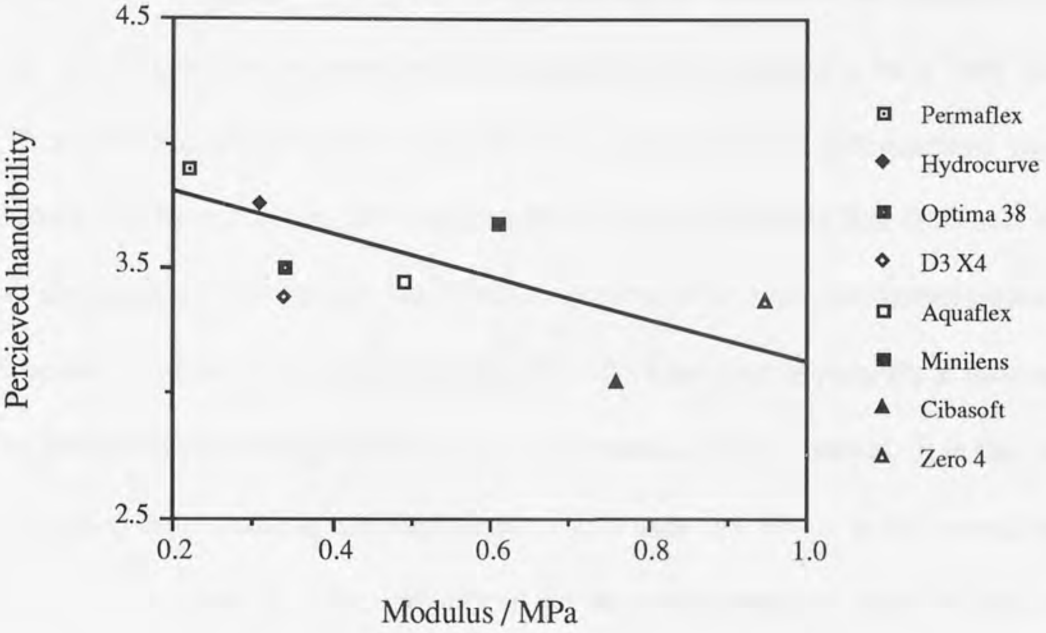


Figure 5.4 Relationship between handling and lens modulus

The explanation for this poor fit lies in the fact that what is referred to as the "handlebility" (ease of handling) of a lens actually covers a whole range of factors. In the quoted study, subjects were asked to consider the following points when rating the handling performance of each lens. 1) How much it (the lens) stuck to itself or one's finger, 2) Its general shape, 3) Its stability, and 4) Its flexure. Of these parameters, only the last 3 could be related in any way to the modulus of the material, and points 2 and 3 are likely to be influenced as much by lens design, as by modulus. Thus given the complex nature of the problem, it is not too surprising that only a casual relationship could be established between modulus and handling. It is also possible that this could explain why the 0-3 lens performed so badly in terms of its handling, but not for its modulus, in that this particular type of lens may be markedly "stickier" than any of the other lenses used in this trial. It is not clear from Gavett *et al.*'s work whether or not this was the case.

Why might a softer (less stiff) lens be associated with easier handling as these results seem tentatively to suggest ? One possible explanation for this is that the subjects are aware that the lens is going to be worn in the eye and that it is supposed to be a "soft" contact lens. Thus even though the lenses were not worn, there may be a subconscious move to those lenses that have a softer feel being preferred, since something that feels soft to the touch might suggest to the patient that it would necessarily be more comfortable once in the eye. The design of the lens (and perhaps its centre thickness) are apparently at least as important in determining handling performance, as the modulus of the material. It is also important to recognise that handling, although important, is only one factor in the overall lens design, and thus the softest lens may well not be the most comfortable to wear. If one considers the ideal contact lens to be a simple "extension of the cornea" then the most comfortable lens will be the one that matches the properties of the cornea most closely. Tighe (8) in his paper on the design of contact lenses gives a value for the modulus of the cornea as approximately 1.3 MPa. Thus on this basis the Hydron zero 4 material would be the best matched (of those materials tested) to the cornea in terms of its modulus value, and yet it rates poorly in terms of its handling.

In the work at Aston, lenses of power -1, were tested for most of the different lens types, as this would, it was felt minimise the problems encountered with the uneven thickness of the lens. In the case of the Permaflex material all three minus powers were tested, but because of the spread of results, and the fact that only 1 lens from each power was available, it was impossible to say with any degree of certainty that there was any effect on the tensile properties of the lens. In contrast however, the handling / inversion study did show some significant differences between the different powered lenses, - in general a higher minus power was found to be associated with easier handling characteristics. Clearly then the issue of contact lens handling is very complex in its nature and consists of a number of interrelated factors.

5.5 Improved Lens Design - Problems of Deposition and Staining

5.5.1 Anti-Deposit Lenses

One of the long standing drawbacks encountered in contact lens wear is that of the build up of protein deposits on the lens, a problem which is the target of much current research, particularly at Aston.(86) It would be of great commercial interest if a lens could be developed that was "non adhesive" to proteinaceaous material. To do this either requires a totally new material, or some form of novel surface treatment. It is well known in the field of biomaterials science that some synthetic polymers and molecules are less adhesive to biological species than others, and therefore incorporation of such a material into the lens is one valid approach. It is important to bear in mind, however that the other factors affecting lens performance must not be altered significantly, and that the appropriate regulations controlling the development of such devices (such as the F.D.A.) must be adhered to if the new material is to become commercially viable.

A range of new materials have been synthesised at Aston,(87) which it is hoped, will produce fewer deposits when worn in the eye. Some of this new material, which is based on an existing lens material consisting of NVP/MMA, was made into lenses and then the tensile properties were evaluated. The results are summarised in Table 5.7.

	Tensile Strength / MPa	Initial Modulus / MPa	Elongation to Break / %
1 (AD 05)	0.76 ± 0.06	1.10 ± 0.20	116 ± 11
2 (AD 06)	0.81 ± 0.04	1.22 ± 0.05	74 ± 3
3 (AD 07) (C)	0.50 ± 0.04	0.81 ± 0.07	87 ± 19
4 (AD 10)	0.34 ± 0.06	1.05 ± 0.14	37 ± 12
5 (AD 11) (A)	0.62 ± 0.08	1.22 ± 0.10	75 ± 15
6 (AD 12) (A)	0.64 ± 0.23	1.38 ± 0.18	66 ± 27
7 (AD 3 A1)	0.46 ± 0.05	1.08 ± 0.02	53 ± 7
8 (AD 3 B1)	0.45 ± 0.14	1.17 ± 0.02	45 ± 13

Table 5.7 Tensile properties of some anti-deposit lens materials

In general the results are quite interesting since they appear to produce a hydrogel that is of relatively high modulus, and low elongation to break. This is significant in that one of the design parameters was to produce lenses that had a similar equilibrium water content to those of conventional poly HEMA lenses. It is known that the only difference between lenses 7 and 8, is that sample 8 contained twice the amount of the material that was added to make the lens non adhesive, as sample 7, and this could explain the higher modulus and lower elongation to break of 8 when compared to sample 7. Furthermore, lens 3 is of the same composition as sample 7, but a different set of polymerisation conditions has been used. Any further conclusions are difficult to draw, since all the information is not available, but the results do show that the technique can be successfully used in order to compare the properties of new lens materials with existing ones, and so provide useful design information.

5.5.2 Corneal Staining

Another quite common problem found in contact lens wear is that of corneal staining. The precise explanation behind this phenomena is still not entirely clear, but there is a school of thought that it may be in part caused by lens dehydration. If the lens dehydrates on the eye, its properties will change - since the loss of the plasticising effect of the water results in a stiffer, and harder material. As a consequence of this the lens may not behave in the eye as it is designed to. The result could be increased friction and abrasion, leading to damage to the cornea, particularly if the lubricating effect of the tear film becomes disrupted in some way. This may very well have design implications, in that the stiffer lens may need to be redesigned to allow for a degree of movement on the eye (rather in the way a typical "hard" contact lens is allowed to move) so that the tear film can wash uniformly over the whole cornea. It is therefore important to know what effect the modulus of the lens has on the fitting and also the patients comfort (or discomfort). Such a study is complicated by the interrelation of modulus and water content in most commercially available lenses, those that have a high water content tending to have a low modulus and *vice versa*. To counter this, we attempted to make a series of new materials (all based on the existing approved contact lens monomers) that would cover a range of stiffness values, and yet have the same equilibrium water content. A target water content of 55% was set, and the materials prepared in the form of flat membranes, as described previously. They were then tested in order to determine their tensile properties, and water content. (see chapter 6). Once this had been shown to be successful, the same compositions were used to polymerise rods, which were eventually cut into the form of lenses. These lenses were then evaluated again for mechanical properties using the testing approach that has been used throughout this chapter.

At the same time, lenses of the same compositions were sent to a participating laboratory (The C.C.L.R.U. in Sydney) where they would do their own modulus evaluation. The results of the two trials are compared below. (Table 5.8)

	Aston	Sydney
1 NVP/MMA 60-40	9	6.33 (0.5 mm/min) 8.71 (2 mm/min) 9.68 (5 mm/min)
2 NVP/HexMA 67-33	2.5	1.68 (0.5 mm/min) 2.22 (2 mm/min) 2.59 (5 mm/min)
3 NVP/CHexMA 74-26	33	8.32 (0.5 mm/min) 14.54 (2 mm/min) 9.67 (5 mm/min)

Table 5.8 Comparison of modulii values (MPa) for new lens materials as determined by two different labs

These results require discussion, since the tests at Sydney were carried out under slightly different conditions. At Sydney a dogbone (dumbbell) shaped sample was used of gauge length 6mm and width 2mm, and the tests were carried out immersed in saline, and at room temperature. Tests were carried out at different crosshead speeds as indicated. Finally the measured lens centre thickness was used for their calculations of modulus. Fortunately the thickness of the lenses made, did not vary substantially across the lens, and values of thickness used were almost identical to those determined here. Although the first two materials give very good agreement for modulii values as found by the two labs, the stiffer material seemed to cause problems for the Sydney group, which they explained was due to the marked nonlinearity of the of the stress strain response. This then, could explain the differences in value as found by the two groups. The situation may not be quite as simple as this, in that we at Aston found material based on NVP/MMA to be the most non-linear of the three materials tested (see chapters 4 and 6) and believe the difference could be caused by problems the Sydney group experienced in gripping the material. Overall however, it is felt that the results give remarkably similar values considering the slightly different approaches used, and it is interesting to note the sensitivity to strain rate that was observed by the Sydney group. Regrettably results from the study on the effect of modulus on fitting and comfort are not yet available.

5.6 Concluding remarks

In this chapter we have shown just how powerful a technique tensile testing can be. It has been demonstrated that an average batch of contact lenses can be quite variable in terms of its mechanical properties, and that routine testing could be used to assess existing production methods. Secondly such tests can be particularly useful for comparative purposes, either within a run, or as on a basis for new lens design. Furthermore the effect that the modulus of the material has on both the handling of the lens and in terms of its comfort have been discussed. Finally further evidence has been presented of the reproducibility of the technique, thereby further enhancing its value. Thus despite its limitations, the methodology developed in the preceding chapter has several important applications within the contact lens field.

Chapter 6
The Design of Hydrogels of Improved Mechanical Properties - Towards a Synthetic Cartilage Material, Part I

6.1 Introduction

In the general introduction in chapter 1, the properties of two of the body's natural hydrogel composite structures were discussed. The cornea, by a unique arrangement of collagen fibrils in a water and proteoglycan matrix, allows visual acuity, and remains quite tough and elastic in order to resist the deforming forces caused by the eyelid during the blink cycle. Another body tissue that can withstand much greater physical stresses than the cornea, and yet consists of essentially the same fundamental "building blocks" exists in the form of articular cartilage. Through the process of evolution, nature has provided a remarkably efficient bearing material in cartilage, one that is stiff and strong, tough and durable, and that excels in its tribological behaviour. It is unfortunate however, that this process of design does not allow for the complete regeneration of damaged tissue, (although some limited repair can occur). The dehabilitating consequences of cartilage damage are well known to all arthritis sufferers, and hardly need to be elaborated upon here.

The gauntlet, then, has been thrown down; all that remains is for someone to pick up this unique and challenging opportunity in materials design. Hydrogel materials, because of their unique properties offer one approach to this problem. Their structural similarity to cartilage in terms of bound water, and their demonstrated biocompatibility, makes them a natural starting point for this sort of application. Few, if any of the synthetic hydrogel materials currently available possess the sort of mechanical durability that would be required for a synthetic cartilage material. The major failing of hydrogel materials in this respect is their lack of strength, and in particular stiffness - cartilage is roughly 200 times more stiff than poly HEMA for example, whilst containing twice the amount of water. Is it possible to produce a hydrogel material that will overcome some of these difficulties ?

6.1.1 Synthetic Strategy

The initial design problem then, is to develop a hydrogel material of improved strength and stiffness, without compromising its water content (since this is likely to render it less biocompatible). Such a material could be utilised as the matrix for a synthetic cartilage, and this matrix could then be used for further design modifications. In order to develop the matrix for this purpose, it is necessary to improve the mechanical properties of some of the existing hydrogels quite substantially, since the homopolymers are obviously too weak for this type of demanding application. A particularly useful way in which to start to make such improvements in strength, is the use of copolymerisation. Intelligent choice of comonomers may enable the development of the sort of hydrogel material that is required, but in order to be able to make this sort of choice, it is first necessary to gain an appreciation of the sort of improvements that are possible, and the fundamental structural reasons behind these changes. Only once this has been done, will it be possible to tailor the design so that the properties of cartilage itself are better reproduced. Figure 6.1 gives a schematic view of the sort of strategy that might be adopted in the design of a potential cartilage material.

In this chapter, a number of structure/property relationships in hydrogel chemistry are investigated, in order to gain a more thorough understanding of the mechanical behaviour of hydrogel materials. The production of a stiff strong hydrogel matrix (the first stage in the development of a potential synthetic articular cartilage material) by using the technique of copolymerisation, remains a central theme throughout this section of the work. In the subsequent chapter the potential of hydrogel materials for this application is further investigated, and some other synthetic strategies (outlined in figure 6.1) described. Other important design considerations will start to be taken into account, as the strategy, and testing procedures become more focussed.

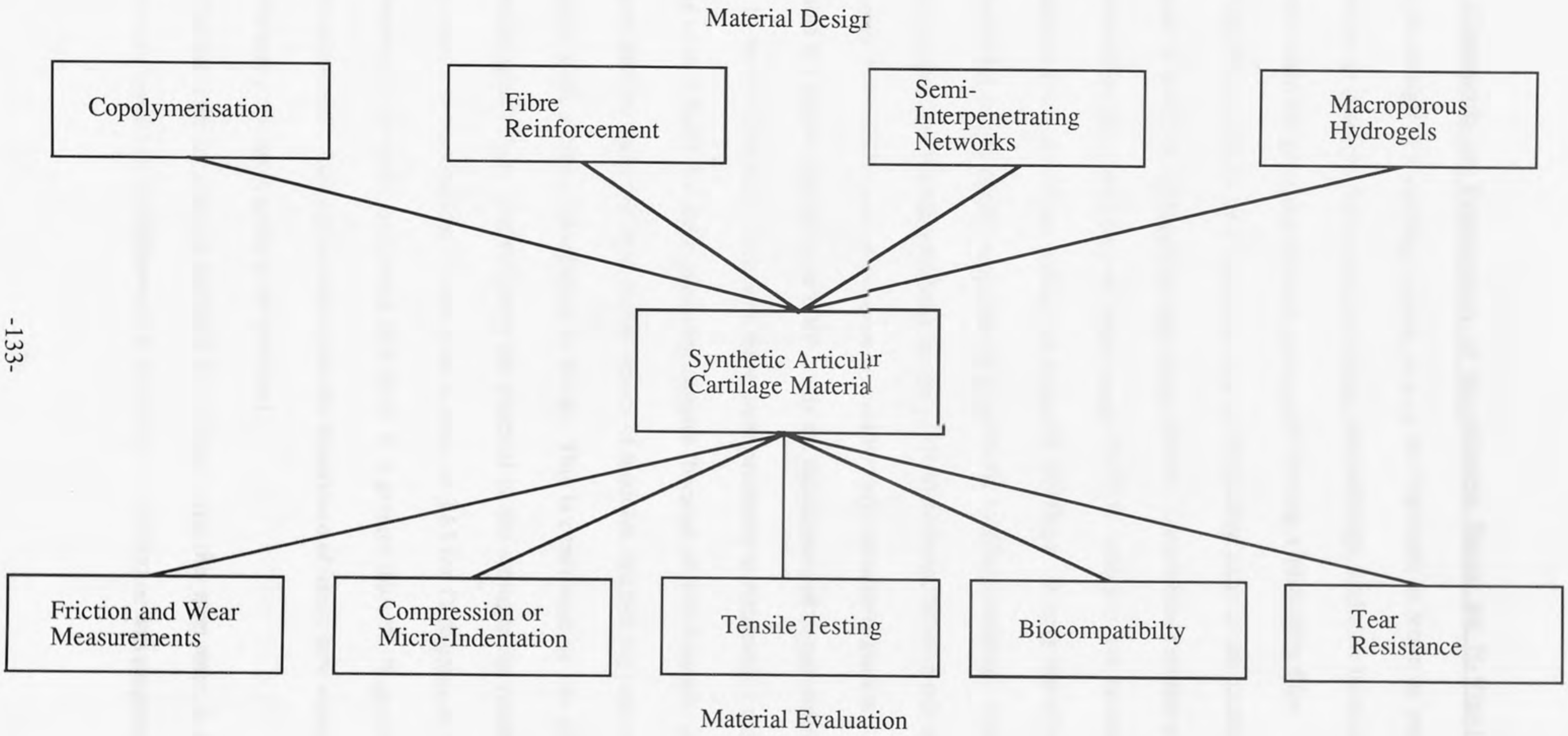


Figure 6.1 Schematic strategic overview

6.2 Comments on Preparation of Membranes Based on N-Vinyl pyrrolidone

In the design of a cartilage matrix, it may be important to retain as much water in the structure as possible, for reasons of tissue compatibility, and also because water may be exuded when the gel is compressed, potentially forming a lubricating film.

N-vinyl pyrrolidone is a monomer that is frequently used in the contact lens industry because it produces hydrogels of high water content. Lenses based on this material typically have equilibrium water contents in the range 70-75 %, which it will be remembered is not dissimilar from the water content of articular cartilage. It may therefore be a suitable hydrogel for use in the development of a synthetic cartilage material. Unfortunately, this monomer poses particular problems for the polymer chemist, because not only is it difficult to purify, but it is also one of the most unreactive vinyl monomers known.

Table 6.1 shows the effect of NVP purity on membranes of composition 85 wt % NVP and 15 wt % CHexMA. Although there were problems in obtaining a valid modulus and elongation to break for these particular samples (because of initial sample slack), the results suggest that the materials have similar values of modulus, but that the pure monomer gives a polymer with a higher elongation to break. This is confirmed by the values for tensile strength, which show that the purer the material is, the stronger the resultant membrane. Application of the students "t" test gives a value of 2.63 for 11 degrees of freedom for this difference in strength, indicating that there is a greater than 95 % probability that this difference is real. This again emphasizes the importance of using pure starting materials if a satisfactory polymer is going to be produced.

A further note concerning hydrogel fabrication using this monomer, is that of potential anisotropy caused by the differences in reactivity. A membrane was prepared from a

	Tensile Strength / MPa	Approximate Modulus / MPa	Approximate Elongation / %
Unpure NVP	2.42 ± 0.09	11	50
Pure NVP	2.57 ± 0.05	10	70

Table 6.1 Comparison of membranes of composition NVP 85 CHexMA 15 made using pure and unpure starting monomer

	Tensile Strength / MPa	Initial Modulus / MPa	Elongation to Break / %
Top	5.8 ± 0.6	54 ± 4	138± 30
Bottom	5.6 ± 0.3	~ 58	109 ± 35

Table 6.2 Comparison between samples cut from the top and bottom of the same membrane (composition NVP 50 MMA 50)

Crosslinker	Tensile Strength / MPa	Initial Modulus / MPa	Elongation to Break / %	EWC / %
1 wt % AllylMA	2.5 ± 0.2		113± 18	67
1 wt % (Allyl 50 EGDM 50)	3.4 ± 0.1	~ 12.5	99 ± 6	62
1 wt % EGDM	4.1 ± 0.2	~ 22	45 ± 6	58

Table 6.3 Effect of crosslinking agent on the mechanical properties of an NVP based hydrogel (NVP 80 ChexMA 20)

monomer mixture consisting of 50 wt % NVP and 50 wt % of methyl methacrylate, which was allowed to stand upright in the oven during curing. MMA was chosen on the basis of its very different reactivity when compared to NVP, and by standing the mould upright in the oven it was hoped to induce some non-uniformity into the membrane. The results given in table 6.2 suggest that this was not achieved, since samples from the top of the membrane were not substantially different from those taken from the bottom. In addition to these results however, it was observed that there was a region towards the top centre of the membrane, that was noticeably thinner than the surrounding material. It is probable that this area was the last region to cure, and was therefore richer in the unreactive NVP. On subsequent hydration the unreacted material would be leached out, and this could explain why a thinner region of membrane developed. This demonstrates that caution needs to be exercised in the choice of monomer pairs, and also shows the importance of polymerisation conditions.

In chapter 3 it has already been shown that the choice of crosslinking agent is a particularly important parameter in hydrogel chemistry. This is never more the case, than with a relatively inert monomer such as NVP, as the results in table 6.3 clearly indicate. As anticipated AllylMA is seen to be a more efficient crosslinking agent with NVP, producing polymers with a much improved elongation to break, when compared to those using EGDM. There is also a reduction in the water content of the hydrogel if EGDM is used as the crosslinker, and this is accompanied by the production of a significantly stiffer material. Since the design of a stiffer material was one of the prime objectives for this section of the work, generally EGDM was the crosslinker of choice here. Using this reagent also had the added benefit of producing a material with a more linear stress/strain response in the 0-20 %

strain region, than similar polymers prepared using AllylMA, and this was felt to be desirable for the design of the cartilage matrix.

6.3 Comparison of HEMA Based and Vinyl Pyrrolidone Based Hydrogels

As has been suggested in the section above, NVP may make a useful potential cartilage matrix material because of its high water content. However it still may be necessary to reduce the water content of the hydrogel in order to provide a stiff enough matrix, and so the use of HEMA copolymers would provide both a suitable starting point, and a basis for comparison with the NVP based polymers.

Table 6.4 demonstrates what sort of range of properties can be obtained by copolymerisation. In this case, increasing proportions of the comonomer tertiarybutyl methacrylate (TBMA) were added to make a series of NVP based and HEMA based hydrogels, which were then tested in tension in the manner described in chapter 3. The results show that as the proportion of comonomer is increased, so in general do the failure strength and modulus of the membranes. As if to counter-balance this increase, it will be noticed that there is both a drop in water content, and a significant reduction in the elongation to break of the gels, as one might have predicted. Strengths of an order of magnitude improvement over the homopolymers can be achieved by the addition of 30 wt % of TBMA, and in terms of the modulus the increase is even more dramatic - several hundred times better in the case of the HEMA based membranes.

At first sight it might be tempting to suggest that the first objective has been achieved, since stiffnesses of a similar order of magnitude to that of cartilage are clearly possible by means of copolymerisation, and indeed may even be improved upon. Unfortunately most of these hydrogels would still be unsuitable as a cartilage matrix material. The reason behind this lies in the nature of the stress/strain behaviour of the polymers, which are depicted in

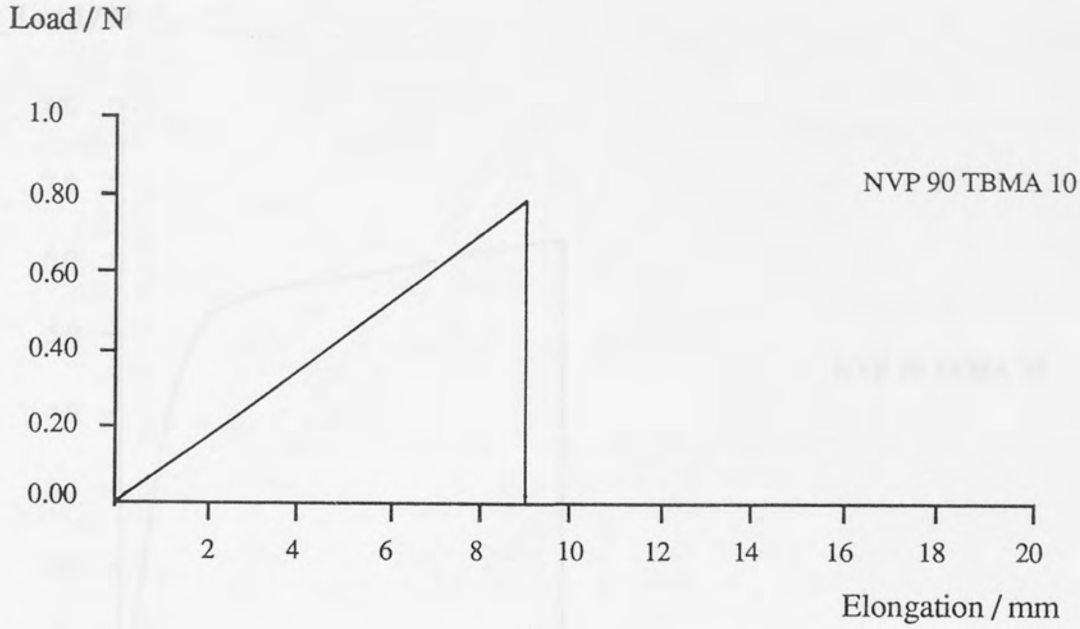
Composition wt %	Tensile Strength / MPa	Initial Modulus / MPa	Elongation to Break / %	EWC / %
NVP 90 TBMA 10	0.55 ± 0.06	0.51 ± 0.03	120 ± 27	81.0
NVP 80 TBMA 20	2.46 ± 0.07	12.0 ± 1.1	81 ± 13	66.4
NVP 70 TBMA 30	5.95 ± 0.20	48.8 ± 2.4	59 ± 9	52.2
HEMA 90 TBMA 10	2.13 ± 0.16	1.2 ± 0.2	347 ± 11	26.6
HEMA 80 TBMA 20	9.82 ± 0.73	26.7 ± 2.9	289 ± 14	18.0
HEMA 70 TBMA 30	23 ± 2	~ 350	30 ± 10	12.5

Table 6.4 Comparative tensile properties of NVP and HEMA based hydrogels

figures 6.2, 6.3 and 6.4.

In the case of the NVP based polymers the response changes from an almost linear shape, with moderate elongation, to a significantly more brittle material which has a pronounced yield point occurring at about 10 % strain. For the intermediate composition, there is no distinct yield point, although there appears to be a more gradual yielding which results in the markedly curved shape of the stress/strain curve for this particular sample.

In the case of the HEMA based materials the change in behaviour with increasing comonomer content is very noticeable. At the 10 % additive level, the stress/strain curve is very similar in shape to that of lightly crosslinked poly HEMA without the addition of a comonomer, and shows the sort of response that is characteristic of elastomeric materials.



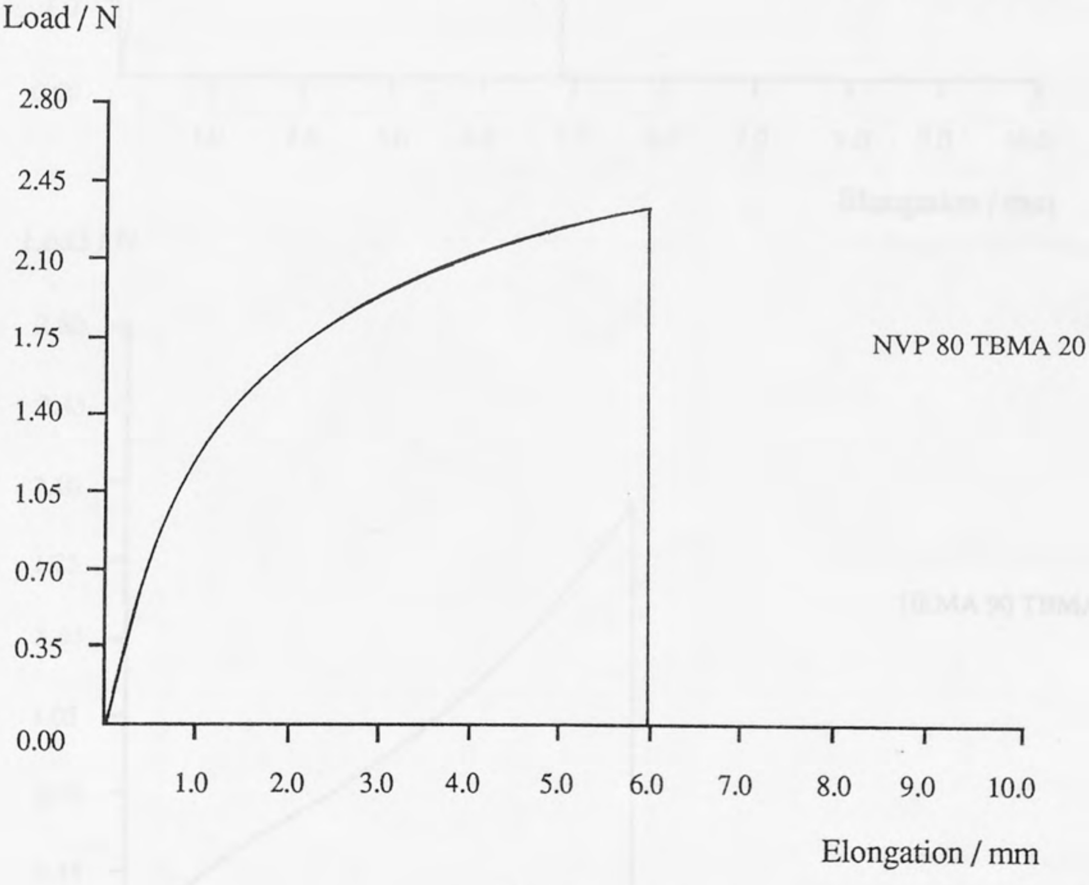


Figure 6.2 Load/elongation curves for some hydrogel copolymers

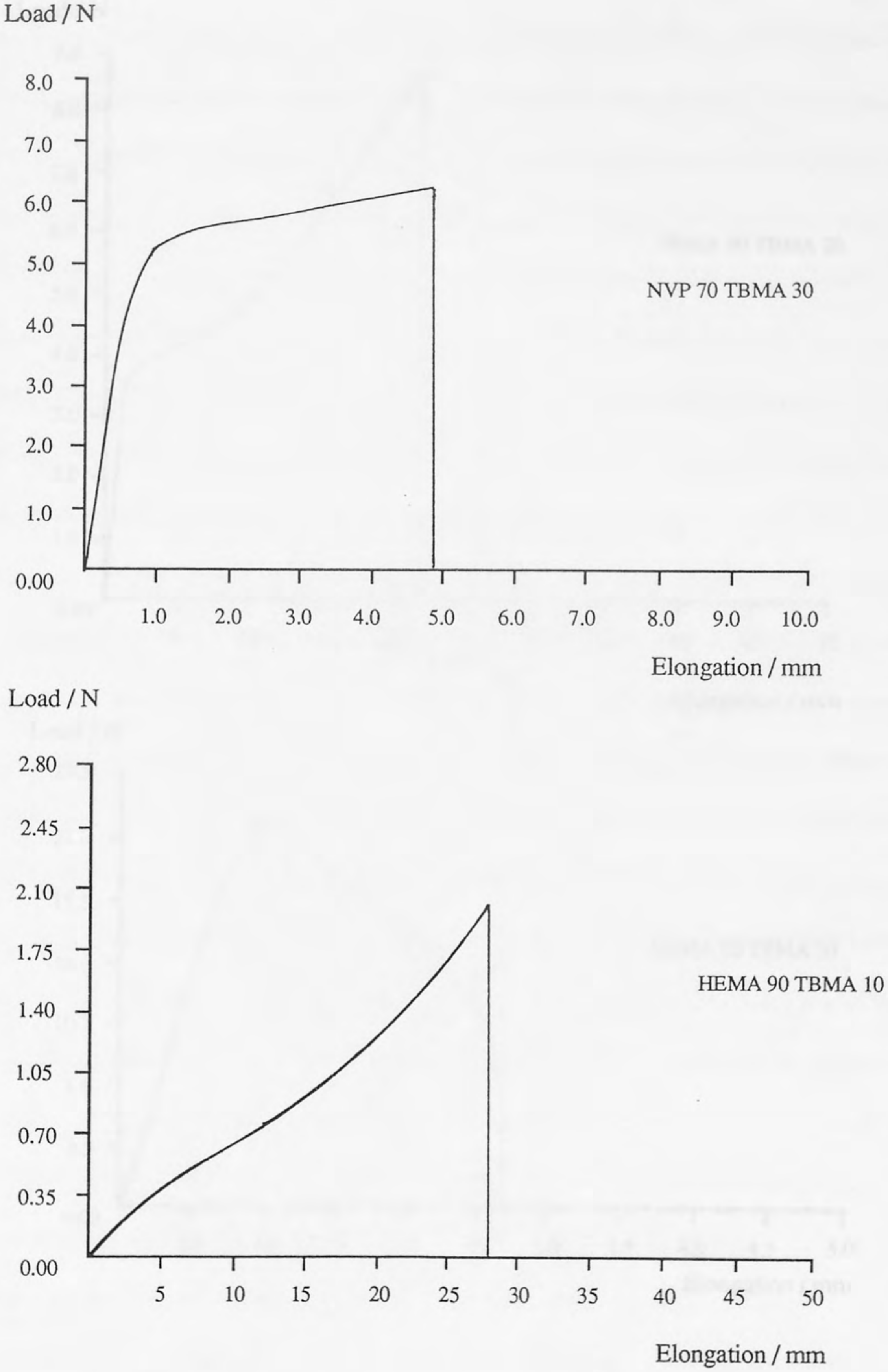


Figure 6.3 Load/elongation curves for some hydrogel copolymers

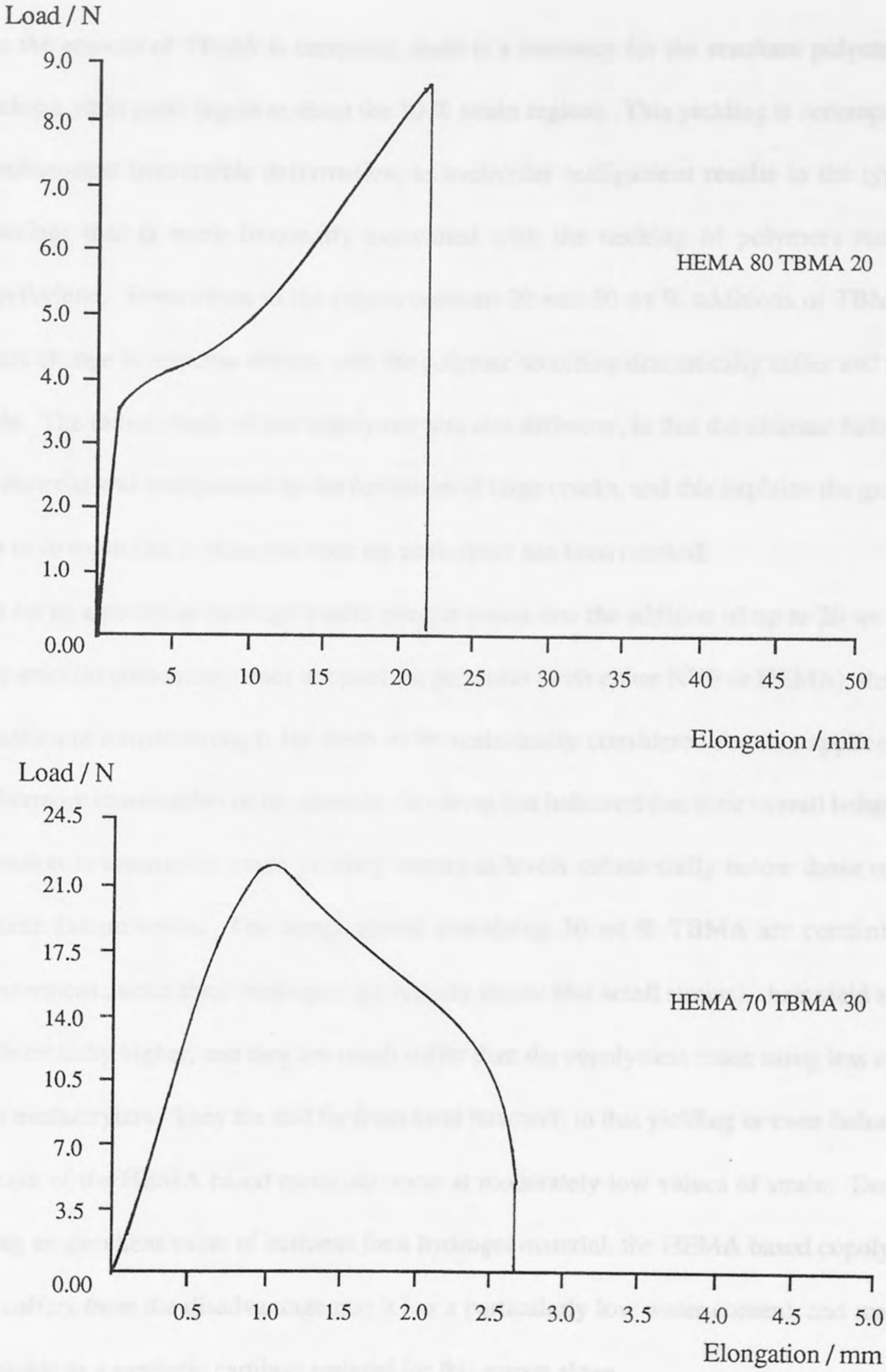


Figure 6.4 Load/elongation curves for some hydrogel copolymers

As the amount of TBMA is increased, there is a tendency for the resultant polymers to develop a yield point (again at about the 10 % strain region). This yielding is accompanied by subsequent irreversible deformation, as molecular realignment results in the type of behaviour that is more frequently associated with the necking of polymers such as polyethylene. Somewhere in the region between 20 and 30 wt % additions of TBMA, a further change in response occurs, with the polymer becoming dramatically stiffer and more brittle. The failure mode of this copolymer was also different , in that the ultimate failure of this material was precipitated by the formation of large cracks, and this explains the gradual drop in strength that is observed once the peak stress has been reached.

As far as a potential cartilage matrix goes, it seems that the addition of up to 20 wt % of this particular comonomer does not produce polymers (with either NVP or HEMA), that are of sufficient tensile strength for them to be realistically considered for this application. Furthermore examination of the stress/strain curves has indicated that their overall behaviour in tension is unsuitable, since yielding occurs at levels substantially below those of the ultimate failure stress. The compositions containing 30 wt % TBMA are certainly an improvement , since these hydrogels are linearly elastic (for small strains), their yield stress is substantially higher, and they are much stiffer than the copolymers made using less of the butyl methacrylate. They are still far from ideal however, in that yielding or even failure (in the case of the HEMA based material) occur at moderately low values of strain. Despite having an excellent value of stiffness for a hydrogel material, the HEMA based copolymer also suffers from the disadvantage that it has a particularly low water content, and may be unsuitable as a synthetic cartilage material for this reason alone.

On the basis of the above argument, N-vinyl pyrrolidone based copolymers seem to offer the greatest potential for the application being considered. There were however, quite important differences in behaviour between the NVP based series of copolymers and those based on HEMA, which are worthy of further discussion. The main reason behind these differences can be found in the low reactivity of the NVP monomer. At the lower comonomer contents, the NVP materials have a much lower elongation to break than their HEMA counterparts, and this is explained partly by the choice of crosslinker, which as we have already seen is less efficient with the unreactive NVP monomer, and also due to the difficulty of obtaining this monomer in a sufficient degree of purity. The effect caused by this crosslink distribution would also explain why the stress/strain behaviour of the NVP materials is not typically elastomeric in response, unlike that of the similar HEMA copolymers. At higher levels of comonomer addition both the HEMA copolymers and the NVP copolymers show a greatly increased stiffness over their respective homopolymers. In both cases this can be explained by the corresponding reduction in water content, the loss of the water that is not associated with the polymer matrix meaning that the resultant material is less plasticised. In the case of the NVP material, there may also be a further effect that could help to explain the increased stiffness, and this again is related to the unreactivity of this particular monomer. The theories of copolymerisation tell us that if two monomers of very different reactivity are used, then it is likely that one will react more with itself than its comonomer, resulting in the formation of a block copolymer. It is therefore probable that the structure of the NVP/TBMA material consists of long sequences of methacrylate, and that this blockiness results in a polymer that is stiffer than an equivalent alternating or random copolymer might be.

6.4 The Effect of Different Comonomers on the Mechanical Properties of NVP Based Hydrogels

In previous section it was shown that NVP and HEMA based hydrogels can be improved by the use of copolymerisation, and it was also suggested that NVP based hydrogels could be used as the basis for further research in the development of a synthetic cartilage material. The choice of TBMA as a comonomer in section 6.3 was essentially a random one, and in order to optimise the design it is necessary to try and understand the structure/property relationships that are found in a range of NVP based copolymer hydrogels. With this in mind ranges of hydrogel membranes were prepared, mostly based on NVP, which contained increasing proportions of different comonomers. Generally, at least 3 membranes were made and tested for each particular monomer pairing, using concentrations of 10, 20 and 30 wt % of the more hydrophobic reagents.

As expected the greater the amount of comonomer added, the greater the strength and modulus of the membranes. Again, the increased properties are offset by a reduction in the overall water content of the gels, and by a drop in the elongation to break. If sufficient compositions are tested, then it is possible to construct a master curve of a specified property (tensile strength for example) against the equilibrium water content of the gel, and this is done in figure 6.5 for two series of hydrogel copolymers based on NVP. This figure shows that the relationship between the total water content of the gel and its tensile strength is not linear, and that it is only for additions above 20 wt %, that there is any appreciable effect on the mechanical properties of the polymers produced.

This sort of curve is particularly valuable, since it may enable further predictions to be made. For instance it may be useful to know what sort of mechanical properties can be achieved for a copolymer of 50 % equilibrium water content. Similarly the approximate

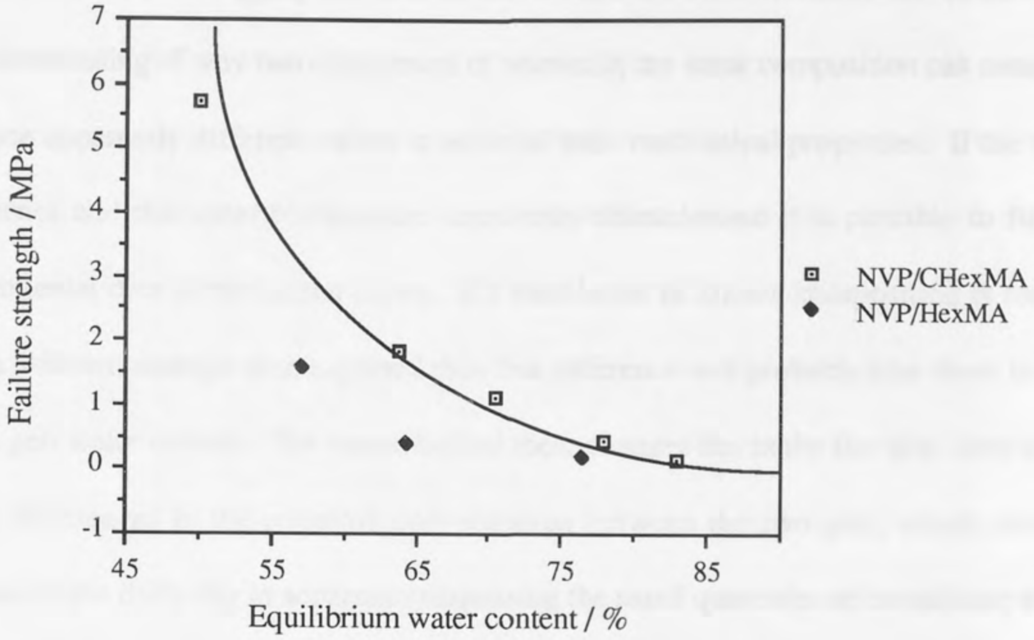


Figure 6.5 Failure strength versus equilibrium water content for two series of hydrogel copolymers

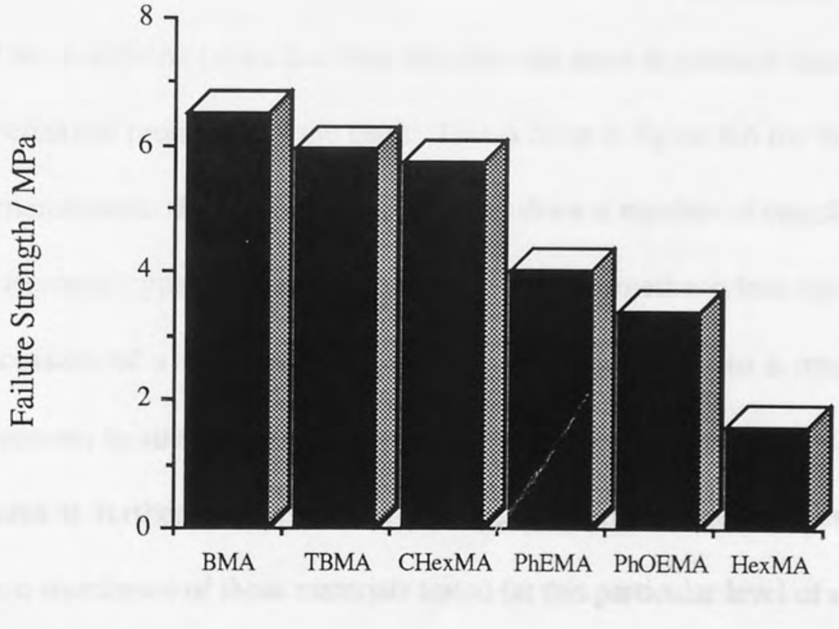


Figure 6.6 The influence of different comonomers on the tensile strength of NVP based hydrogel copolymers (all at 70 wt % NVP)

copolymer composition that is required to give gels a particular strength or water content can be estimated from the appropriate master curve. The use of such master curves also offers an understanding of why two copolymers of nominally the same composition can sometimes produce apparently different values in terms of their mechanical properties. If the tensile properties and the water contents are accurately characterised it is possible to fit other experimental data to the master curve. If a membrane of known composition is found to give a different strength than expected then this difference will probably also show in terms of the gels water content. The reason behind these changes lies in the fact that there may be slight differences in the crosslink concentration between the two gels, which can arise because of the difficulty in accurately dispensing the small quantities of crosslinker that are required to make a membrane.

We are now in the position where we can start to investigate structure property relationships in a little more detail. This can best be done by comparing the copolymers at the 30 wt % addition (since less than this does not seem to produce significant differences in the mechanical properties of the gels). This is done in figure 6.6 for the tensile strengths of these membranes. From this it is possible to draw a number of conclusions. Comparison of the isomeric cyclohexyl methacrylate and n-hexyl methacrylate clearly demonstrate that the inclusion of a ring into the hydrogels structure leads to a much more significant improvement in strength (and modulus) than the more linear form. The influence of ring structures is further emphasised by the benzyl methacrylate copolymer which gave the strongest membrane of those materials tested (at this particular level of comonomer content). Following on with this argument, figure 6.6 shows that the phenyl monomers also offer an improvement in strength over the HexMA material as one might have anticipated. It is interesting to note the difference between the phenylethyl and the phenoxyethyl methacrylates, where the phenoxy compound is seen to be slightly less stiff and less strong than its neighbour. Examining the respective structures of these monomers shows why this might be the case. The main structural difference between these two methacrylates is that the phenoxyethyl material incorporates the addition of an extra oxygen atom in the form of a flexible linkage or bridge (figure 2.2). This makes this part of the molecule more susceptible to the plasticising influence of the water in the hydrogel and explains why it is less good mechanically, than the phenylethyl methacrylate copolymer.

The NVP/TBMA copolymer (used in the comparison between NVP and HEMA membranes) also gives a strong membrane, and in terms of its tensile failure strength is slightly better than the cyclohexyl methacrylate, but not as good as the benzyl material. In this case it is the bulky nature of the three methyl groups that causes the observed increase in strength and stiffness. It is reasonable to predict that the preparation of membranes using the monomers isobutyl methacrylate and n-butyl methacrylate will give hydrogel membranes whose tensile properties will fall somewhere between those of the tertiarybutyl copolymer and those of the n-hexyl methacrylate one.

These results indicate that the incorporation of bulkier more hydrophobic groups into the hydrogel backbone produce greater increases in mechanical properties (for a similar concentration of comonomer) than those of monomers having a more linear structure. These bulkier groups generally correspond with those methacrylates that have a higher value of glass transition temperature (see table 6.5). The Tg of the comonomer however, is only one factor, and the complete structure/property relationship is considerably more complex than this. Some of the reasons for this have already been hinted at, for example, the difficulty in obtaining pure starting materials, and the effects of the polymer sequence distribution. This latter point is illustrated by the copolymers of NVP/MMA in section 6.3. Here the polymer

Polymer	Glass transition temperature /°C
Poly (tertiarybutyl methacrylate)	114
Poly (methyl methacrylate)	105
Poly (cyclohexyl methacrylate)	83
Poly (benzyl methacrylate)	54
Poly (phenylethyl methacrylate)	26
Poly (n-hexyl methacrylate)	-5

Table 6.5 Glass transition temperatures of some methacrylate polymers

produced at 50 wt % MMA is noticeably better in terms of its elongation to break than might be expected for a similar content of the hydrophobic benzyl material for example. In addition the more linear of the comonomers can sometimes produce hydrogels of a relatively high elongation, under the right conditions. In the case of the HexMA copolymers, the elongation to break of the 30 wt % copolymer is actually much better than the same reagents used in a 90/10 ratio. A possible explanation for this again may rest with the sequence distribution of the copolymer. It is also possible however, that the low elongation found in the 10 and 20 wt % is caused more by a lack of purity of some of the monomers used, rather than the resultant structure of the membrane itself.

In terms of the stress/strain behaviour of these different copolymers, there were in fact few differences between them. The types of behaviour that were shown are very similar to those of the NVP/TBMA copolymers, which has already been described elsewhere. Only the three strongest comonomers (benzyl, cyclohexyl, and tertiarybutyl methacrylates) produced a sharp yield point at high wt %, the other materials giving a more gradual yield as that in figure 6.2 (bottom). The 30 % HexMA material showed yielding almost immediately although the general form of the curve was similar to that in figure 6.2 (80/20 blend), except with a greater elongation to break. The NVP/MMA material discussed, behaved rather like polyethylene, in this case the formation of the neck was much more stable in that the stress remained constant for quite a considerable amount of strain, before final failure. (Compare this with the 80/20 HEMA/TBMA material).

An extremely important factor that has not yet been discussed in any detail, is the influence of water on the polymers properties. Although it has been shown that different comonomers can produce hydrogels of quite different mechanical properties, it may be that some important differences are being masked because of the varying levels of water contained within the structures. This issue will be dealt with in the next section.

6.5 Comparison of Hydrogel Copolymers of Different Compositions, but Similar Equilibrium Water Content

In the general introduction, the importance of water in hydrogel structures was described. In particular, the nature of this water, whether it is bound or free, and the controversy surrounding these various descriptions were discussed. The presence of water is of particular relevance to the mechanical properties of hydrogels, since water has a considerable plasticising effect on these particular materials.

Using the type of master curve that was outlined in the previous section, it was possible to prepare a range of hydrogel copolymers that had a similar total equilibrium water content. Because they were later also intended to be made into lenses (Chapter 5) an intermediate value of water content was chosen, and in addition a mixed crosslinker was used which consisted of 50 % AllylMA and 50 % EGDM. Having prepared and tested these materials in tension, it is now possible to make more meaningful comments concerning the structure property relationships in hydrogel materials. For similar water contents, the results shown in table 6.6 show that variations in modulus of at least an order of magnitude can be achieved solely by changing the comonomer, although the increase in failure strength is less dramatic, a factor of roughly 3 was achieved for the range of hydrogel polymers that were tested here.

Some of the structural features that were outlined previously are seen to be still valid at these similar levels of water content, in particular the greater improvement in strength and stiffness that is associated with the ring structures as opposed to the more linear polymers, and also the improved elongations to break that are achieved with the more linear arrangements. Again the MMA copolymer is particularly extensible, confirming the theory that the polymer sequence distribution plays an important role in determining the properties of this particular

Composition / wt %	Tensile Strength / MPa	Initial Modulus / MPa	E (0.06) (0.13) / MPa	Elongation to Break / %	EWC / %
NVP 60 MMA 40	2.8 ± 0.1	~ 3.7	3.5 ± 0.6	223 ± 12	56.8 ± 0.7
NVP 70 PhOEMA 30	3.7 ± 0.2	~ 6.8	5.6 ± 0.9	135 ± 15	56.3 ± 0.6
NVP 74 CHexMA 26	5.0 ± 0.2	~ 30	22 ± 1	87 ± 8	56.3 ± 0.4
NVP 67 HexMA 33	1.8 ± 0.2	~ 2.2	1.7 ± 0.3	151 ± 18	56.5 ± 0.8
NVP 73 CHex 18 Hex 9	4.4 ± 0.3	~ 15	14 ± 3	98 ± 10	58.8 ± 0.2
NVP 70 CHex 10 Hex 20	4.7 ± 0.2	~ 22	19 ± 3	111 ± 8	55.0 ± 0.3
NVP 57 CHex 21.5, EOEMA 21.5	4.6 ± 0.1	~16		158 ± 9	55.8 ± 0.6

Table 6.6 Comparison of the tensile properties of a range of hydrogel polymers, having the same total equilibrium water content

copolymer blend. The effect of the mixed crosslinker is also quite clear, in that the elongations to break for this set of polymers are improved with respect to those of the copolymers based on 1 % EGDM used in the earlier section on copolymerisation.

A number of other minor structural variations were also made in this section of the work. For instance, terpolymers were made consisting of NVP with the two hexyl methacrylates in the proportions 2 to 1 and 1 to 2 to see if this made any significant difference to the resultant tensile properties. In actual fact these particular hydrogels behaved in a very similar manner, the stress/strain curves being almost identical. In terms of the figures produced for the tensile properties, there were some minor differences, in that the blend containing the greater proportion of cyclohexyl methacrylate was slightly less extensible than its partner. Failure strengths were very similar and this is because although the one had a greater elongation to break, this improvement was primarily restricted to the post yield region, where there is little change in stress for quite large variations in strain. Surprisingly the polymer with the greater cyclohexyl methacrylate content did not produce the stiffer material, although this is most likely due to its slightly higher water content (~ 59 %).

A further point concerns the use of the monomer ethoxyethyl methacrylate. This was incorporated into a terpolymer in the hope that a more flexible hydrogel might be produced, on the basis that this monomer is easily plasticised by water, and that its reactivity is more compatible with both that of the NVP and that of the allyl ends of the crosslinking agent. This strategy appears to have been quite successful, in that the elongation to break of this hydrogel is markedly better than that of a comparable copolymer or terpolymer containing similar amounts of the cyclohexyl methacrylate monomer. Even so the polymer still shows a yielding at around 10 % strain, so that this increase in elongation is probably of little consequence in engineering terms, and in particular does not make it any more suitable as the matrix for a cartilage replacement material.

At this juncture it is worth emphasising that these copolymers and terpolymers were prepared on the basis of trying to achieve similar total equilibrium water contents. This does not necessarily make them directly comparable since water is known to exist in two different states in hydrogel materials. In order to determine the relative proportions of free and bound water, the use of differential scanning calorimetry (DSC) was employed. By quenching the polymer rapidly to a temperature below that of the freezing point of water, and then allowing it to heat up at a constant rate, it is possible to determine the amount of freezing water, which is equivalent to the water that is not associated with the polymer matrix (the so called free water) Preliminary work with the DSC showed that for most of the polymers in this section a similar behaviour was found, and that the water structuring showed little dependence on the comonomer type. This is a particularly striking observation since it shows that the water structuring is still dominated by the NVP (at this particular level of total EWC), even though in order to obtain a similar EWC, the proportion of NVP varies from 60 to 75 %. Thus at these moderate water contents the nature of the imbibed water is independent of the type of comonomer used.

6.6 Conclusions

The results from this chapter have shown that copolymerisation can substantially improve the tensile properties of hydrogel membranes, and that copolymers based on NVP are able to provide the sort of properties that might be useful in the first stage of the design for a synthetic cartilage material. By using a variety of comonomers, and preparing a range of polymers of similar water content, it was possible to gain some insight into the structures and the resultant tensile properties that were obtained. Although considerable improvement is still necessary, this part of the work has enabled the selection of potential cartilage materials on a more logical basis. Further development can now be continued, using this sort of hydrogel as the basis for more applied research.

Chapter 7

Towards a Synthetic Articular Cartilage Material, Part II

7.1 Introduction

Copolymerisation then, can produce hydrogels of improved strength and stiffness. Nevertheless, this type of material is not going to be of much use as a synthetic cartilage replacement, because the requirements for such a prosthesis extend far beyond those of just failure strength and stiffness. In this chapter, the further optimisation of synthetic analogues to articular cartilage are discussed. This can best be done by following the format that was outlined in figure 6.1. Each of the remaining areas will now be dealt with in turn.

7.2 Synthetic Strategies

7.2.1 Fibre Reinforcement

The use of composite structures is widely adopted by nature in her design of body tissues, as we have already seen in chapter 1. Similarly, the use of stiffer fibres to reinforce a more pliant matrix material is a technique that has successfully been employed in the design of high performance engineering composites such as carbon fibre reinforced, and kevlar reinforced plastics. In order to develop a successful synthetic cartilage material it will almost certainly be necessary to make use of a composite structure, the matrix of which could well be based on the types of hydrogel copolymer we have already seen.

The appropriate choice of the reinforcing agent is the next problem (although this need not necessarily exist in the form of fibres - see section 7.2.2) Carbon fibres have already had some success in prosthetic devices such as artificial ligaments and tendons, and may therefore be one potential way forward. In the last couple of years, the use of a carbon fibre mesh has been proposed as a partial cartilage replacement, and initial trials appear to have been relatively successful (chapter 1), although such a hard, brittle material hardly seems to be the ideal solution, and this idea is still treated with scepticism by a number of orthopaedic surgeons.

An interesting alternative approach might be to make use of a more obviously compatible reinforcement, for instance collagen fibres could be employed as the reinforcing agent. The idea of using collagen is not a new one, and the use of collagen graft copolymers (88, 89) for instance, has been tried in a number of potential biomedical applications, with some limited success. It has been demonstrated that reconstituted collagen fibres can be produced with quite high values of tensile strength, the sort of values obtained matching that of collagen found in tendons for example (90). However it is not yet clear whether this strength can be amply transferred to that of a softer matrix material, in order to produce sufficient reinforcement for a demanding application like that of synthetic cartilage material. To date, although collagen fibres have been successfully incorporated into hydrogel structures, they have only been able to provide the sort of strengths that are necessary to support light loading. A good instance of this is the case of a typical hydrogel wound dressing material, where the collagen fibres form a supporting scaffold, around which the natural processes of healing are allowed to develop. Consequently, although the use of collagen fibre reinforcement seems to possess a high degree of potential, it has not been pursued any further.

7.2.2 Semi-interpenetrating Networks

The previous section outlines a method where the reinforcement of the composite structure is on an essentially macro scale, the fibres being used rather as they might in a conventional fibre reinforced plastic, and existing as a distinct separate phase. Reinforcement can also be achieved at a macromolecular level however. One manner in which this can be done is by means of a semi-interpenetrating network. Here, one polymer is synthesised around another, to form a structure that is somewhat analogous to that of ivy growing on a trellis. Thus a lightly crosslinked hydrogel material can be formed around a stronger polymer, which will then act as the reinforcing agent. Corkhill *et al*,(91) have shown that cellulose acetate and cellulose acetate butyrate are particularly successful as this type of reinforcing material. In addition it has been shown that the molecular weight of the reinforcing polymer has an important influence on the resulting mechanical properties of the polymer, the higher the molecular weight, the better the strength of the structure. A semi-interpenetrating network polymer has been synthesised that consisted of a matrix of a NVP/MMA copolymer, and this was then reinforced using cellulose acetate butyrate (CAB). This material was tested in tension and found to have a tensile strength in the range 7-8 MPa and an initial modulus of approximately 80 MPa. The water content of this hydrogel was still quite substantial and was approximately 50 %. Even better mechanical properties can be achieved, although in order to do this, there is a penalty, in that the water content of the material has to be allowed to drop to nearer 40 %. The elongation to break for these types of IPN materials is also quite reasonable, and is certainly equivalent to that of normal articular cartilage (about 80 %). This sort of synthetic approach then, shows particular promise, and a number of hydrogel materials of this nature are currently undergoing further trials.

7.2.3 Macroporous Hydrogels

At first glance, the use of a macroporous hydrogel matrix seems somewhat of an ironic contradiction to all the previous work. The strategy to date has been concerned with making hydrogels stronger and stiffer, and yet now it is being suggested they be made weaker by the deliberate inclusion of porosity. This perhaps deserves some explanation. The use of a macroporous material is a vital part of the design strategy used in this work. As has already been suggested in chapter 1, the inclusion of porosity may permit the formation of bone ingrowth. This is a highly desirable objective, in that bone ingrowth would overcome one of the main problems that is associated with that of a cartilage graft, namely that of anchorage to the subchodral bone.

One way in which hydrogels can be made macroporous is to polymerise the hydrogel in a water/ethylene glycol mix. The polymer is then synthesised around ice crystals, which on subsequent warming to room temperature melt, rendering the resultant structure porous. This method of preparation is less than ideal however, in that it is difficult to control the pore size, and that the pores that are produced generally tend to be quite large. (The ideal size of pores suitable for bone ingrowth is thought to be quite small, and is of the order of 50 μm). A further factor to the disadvantage of these simple macroporous gels is that, in order to give them structural integrity it is necessary to make use of quite a high crosslink concentration (approximately 10 %), and this makes the materials unsatisfactorily brittle.

The solution lies with the use of the IPN's that were described in the previous section. Here, the materials are already mechanically strong, so that the use of a high crosslink density is no longer required. In order to overcome the problem associated with the pore size, instead of polymerising the structure around ice crystals, it is possible to use dextrin as the scaffold instead. This can then be dissolved out by autoclaving the polymer in the presence of weak acid, whereby the dextrin is removed via a process of hydrolysis. The resulting polymer has a porous structure, with pores of approximately 30-60 μm depending on the original size of the dextrin particles used. Such a structure is illustrated in plate 5.

The use of autoclaving is in fact quite significant, since the material will have at some stage, to be sterilised in some way before implantation, and a convenient form of sterilisation is to autoclave the material. It could therefore be demonstrated that the use of autoclaving (at a temperature of about 120°C) does not significantly affect the material's mechanical properties, so that another potential problem seems to have been overcome, although it must be said that autoclaving is not the only acceptable method of sterilisation for implant materials.

Tensile tests on this type of structure (i.e. a macroporous semi-IPN), have indicated that tensile strength and modulus are not appreciably reduced by the inclusion of porosity, provided that the pores are smaller than about 60μm, although they are slightly more brittle than a similar structure without pores. Thus the formation of inter-penetrating networks and the production of macroporous structures form an integral part of the strategy employed here to develop a synthetic articular cartilage material.

7.3 Characterisation and Evaluation

7.3.1 Biocompatibility Testing

The evaluation of a material's so called biocompatibility is a science in itself. Because of its critical importance to the successful adoption of any prosthesis, a brief mention of this science will be made here. The use of cell culture techniques to assess compatibility of various materials for biomedical applications has been well documented, and in particular the application of cell culture techniques to hydrogel materials has been studied extensively within the speciality materials group at Aston.(92) Initial tests on possible substrate materials, are often carried out using baby hamster kidney (B.H.K.) cells, although other cell lines can of course be used. There are essentially two stages in cell response, the first of which is cell attachment, and the second of which is cell spreading.

Cell attachment on its own is rarely a sufficient indicator of compatibility, and therefore the degree of cell spreading also needs to be assessed. This is usually done by comparison of the trial substrate, with the response of that of the same cell line on a known standard,

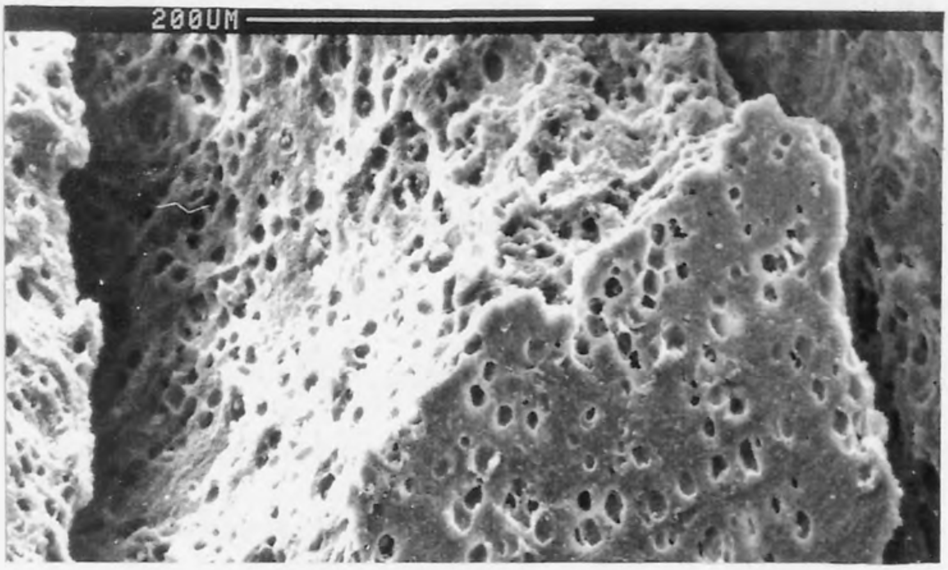


Plate 5 Macroporous IPN hydrogel showing characteristic porosity.

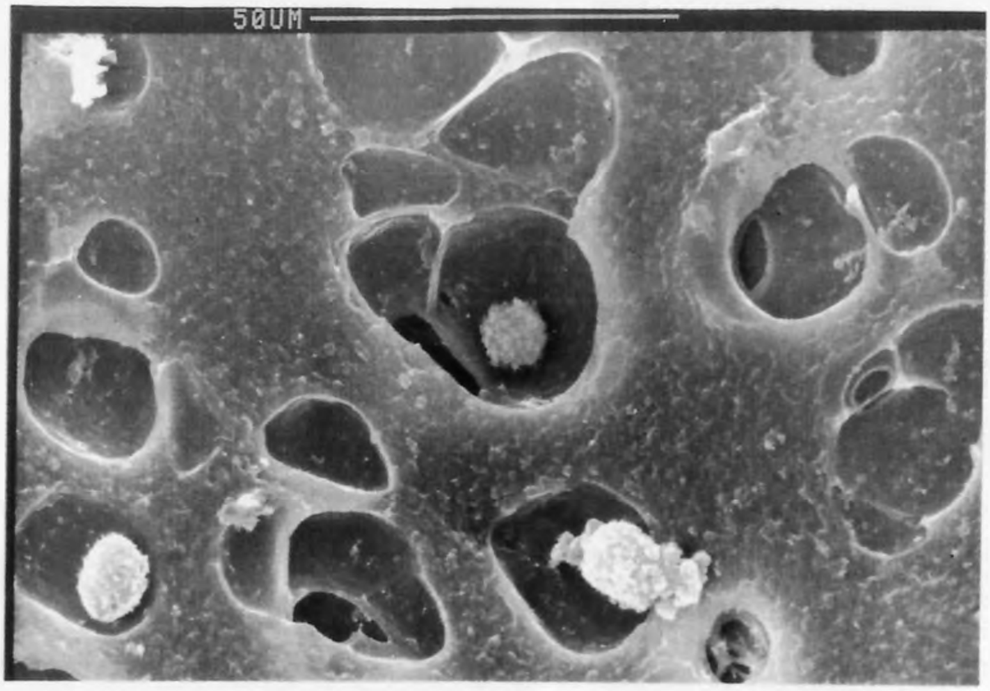


Plate 6 Rabbit chondrocyte adhesion on a macroporous IPN hydrogel expressing correct rounded morphology.

such as tissue culture plastic. It is important to keep the cell testing relevant to the particular application in mind. For instance in the case of a soft contact lens, it is not desirable to have any cell attachment, but it is important that the epithelial cells the material comes into contact with during service, are not poisoned. Other applications (such as our synthetic cartilage material for example) may need to support the spreading and growth of certain types of cell.

The choice of what cell line to use is therefore an important one, and in this work a line of rabbit chondrocytes were cultured, and these were then used to to evaluate the response of some of the more promising materials. Plate 6 shows rabbit chondrocytes growing on a typical macroporous IPN hydrogel, and clearly shows the attached cells are within the pores of the material. Notice also the "rounded" morphology of the cells. This is particularly important, because in order for the chondrocytes to produce the right biological response (to make new cartilage), they must maintain this phenotypic expression.(93, 94)

Such *in vitro* testing is particularly useful, as it gives a first assessment of the likely cell response. On their own however, such tests are insufficient to completely characterise the materials long term response. This can only really be done satisfactorily in the *in vivo* situation. Some of the materials developed here have shown such promise that they are currently being tested in the knees of young rabbits. A complete histological examination will then be possible, but because of the long term duration of such tests, the results are not yet available.

7.3.2 Compression Properties

Thus far little mention has been made of the compression properties that might be required for a synthetic cartilage material. Clearly, for a tissue that is under compression for much of its lifetime, the importance of this type of loading should not be overlooked. Consequently an assessment needs to be made of the compressive properties of our hydrogel materials, particularly with respect to the compressive modulus of the polymers. Unfortunately compression testing is slightly more difficult to perform than similar testing in tension. Several factors need to be taken into account, such as whether the sample is going to be confined or unconfined, the importance of accurate axial alignment, and the geometry of the test specimen. Ideally the sort of study that was carried out in chapter 3 needs to be performed, although it may be possible to adopt existing standards such as B.S. 903.

The compression properties of a number of hydrogels have however been measured, by Huglin and Davis for example.(77) These authors determined the compression modulus of a range of HEMA/NVP based copolymers. In particular they quote a value for the compression modulus of 70/30 copolymer crosslinked with 1 % EGDM as 1.75 MPa. A similar copolymer made in these labs having nominally the same composition was found to give a modulus in tension of 0.75 MPa. This result is particularly encouraging, in that it would appear that the values of modulus in compression are unlikely to be less than those determined in tension, and may indeed be even greater.

There are in fact other methods available to determine the compressive properties of polymers. One such method that has been used, particularly in the early work on the compressive properties of cartilage, is that of indentation. By making certain assumptions about the material being tested, which are based on the Hertzian theory of contact, it is possible to derive the following relationship for the modulus of the material :

$$E = (3\,(1-\upsilon^2)\,m\,g) / (4\,r^{1/2}\,h^{3/2})$$

Where E = Youngs Modulus,
υ = Poissons ratio,
m = Applied load,

g = Acceleration due to gravity,
r = Radius of the indentor,
and h = depth of indentation

Preliminary work on some hydrogel polymers was carried out using the I.C.I. pneumatic microindentation apparatus. In addition to the modulus of the material, the load/indentation curves obtained from this instrument also make it possible to derive information concerning the viscoelastic response of the polymer being tested, and thus this is a potentially very useful technique.

Unfortunately, practical difficulties meant that no meaningful results were obtained from this technique. One of the main problems encountered was that it was particularly difficult to provide a sufficiently close contact between the hydrogel test piece and the base plate of the instrument. It was therefore uncertain if the indentation was actually occurring in the hydrogel, or whether there was gross movement occurring between it and the base plate which would mask the effects of the true indentation. Other problems were caused by the effects of dehydration, and also because of the small loads that were required (typically 0.1 - 0.2 grams). It is worth saying at this point that the hydrogels tested were not particularly strong, since at the time the synthetic strategies had not been fully developed. It is quite likely that some of the better IPN materials may be more responsive to this technique, and because of their improved stiffness, the assumption made that the substrate is perfectly elastic will be more valid, and furthermore somewhat larger loads can then be applied.

7.3.3 Tear Resistance

Tear resistance or tear strength is perhaps not a property that is obviously associated with the requirements for a synthetic cartilage material. The reason why tear strength might be important for such a material can be found by examining the types of forces that this remarkable body tissue must resist. During normal articulation, the loading cycle that is usually experienced by cartilage, is such that the stresses imposed are of a very complex nature, and in particular quite substantial shear stresses may be set up. In order to resist these forces, apart from the necessary shear strength, the tear resistance of the material will also be important. In addition to the shear forces, damage might also arise from the impact loads that occur during the walk cycle, and this is another reason why any potential synthetic cartilage materials must have adequate toughness.

In order to assess the tear resistance of the hydrogel copolymers that have already been discussed in chapter 6, "trouser tear" tests were employed, as this was felt to be the most appropriate (and convenient) method of testing the polymer membranes that were usually produced. The results from this study are given in table 7.1.

The arguments that were given in the previous chapter are also seen to be valid for the tear strength of the membranes, so that incorporation of rings produces a more tear resistant material than the more linear monomers do. Similarly the use of EGDM produces a tougher material than AllylMA, and the addition of flexible oxygen linkages gives a slightly less resistant material than those without this linkage, as illustrated by the phenylethyl methacrylate and phenoxyethyl methacrylate copolymers.

In general the tear strengths of the NVP based hydrogels seems to lie in a fairly narrow band, with only a small increase in tear strength for quite large drops in equilibrium water content. Again this is quite similar to the effect of copolymerisation on tensile strength, where it was shown that only for additions of comonomer above about 20% was any significant improvement in tensile strength produced. The relationship between EWC and tear strength is shown in figure 7.1 for the various hydrogels tested. From this figure it can be seen that the HEMA based hydrogel materials are considerably tougher than the

Composition / wt %	EWC / %	Approximate Tear Strength / Nmm^{-1}
HEMA	38	0.10 ± 0.05
HEMA 90 TBMA 10	27	1.8 ± 0.1
HEMA 80 TBMA 20	18	5.8 ± 1.1
HEMA 90 HexMA 10	-	1.7 ± 0.05
HEMA 70 HexMA 30	12	5.8 ± 1.0
NVP 90 TBMA 10	81	~ 0.04
NVP 80 TBMA 20	66	0.20 ± 0.2
NVP 90 PhOEMA 10	-	~ 0.03
NVP 80 PhOEMA 20	-	0.15 ± 0.02
NVP 70 PhOEMA 30	-	0.45 ± 0.06
NVP 90 PhEMA 10	-	~ 0.04
NVP 80 PhEMA 20	-	0.17 ± 0.01
NVP 70 PhEMA 30	-	0.57 ± 0.09
NVP 80 HexMA 20	64	0.13 ± 0.05
NVP 70 HexMA 30	53	~ 1.6
NVP 70 CHexMA 10 HexMA 20 (m)	55	0.53 ± 0.04
NVP 60 MMA 40 (m)	57	0.19 ± 0.04
NVP 67 HexMA 33 (m)	57	0.18 ± 0.01
NVP 74 CHexMA 26 (m)	56	0.71 ± 0.02
NVP 70 PhOEMA 30 (m)	56	0.38 ± 0.03
NVP 73 CHexMA 18 HexMA 9 (m)	59	0.49 ± 0.08
NVP 57 CHexMA 21.5 EOEMA 21.5 (m)	56	0.83 ± 0.05
NVP 64 CHexMA 18 EOEMA 18 (m)	61	0.28 ± 0.03
NVP 50 CHexMA 25 EOEMA 25 (m)	-	1.53 ± 0.27
NVP 50 MMA 50	38	2.2 ± 0.6
NVP 80 CHexMA 20 (1 % EGDM)	58	~ 0.37
NVP 80 CHexMA 20 (0.5 % EGDM 0.5% AllylMA)	62	0.34 ± 0.04
NVP 80 CHexMA 20 (1 % AllylMA)	67	0.21 ± 0.02

Table 7.1 Tear strengths of various hydrogel polymers

N.B. (m) denotes the use of a mixed crosslinker (0.5 % EGDM 0.5% AllylMA)

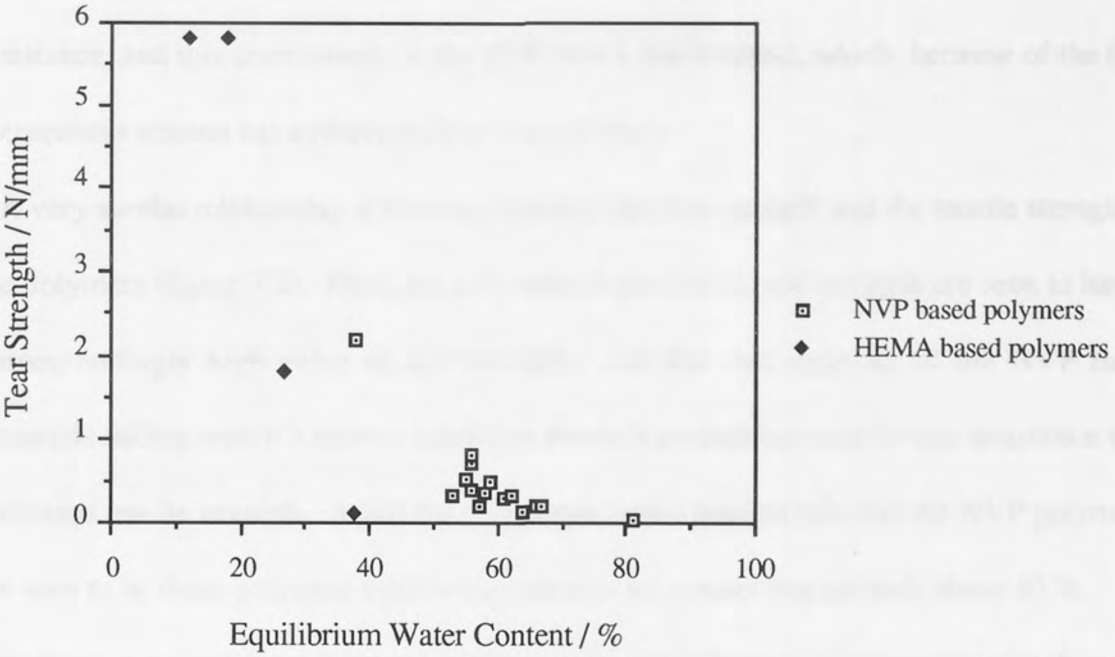


Figure 7.1 Tear strength versus EWC for a range of hydrogel polymers

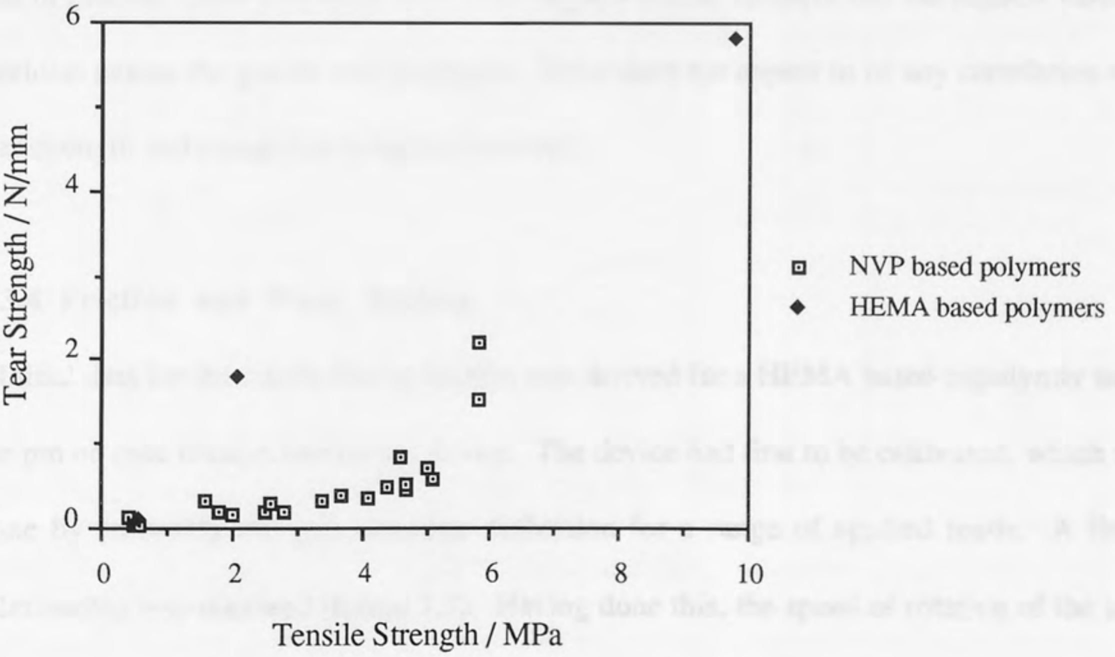


Figure 7.2 Tear Strength versus Tensile Strength for a range of hydrogel polymers

NVP materials. Only one of the NVP materials shown has a particularly high level of tear resistance, and this corresponds to the NVP/MMA 50/50 blend, which, because of the high comonomer content has a relatively low water content.

A very similar relationship is obtained between the tear strength and the tensile strength of the polymers (figure 7.2). Here, the polymers of greatest tensile strength are seen to have a correspondingly high value of tear strength, with the vast majority of the NVP based materials falling within a narrow band that shows a gradual increase in tear resistance with increased tensile strength. Again the exceptions to this general rule (for the NVP polymers) are seen to be those polymers that have a comonomer content that exceeds about 40 %.

In the previous chapter it was possible to compare polymers of approximately the same equilibrium water content, and those same polymers were also evaluated for tear strength. Comparison of the appropriate of the data from table 7.1 and that shown in table 6.6 show that in general, those polymers having the highest tensile strength and the highest value of modulus posses the greater tear resistance. There does not appear to be any correlation with tear strength and elongation to break, however.

7.3.4 Friction and Wear Testing

Initial data for the coefficient of friction was derived for a HEMA based copolymer using the pin on disk friction measuring device. The device had first to be calibrated, which was done by recording the galvanometer deflection for a range of applied loads. A linear relationship was obtained (figure 7.3). Having done this, the speed of rotation of the steel counterface was varied, and the corresponding galvanometer deflection recorded as a function of the speed of rotation. This produced the sort of curve that is shown in figure 7.4, where the frictional force is plotted against the speed (in rpm). Initially, the frictional force is seen to rise steeply, as the speed is increased, but seems to level off, with a value

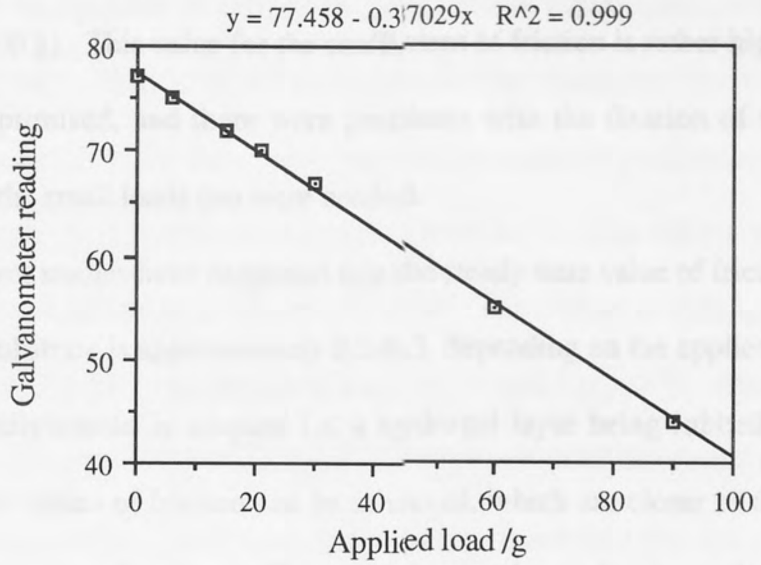


Figure 7.3 Calibration curve for friction measuring device

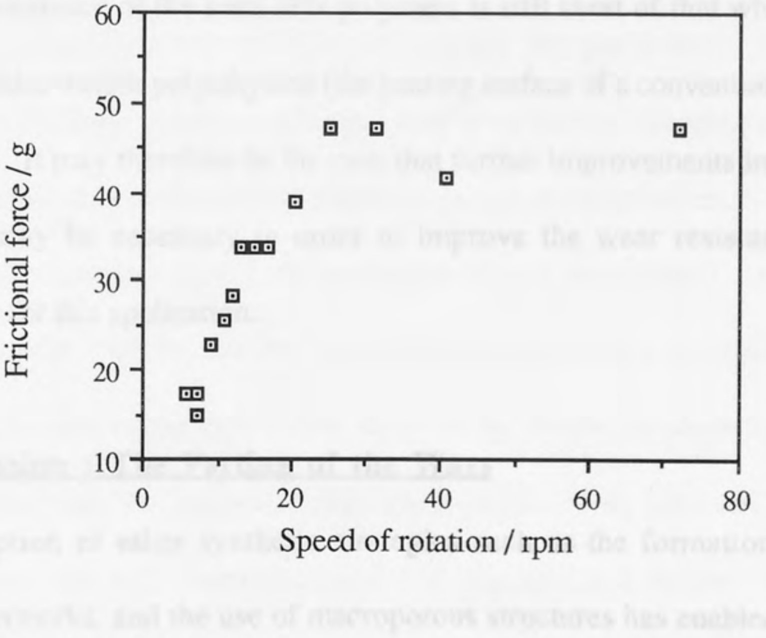


Figure 7.4 Plot of frictional force against counterface speed for a hydrogel polymer

for the coefficient of friction approaching a limiting value of about 0.5. (The applied normal load was 100 g). This value for the coefficient of friction is rather high, but the testing had not been optimised, and there were problems with the fixation of the hydrogel pin and because of the small loads that were needed.

More recent studies have suggested that the steady state value of friction for a hydrogel pin on a steel substrate is approximately 0.2-0.3, depending on the applied load. If however the reverse configuration is adopted *i.e.* a hydrogel layer being rubbed by a steel substrate, much lower values of friction can be achieved, which are closer to those found in natural joints. Low values for the coefficient of friction have also been obtained for NVP based copolymers by Nagaoka and Akashi,(95) who suggested that in order to achieve these low values of friction molecular weights for the polymer must exceed 400,000.

In terms of the wear resistance of these materials, preliminary studies have suggested that the wear resistance of the semi-IPN polymers is still short of that which is found for ultra high molecular weight polyethylene (the bearing surface of a conventional Charnley style hip prosthesis). It may therefore be the case that further improvements in the strength of these materials may be necessary in order to improve the wear resistance of the polymers sufficiently for this application.

7.4 Discussion : The Parting of the Ways

The adoption of other synthetic strategies such as the formation of interpenetrating polymer networks, and the use of macroporous structures has enabled the production of a range of hydrogel polymers with greatly improved tensile properties, compared to the unreinforced polymers. These new polymers show great potential as synthetic cartilage materials. A particularly exciting aspect of these new materials, is the development of the macroporous IPN hydrogels. This particular range of polymers have the potential to facilitate bone ingrowth, thereby overcoming one of the potential problems associated with the development of a synthetic articular cartilage material. Furthermore, by using the macroporous hydrogels, the appropriate cell response to produce new cartilage has been demonstrated. This sort of material then, may be of value for the partial replacement of damaged cartilage, rather in the manner of the carbon fibre prostheses used by Muckle and Minns,(59) or the cartilage allografts used by Shagaldi *et al.*(60). Although the mechanical properties of this type of hydrogel are still a little short of that found for articular cartilage, this may not a serious problem, since it is envisaged that the device acts primarily as a supporting framework around which new cartilage can form. Thus although the mechanical properties of this device are important initially, it is the formation of new cartilage that is the main objective for this particular potential synthetic cartilage material.

Alternatively the IPN polymers developed may be sufficiently durable to be used as the lining for the acetabular cup of a conventional hip prostheses. Potentially the water contained within the polymers structure may give rise to "squeeze film" lubrication. The aspect of lubrication in artificial joints has received much attention in the literature, and the hydrogel polymers that have been developed may be particularly useful as "cushion form bearings" for the artificial hip.(96) The property requirements for this particular application are seen to be somewhat different to those of the partial cartilage replacement discussed above. In this case the materials tribological properties are the main consideration, and in addition the mechanical property requirements may need to be improved.

Thus the future development of these materials may need a slightly revised strategy, where the synthesis and characterisation procedures are appropriately weighted towards each of these two slightly different applications.

Chapter 8 Concluding Summary

Hydrogel polymers are particularly well suited for use as biomaterials, since the water contained within these polymers enables the body to tolerate them more readily. Unfortunately, the presence of this water tends to make such polymers rather weak and fragile. Consequently the use of hydrogels as biomaterials, has been restricted primarily to those situations where the mechanical stresses involved are low, as in the case of the soft contact lens for example.

A variety of methods have been used to try and improve the mechanical properties of this range of materials, with a fair degree of success. In most of these cases, the static tensile properties are the ones chosen to demonstrate any improvements, partly because such testing is relatively straightforward to perform. However, there seems to be no universally accepted standard procedure, with which to test these materials in tension. This fact helps to explain the wide variation in values of strength that have been quoted for nominally the same material. Because of the unique nature of hydrogel polymers, existing standards for tensile testing (such as that for testing rubber sheeting) are not directly applicable to these materials. It may therefore be necessary to modify an appropriate existing standard, to devise a suitable testing procedure for this class of polymers. The problem is further compounded, because hydrogels can be prepared that cover a broad spectrum of mechanical properties. At one end of the scale, lightly crosslinked high water content hydrogels behave in tension rather like a typical elastomer, with high elongations to break, whereas at the opposite end of the spectrum, those of lower water content can be quite characteristically brittle.

Once such an accepted procedure exists, then the use of tensile testing becomes a powerful research tool. Advantages of using such a technique lie partly in its sensitivity to small structural variations, and partly because in one test it is possible to to derive a considerable amount of information about the polymer. Comparison between similar polymers then enables a better understanding of the structural factors responsible for any changes in properties, so that continued development may be facilitated in this manner.

The development of an appropriate testing methodology for hydrogel membranes was therefore an important aspect of this work. The methodology derived, was then applied to a range of hydrogel polymers and copolymers, which demonstrated the value of being able to produce comparative data of this nature. The importance of monomer purity on the resulting tensile properties was emphasised, and a clearer understanding of the effects produced by adding different comonomers has been achieved.

In the wider context of the design of new materials, it is also very important to be able to generate meaningful mechanical property data. This was illustrated in the design strategy that was employed to develop a synthetic articular cartilage material. In this case, one of the underlying criteria that was applied, was to try and match the properties of the natural material as far as possible. A survey of the existing literature on the mechanical properties of cartilage demonstrated that it is particularly difficult to obtain reliable data from natural materials. Even so, an appreciation of the sort of properties that are found in cartilage is vital if a synthetic analogue to this material is to be produced.

Having derived a suitable method to test hydrogel polymers in tension, and knowing the magnitude of some of the more important mechanical properties of cartilage, an intriguing design challenge then emerges. The adoption of suitable synthetic strategies, particularly the use of semi-interpenetrating polymer networks, and macroporous hydrogels, has enabled the first stage in the development of a synthetic cartilage material to be achieved. Hydrogel polymers have been prepared and tested that have demonstrated tensile strengths and stiffnesses that are comparable to those found for the natural material. The use of tensile testing as a research tool to provide preliminary design data of this nature makes it a particularly valuable technique. Once properties of the right order of magnitude have been achieved, it is then possible to tailor the design strategy to meet the more specific requirements needed for such a prosthesis.

During the process of development of the synthetic cartilage material, it became apparent that hydrogel polymers may find uses both as a potential cartilage replacement material and as a bearing surface inside a conventional hip prosthesis. The property requirements for these two applications are seen to be different. In the case of the partial cartilage replacement, the idea was to match the mechanical properties of the candidate material to those of natural cartilage, and it was also vital for the polymer to induce the right biological response. In the case of the surface lining for a hip replacement, the property requirements for the material are different because the prosthesis is designed to function in a different manner. Here the polymers tribological properties are one of the main concerns. Additionally the mechanical properties for this type of application are likely to be more demanding than those required for the partial cartilage replacement, so that further development may be necessary in this area.

The characterisation of subsequent materials needs to be very carefully considered. In particular, great attention must be paid to the appropriate design requirements, and new testing procedures that are more relevant to the particular application, may need to be devised.

This was done in another section of the work, where in order to test contact lenses in tension, a methodology had to be developed that would take account of the small size of these devices. Because of the nature of lens design, it is particularly difficult to determine the "absolute" tensile properties of such materials. However, it is possible to provide comparative data on lenses made from different materials, and because of the sensitivity of the technique, differences can be picked up that might not be detected using more conventional means. A further application of this technique could be in quality control or quality assurance, where it may be possible to adopt routine tensile testing to assist in this particular task.

Mechanical testing then, particularly in tension, is an extremely valuable technique. It can be used in research, both to compare similar materials, and also to generate preliminary design data for the development of new materials. Because data of this sort is primarily used for comparative purposes, it is important to keep any testing relevant to the particular application. Consequently a distinction needs to be made between testing used to generate research data, and that used to produce design data. The techniques and methodologies used to generate design information are likely to considerably more complex than those used for research purposes.

In terms of the mechanical properties of hydrogel polymers, there remain several unanswered questions, particularly with respect to the effects of polymer sequence distribution, and those relating to the water structuring of the polymer. Further research into these areas may enable polymers to be produced that have a range of novel properties. Although there still remain some concerns, the development towards a synthetic cartilage material has shown the great potential of hydrogel polymers for this particularly demanding application, and continued development may soon enable a successful prosthesis to be produced.

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