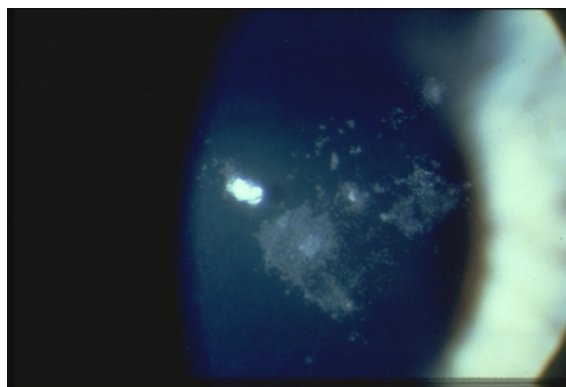


## **Tear film proteins, soft contact lenses and solutions**

**Interaction of tear film proteins with contact lenses and solutions is a key issue in soft contact lens wear. Dr Philip Morgan and Dr Curtis Dobson explore current knowledge of these interactions**

Since the early days of hydrogel contact lenses, tear film components have been known to deposit on and within the contact lens material (Figure 1).<sup>1</sup> Tear film proteins, in particular, have been associated with discomfort,<sup>2</sup> reduced vision<sup>3</sup> and inflammatory reactions such as papillary conjunctivitis<sup>4</sup> during contact lens wear. Understanding the state and role of tear film proteins, and how they interact with contact lenses and with solutions, is important if adverse events in contact lens wear are to be reduced.



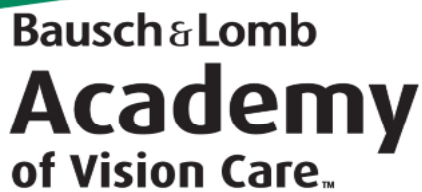
A basic understanding of the structure of proteins is a useful starting point. Proteins are molecules consisting of linear chains of around 20 or more amino acids connected by peptide bonds between the carbonyl and amino groups of adjacent amino acids. The term peptide is often used to describe shorter chains (around 40 amino acids or fewer); chains of increasing length are associated with greater molar mass.

Protein structure is described at four levels, which reflect the organisation of individual protein molecules and multiple molecules. Primary structure (or 'sequence') relates to the order of amino acids within a single protein chain. Secondary structure describes the localised folding of that chain in various configurations, often within the same protein molecule, held in place by hydrogen bonds. Tertiary structure describes the folding of secondary structural features and attractions between them within a single protein molecule, whereas quaternary structures consist of more than one different protein molecules.

'Denaturation' describes important changes to the structure of proteins that do not affect the primary structure, but can change the other forms of structural organisation. When denatured, most proteins lose their biological function although the process can be reversible. Unaltered proteins are usually described as being in their 'native' state. Protein 'conformation' refers to the secondary, tertiary or quaternary forms which a protein can adopt under given conditions.



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Movement between these states (conformational change) often influences the protein's function.

Proteins can be denatured by variations in temperature, pH, radiation, surface hydrophobicity and peroxidising lipids or other chemicals. Under these conditions the bonds and interactions responsible for maintaining secondary or tertiary structure are destabilised. An everyday example of irreversible protein denaturation is that of egg white becoming opaque and hardening when fried.

## **Tear film proteins**

Nearly 500 different proteins have been identified in the human tear film although only four – lysozyme, lipocalin, lactoferrin and secretory immunoglobulin A (sIgA) – are present at high concentrations (Table 1). All major tear film proteins are produced in the lacrimal gland; lysozyme, lipocalin and lactoferrin are secreted by the acini, grape-like masses of cells within the lacrimal gland, whereas sIgA is produced by interstitial plasma cells within the gland but outside the acini.

These different sites of production influence the diurnal variation of tear film proteins. The acini produce a watery secretion which is reduced in volume overnight, as are the three proteins produced within the acini. In contrast, the production of sIgA continues during sleep and, coupled with reduced water volume, gives rise to a steep rise in concentration.

The altered state of the tear film during overnight wear, including the rise in sIgA concentration and an increase in the number of polymorphonuclear white blood cells, has led some to describe the overnight closed eye environment as one of 'subclinical inflammation'.

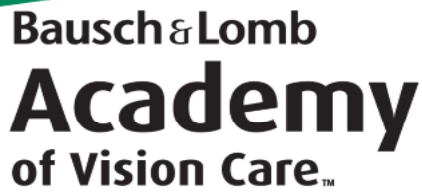
## **Roles of major proteins**

Each of the major tear film proteins plays its part in preventing infection and maintaining ocular health. Lysozyme is a potent antibacterial enzyme which hydrolyses bonds in bacterial outer cell walls, particularly those of Gram positive bacteria. The principal bacteria in the tear film that are attacked by lysozyme are species of *Streptococcus* and *Staphylococcus* which can cause conjunctivitis.

Lipocalin appears to play a lipid-binding role within the tear film and has a strong affinity to fatty acids. This gives rise to two important properties: binding between lipocalin and lipids determines the surface tension of tears and also prevents long chain fatty acids from inactivating lysozyme, indirectly enhancing the antimicrobial action of the tear film.



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Lactoferrin can bind to both Gram positive and Gram negative bacterial membranes and inhibits the growth of various bacteria including *Escherichia coli*, *Haemophilus influenzae*, and species of *Streptococcus*, *Staphylococcus* and *Pseudomonas*. There is also some evidence of synergistic action between lactoferrin and lysozyme; for example, *Staphylococcus epidermidis* is only susceptible to lactoferrin in the presence of lysozyme. The antimicrobial action of lactoferrin is enhanced by its ability to bind to free iron in the tear film, reducing the availability of iron for bacterial growth.

Lysozyme, lipocalin and lactoferrin are responsible for background or 'innate' defence mechanisms of the tear film but sIgA is important in the adaptive response system. It protects the eye by preventing the adhesion of bacteria to the ocular surface and enabling their destruction.

## Contact lens materials and proteins

Tear film proteins quickly deposit onto (and into) contact lens materials during wear, perhaps within hours.<sup>6</sup> Deposition is closely related to material type; ionic lenses containing methacrylic acid attract much higher levels of protein than other materials, including non-ionic lenses containing n-vinyl pyrrolidone.<sup>7</sup> Lysozyme, in particular, carries a high positive charge and is attracted to the negative charge of some materials.

Although, from a clinical perspective, the attraction of proteins onto and into soft contact lenses is generally regarded negatively, an aggregation of proteins with anti-microbial characteristics into a contact lens might be considered desirable. This hypothesis is supported by the levels of bacteria which attach to worn and unworn contact lenses; the number of viable Gram negative bacteria on worn lenses is less than on new, unworn lenses.<sup>8</sup> This may be of clinical benefit given the ability of such bacteria to cause adverse events during lens wear.

Since the behaviour of proteins is changed by denaturation, any potential protective benefit of protein-deposited contact lenses may relate to the state of tear film proteins. Denaturation of lysozyme, for example, causes a reduction in its bactericidal action.<sup>9</sup> Papillary conjunctivitis is associated with the presence of denatured proteins<sup>4</sup> and other negative responses to contact lens wear such as reduced comfort<sup>2</sup> and vision<sup>3</sup> may also be related to the level of protein denaturation. Further research is required to more fully understand these effects.

Various studies have investigated the relationship between proteins and different contact lens materials. Etafilcon lenses show a relatively high level of lysozyme after wear (1mg/lens) compared with balafilcon (10µg/lens) and lotrafilcon (2µg/lens) lenses.<sup>10</sup> The level of denaturation also varies between lens types with



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protein bound to lotrafilcon, balafilcon and etafilcon materials measured as 80%, 50% and 22% denatured, respectively.

Suwala *et al*<sup>11</sup> looked at the amount of deposited lysozyme and the degree of its denaturation on a range of soft lens materials and found that levels of activity are highly variable (Figure 1: Soft lens deposits (courtesy of Bausch & Lomb Image Library)

Figure 2a and 2b). Other researchers have also reported that lysozyme denatures during soft contact lens wear.<sup>12</sup>

Figure 2a: Total lysozyme on a range of contact lens materials<sup>11</sup>

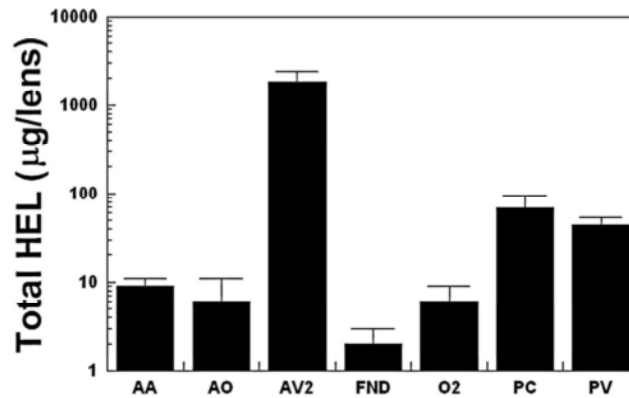
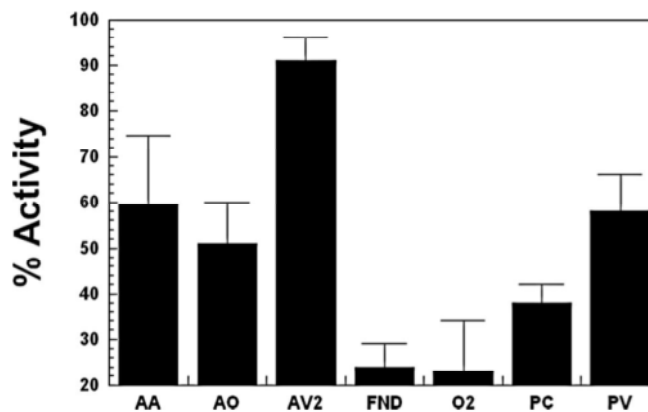


Figure 2b: Measures of denatured lysozyme (less activity signifies greater levels of denaturation) on a range of contact lens materials<sup>11</sup>



Key:

AA Acuvue Advance

FND Focus Night & Day

PV PureVision

AO Acuvue Oasys

O2 Air Optix

AV2 Acuvue 2

PC Proclear



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### **Contact lens solutions and proteins**

Compared to the relationship between proteins and lens materials, there are relatively few reports on interactions with solutions. One study conducted under no-rub conditions found more protein was removed from contact lenses soaked with OptiFree Express than with ReNu MultiPlus or SOLO-care Plus.<sup>13</sup> Other researchers examined the range of tear proteins in tears collected from contact lens wearers using a range of lens care products.<sup>14</sup> They concluded that 'protein patterns' tend to be more similar to those of non-contact lens wearers with some care products than with others.

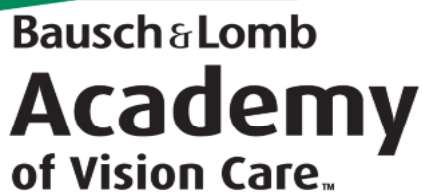
A more recent study found that OptiFree Express removed the greatest amount of protein (compared to ReNu with MoistureLoc, Complete MoisturePlus and AQUify), and that these results were dependent on the contact lens material.<sup>15</sup> The range of proteins removed also varied by solution type and lens material.

To date there appears to be little information in the literature about the conformational state of tear film proteins in relation to contact lens solutions. Further studies will investigate whether solutions vary in their ability to reduce protein denaturation and the clinical significance of any such differences.

### **Conclusions**

Tear film protein have an important physiological role. The potential denaturation of proteins on contact lens surfaces and by contact lens solutions is associated with some adverse consequences of contact lens wear. Better understanding of the interaction between tear film proteins, soft contact lenses and solutions may lead to new strategies to reduce the level of adverse events and maintain or enhance the inherent antimicrobial activity of the tear film.





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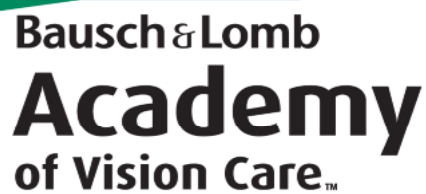
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Dr Philip Morgan is a senior lecturer in optometry and director of Eurolens Research at the University of Manchester, UK. Dr Curtis Dobson is a senior research fellow at the same institution and is CEO of the antimicrobial technology company Ai2 Limited.



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Table 1: Major tear film proteins<sup>5</sup>

| Protein       | Molar mass<br>(daltons) | Concentration (mg ml <sup>-1</sup> ) |
|---------------|-------------------------|--------------------------------------|
| Lysozyme      | 14,000                  | 2.07                                 |
| Lipocalin     | 17,500                  | 1.55                                 |
| Lactoferrin   | 90,000                  | 1.65                                 |
| Secretory IgA | 385,000                 | 1.93                                 |

Note: Other tear film protein concentrations are <0.1 mg ml<sup>-1</sup>

Figure 1: Soft lens deposits (courtesy of Bausch & Lomb Image Library)

Figure 2a: Total lysozyme on a range of contact lens materials<sup>11</sup>

Figure 2b: Measures of denatured lysozyme (less activity signifies greater levels of denaturation) on a range of contact lens materials<sup>11</sup>



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