Biotribology of the ageing skin—Why we should care.

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Abstract

Ageing of populations has emerged as one of the most pressing societal, economic and healthcare challenges currently facing most nations across the globe. The ageing process itself results in degradation of physiological functions and biophysical properties of organs and tissues, and more particularly those of the skin. Moreover, in both developed and emerging economies, population ageing parallels concerning increases in lifestyle-associated conditions such as Type 2 diabetes, obesity and skin cancers. When considered together, these demographic trends call for even greater urgency to find clinical and engineering solutions for the numerous age-related deficits in skin function.

From a tribological perspective, detrimental alterations of skin biophysical properties with age have fundamental consequences on how one interacts with the body's inner and outer environments. This stems from the fact that, besides being the largest organ of the human body, and also nearly covering its entirety, the skin is a multifunctional interface which mediates these interactions.

The aim of this paper is to present a focused review to discuss some of the consequences of skin ageing from the viewpoint of biotribology, and their implications on health, well-being and human activities. Current and future research questions/challenges associated with biotribology of the ageing skin are outlined. They provide the background and motivation for identifying future lines of research that could be taken up by the biotribology and biophysics communities.

Key words

1   Introduction

One of the most significant achievements of the last century has been the phenomenal extension in average human life expectancy [1]⸺in Western countries, it is expected to reach 100 years by the end of the century [2]. However, ageing of populations has emerged as one of the most pressing societal, economical and healthcare challenges currently facing most nations across the globe. It has been estimated that, globally, the proportion of people over 60 will nearly double from 12% in 2015 to 22% by 2050 (i.e. 617 million to 1.6 billion) [3]. Between 2001 and 2011, the UK population aged 65 and over increased by 0.92 million [4] while the number of individuals aged 85 and over increased by almost 25% (from 1.01 million to 1.25 million) [5]. As of 2016, these two age groups represented respectively 18 and 2.4% of the UK population [6].

From the viewpoint of healthcare, the significance of these statistics is embodied by two essential features: first, the need for care and medical treatment increases with longevity and, second, of special relevance to the present paper, the ageing process itself results in degradation of physiological functions and biophysical properties of organs and tissues, and more particularly those of the skin.

Moreover, in both developed and emerging nations, population ageing parallels concerning increases in lifestyle-associated conditions such as Type 2 diabetes, obesity and skin cancers. When considered together, these demographic trends call for even greater urgency to find clinical and engineering solutions for numerous age-related deficits in skin function [1], which generally lead to further diseases [7], skin cancers [8] and aggravating conditions including debilitating, costly and life-threatening skin tears and pressure ulcers [9]. Even in their minor form, these afflictions can severely impact on quality of life for the elderly population. As with many other health issues, this puts an alarming economic and social burden on governments and healthcare services [10]. In the UK, average hospital spending for an 89 year-old man is about three times the average for a 70 year-old, and nine times the average figure for a 50 year-old while costs typically escalate more rapidly for men than women [10].

From a tribological perspective, detrimental alterations of skin biophysical properties with age [11-13] have fundamental consequences on how one interacts with the body's inner and outer environments [14-16]. This stems from the fact that, besides being the largest organ of the human body, and also nearly covering its entirety, the skin is a multifunctional interface which mediates these interactions. The latter are encompassed by mechanical, thermal, biological, chemical and electromagnetic processes which typically operate in concert and, more often than not, features non-linear coupling effects [17]. The skin also features important biochemical synthesis functions for the production of vitamin D and immuno-chemical compounds which can be affected by ageing.

The aim of this paper is not to present an exhaustive review but rather to discuss some of the consequences of skin ageing from the viewpoint of biotribology, and their implications on health, well-being and human activities. First, in **section 2**, an overview of the skin structure and essential characteristics of its mechanical behaviour is presented. **Section 3** provides an introduction to ageing and highlights its main manifesting effects in skin. This provides the basis for understanding the microstructural changes in skin induced by ageing (**section 4**), and their consequences on the mechanical and tribological behaviour of skin which are discussed in **section 5**. Finally, in **section 6**, current and future research challenges associated with biotribology of the ageing skin are outlined. They provide the background and motivation for identifying future lines of research that could be taken up by the biotribology and biophysics communities.

2 Essential characteristics of skin microstructure and mechanical properties

2.1 Skin microstructure

From the structural viewpoint, the human skin is a multi-layer assembly composed of an epidermis, dermis and hypodermis. Each of these layers is itself a complex multiscale structure that can be subdivided into further components (**Figure 1**).

The **hypodermis** (**Figure 1-c**) is the layer that separates the dermis from the *fascia*⸺a band of connective tissue primarily composed of collagen⸺and attaches, encapsulates and delineates muscles and other internal organs. The thickness of subcutaneous tissue (i.e. hypodermis) is highly variable within and across individuals. This layer, mainly composed of fat cells (i.e. adipocytes), provides mechanical protection and thermal insulation, can generate heat, and also acts as a reserve of nutrients for period of starvation.

Going outwards from the hypodermis, the next skin layer is the **dermis** which is essentially a fibre-reinforced composite featuring a geometrically complex network of crimped fibres embedded in a ground substance matrix. As a consequence of its fibrous nature and the mechanical properties of its fibres, the dermis is considered to be the main tensile load-bearing element of the skin [13, 18, 19]. The extracellular matrix (ECM) of the dermis, which is mainly secreted by fibroblasts, is constituted of a three-dimensional network of fibrous proteins (mainly type I and III collagen and elastic fibres—namely, elastin and fibronectin) and glycosaminoglycan-rich proteoglycans (i.e. ground substance) [20]. Out of the twenty eight types of collagen identified in humans [21], five can be found in skin [22] and, together with their respective location, structural class and function [23], are listed in **Table 1**. Collagen approximately represents up to 66-69% of the fractional volume of the dermis [13]. Elastic fibres contribute approximately 2-4 % of the dry weight of skin [24].

Table 1. Types of collagen found in human skin as well as their location, structural class and function. Adapted from Mescher and Uchôa Junqueira [25].

Collagen	Location in skin	Structural class	Function
Type I	Forms heterotypic fibrils with collagen Type III. Increased collagen I/collagen III ratio in reticular dermis	Fibril-forming	To resist tension and provide structural support
Type III	Forms heterotypic fibrils with collagen Type I. increased collagen III/collagen I ratio in papillary dermis	Fibril-forming	To provide structural support
Type IV	Found at cell-extracellular matrix boundaries (e.g. at the dermal-epidermal junction separating the papillary dermis from the living epidermis)	Network-forming fibrils	Basement membrane component mediating cell attachment to extracellular matrix
Type VII	Dermal-epidermal junction	Anchoring fibrils	To act as anchoring structural elements
Type VIII	Blood vessels	Network-like	To provide structural support

Proteoglycans are composed of multiple glycosaminoglycans (i.e. mucopolysaccharides) interlaced with back bone proteins. Due to its high hyaluronic acid content, glycosamine produced by dermal fibroblasts is essential in controlling moisture retention in the skin. The ECM provides strength, extensibility and elasticity to the skin and plays a significant bio-chemo-mechanical role in cell adhesion and regulation of cell signalling. The ground substance also contains blood and lymph-derived fluids which are involved in the transport of substances crucial to cellular and metabolic activities. Within the dermis, one can identify three separate layers: the papillary dermis adjacent to the epidermis, the sub-papillary dermis underneath and the reticular layer (**Figure 1**) which is bound by the underlying hypodermis. The papillary layer is defined by rete ridges (i.e. papillae) which are finger-like structures extending into the epidermis and contains thin collagen fibres, sensory nerve endings, cytoplasms and a rich network of blood capillaries. The zone below the epidermis and papillary layer is known as sub-papillary dermis and is constituted of similar structural and biological components to those of the papillary layer.
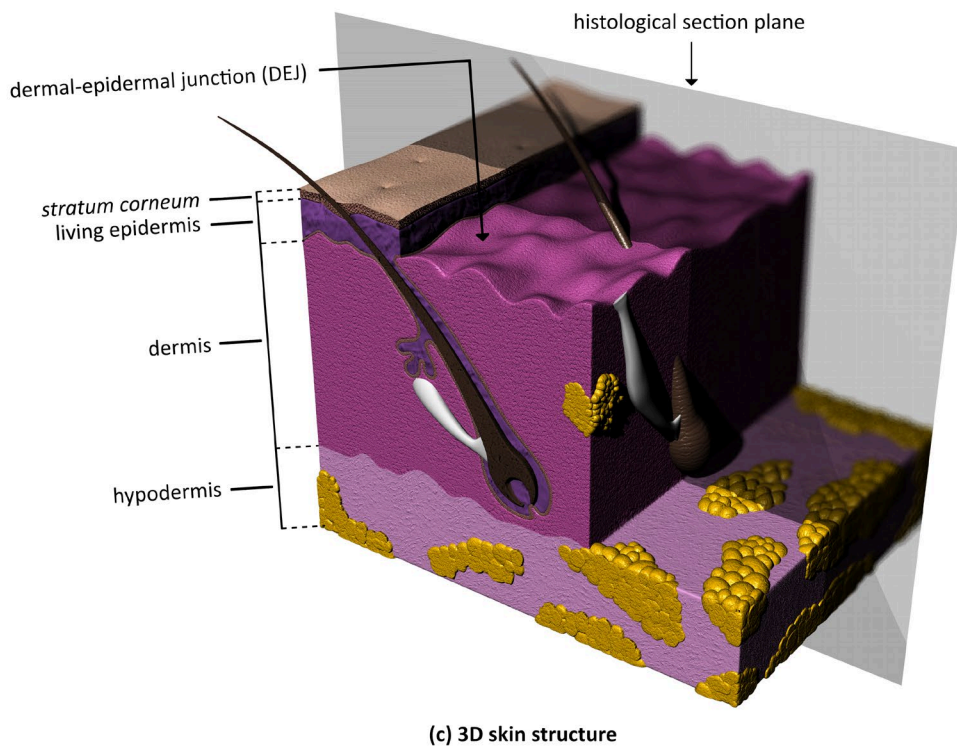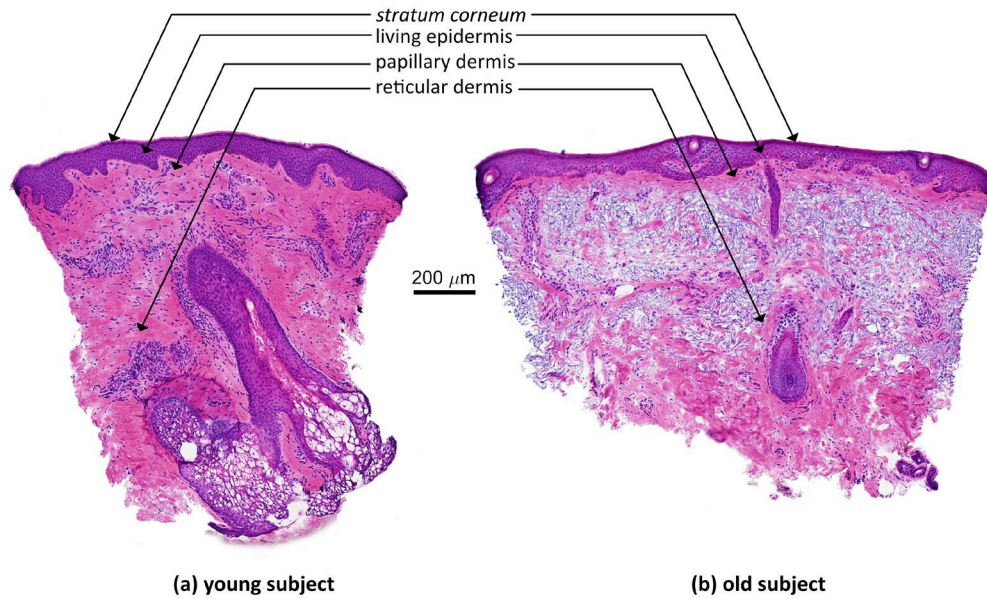
(a) young subject

(b) old subject

(c) 3D skin structure

Figure 1. Histological sections of human facial skin (forehead) highlighting the microstructural features of the epidermis and dermis, in particular, the stratum corneum, living epidermis, papillary dermis and reticular dermis. Sections were cut from biopsies obtained with ethical approval and consent from Caucasian female subjects. (a) 24 year-old female subject; (b) 68 year-old female subject. The original digital histological sections and associated permissions are graciously provided by Bradley Jarrold of The Procter&Gamble Company, Cincinnati, OH, USA. Compared with photo protected and/or young skin (which may be mildly photo-damaged), chronically photo exposed skin is commonly characterised by a flattening of the dermal epidermal junction, the loss of fibrillar collagens, accumulation of glycosaminoglycan content (including hyaluronic acid) and disruption of elastic fibre organisation. (c) schematic representation of the three-dimensional (3D) structure of human skin indicating the main skin layers and the dermal-epidermal junction (DEJ) which is the basement membrane interface separating the epidermis from the dermis (more precisely, the papillary dermis). A plane normal to the external skin surface is also overlaid to specify how histological sections are spatially positioned with respect to the 3D structure of the skin.

The avascular **epidermis** can be decomposed into two main structures: the **living epidermis** containing living cells (keratinocytes) and the ***stratum corneum***, a 15-30 cell-thick layer of dead flattened corneocytes [26]. Besides the abundance of keratin proteins expressed by keratinocytes, the living epidermis is also rich in vimentin, desmin, a-internexin and nestin. Other types of cell including melanocytes, Langerhans's cells and Merkel cells, can also be found [27]. The epidermis is 15 to 40 times thinner than the dermis [27].

Stem cells in the basal layer separating the viable epidermis from the papillary dermis—a 0.5 to 1 μm thick epidermal basement membrane known as *basal lamina* [28]—transdifferentiate into keratinocytes, the main epidermal cell-type that forms the superficial layers of the epidermis. There, they replicate, pushing older cells towards the external skin surface, and, as they move away from the source of nutrients during their migration, progressively lose their nuclei, undergoing a keratinisation process, become corneocytes and eventually die. This process takes place over approximately four weeks [29]. As corneocytes are squashed by migrating cells they get flattened. It is worth pointing out that corneocytes are strongly bonded together by a type of cellular joint called desmosomes. Desmosomes ensure structural integrity of the *stratum corneum* as a multi-layer assembly of corneocytes and are fundamental in contact interactions where they can be subjected to severe tensile and shear loads. As the connecting desmosomes degrade in the more mature corneocytes the latter detach from the rest of the *stratum corneum* in the process known as desquamation. The *stratum corneum* is the primary interface in external skin contact interactions and the physico-chemical properties of this layer are therefore essential in controlling tribological properties and behaviour such as skin friction [30]. The structure of the *stratum corneum* permits penetration of water, lipids and other substances including skin care products into the inter-cellular space. Besides leading to volumetric expansion of the *stratum corneum* [31], increasing relative humidity also alters the mechanical properties of this layer (i.e. softening) and amplifies its sensitivity to variations in temperature. The combined effects of both relative humidity and temperature—collectively embodied by the concept of micro-climate [32]—can therefore modulate the mechanical response of the *stratum corneum* and the underlying layers, particularly during contact interactions. In turn, alterations of the micromechanical environment can play a critical role in conditioning the nature and intensity of contact interactions (i.e. friction) [32-34] and the likelihood of developing skin injuries [15, 35, 36].

2.2 Mechanical behaviour of the skin

When considered at a macroscopic level, the mechanical properties of the skin are anisotropic and inhomogeneous. These properties arise from the complex hierarchical structure of skin and its materially non-linear constituents [17, 37] as well as from the existence of residual tension lines in the skin (i.e. the so-called "Langer lines"), all over the body as first recognised by the Austrian anatomist Karl Langer in his seminal study [38]. In-plane anisotropy of the skin is correlated with the distribution and orientation of Langer lines over the body [18, 39] while out-of-plane (or across-the-thickness) anisotropy is due to the distinct mechanical properties and complex three-dimensional architecture of the skin layers and their basic constituents. Like many other soft tissues of the body [40], the skin can sustain large deformations and exhibits various degrees of non-linear mechanical behaviour according to the level of strain experienced. Under uniaxial tension, the skin exhibits a typical strain hardening response and its macroscopic strain-stress curve features four to five main characteristic portions which can be explained by particular structural deformation mechanisms associated with the skin dermal constituents (**Figure 2**):

(1) Low modulus portion of the strain-stress curve: as the skin is macroscopically subjected to tensile load, it exhibits an initial compliant response where the load is mainly borne by the ground substance and elastic fibres (e.g. elastin) [41] which have very low ground-state elastic moduli. At this stage, most wavy collagen fibres are still in a crimped state, and therefore do not carry any tensile load. The equivalent macroscopic stiffness is low;
(2) Non-linear portion of the strain-stress curve, known as the "toe region": as macroscopic strains continue to propagate to the microscopic level, collagen fibres progressively uncrimp, up to the point when they are fully uncrimped and start to bear load (**Linear region of the strain-stress curve**). Because of the geometrical complexity of the collagen meshwork and the large number of fibres of unequal length, collagen fibres are mechanically and sequentially recruited, and eventually align with the load direction. At macroscopic level this translates into the classically observed non-linear stiffening behaviour that is typically represented by an exponential function [18], as more and more fibres resist loading;
(3) Linear region of the strain-stress curve: in this phase, collagen fibres are fully taut and strongly resist loading. The collective mechanical behaviour of individual collagen fibres in tension gives rise to an approximately linear response. Fully extended collagen fibres are not very extensible, unlike elastin fibres [42];

(4) Plastic region of the strain-stress curve: under high loads, collagen fibres slip with respect to each other or with respect to the ground substance matrix, effectively dissipating mechanical through microstructural rearrangement. At the macroscopic scale this is manifested as plastic behaviour, typically associated with softening. At this stage, fibres are the main load-bearing component of skin.

(5) Failure region of the strain-stress curve: the tensile strength of collagen fibres is reached and fibres begin to sequentially break until they are all fully ruptured which eventually leads to total failure of the whole skin sample.
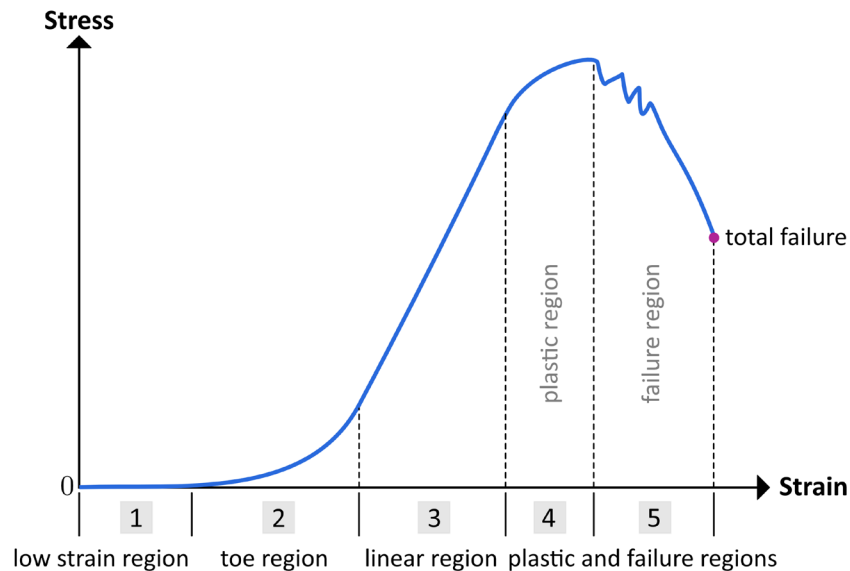

Figure 2. Schematic representation of the essential characteristics of the strain-stress curve of human skin which highlights five key phases, each one of them being associated with specific underlying microstructural mechanisms (see **section 2.2**). The range of strains associated with each region of the stress-strain curve is not necessarily drawn up to scale. For example, in the plastic region the variation of strain might be negligible compared to that observed for the failure region.

The mechanical interplay of collagen and elastin is fundamental for determining the homogenised mechanical response of skin. This micromechanical aspect is crucial in ageing as many manifestations of skin ageing actually arise from a disruption and rebalancing of this interplay. These phenomena will be discussed in more details in the next section, but important observations are briefly presented. By removing elastin from skin through enzymatic degradation (e.g. using elastase) and subjecting skin to tensile loads, Oxlund et al. [43] showed that elastin supports the entire load up to 50% strain after which the strength rapidly increases due to the recruitment of collagen fibres. The elastic modulus of elastin has been measured to be about 1 MPa, which is consistent with Young's modulus of skin at low strain and because elastin is not strong enough to provide much tensile strength at higher strains [44]. There is strong evidence that elastin is responsible for the recoiling of the skin and collagen fibres after mechanical stress is applied [45]. Oxlund et al. [43] also found that, following removal of elastin, for a given tensile load, the post-toe region linear portion of the strain-stress curve (**region 3**) occurs sooner, a result also found in other studies [45-47]. This observation would suggest that without the mechanical contribution of elastin, collagen fibres start to bear load at lower strain levels than when elastin is present. It is reasonable to hypothesise that elastin fibres are intertwined with the collagen meshwork in such a way that they maintain collagen fibres in a crimped state. If elastin disappears, collagen fibres are in a less crimped state in their undeformed configuration. In this situation, they are closer to their fully extended length than would be the case if the elastin meshwork was intact. Therefore, when a macroscopic tensile load is applied to the skin, collagen fibres would be recruited earlier as they do not have to uncrimp as much before they can bear load. The viscoelastic and poroelastic behaviour of the skin is thought to mainly arise from the microstructural properties of the ground substance through its high water content, microstructure and the associated time-dependent interstitial fluid motion within it [13, 19]. Using films of purified and reconstructed collagen obtained upon enzymatic degradation of macromolecules present in the ground substance of rat skin, Oxlund et al. [48] showed that the mechanical response of rat skin in tension was dominated by the mechanical contribution of collagen. Oomens et al. [49] suggests that ground substance is the main load-bearing constituent of soft tissues when subjected to compression. For a more complete description of skin mechanical behaviour and associated constitutive theories, the reader is referred to recent published works [17, 50-52].

3 Definitions and manifestations of skin ageing

Here, it is important to clarify what is meant by ageing. There are two main types of ageing: *intrinsic* and *extrinsic* ageing. **Intrinsic ageing**, sometimes imprecisely called *chronological* ageing, is a series of biochemical molecular degenerative changes occurring as the result of the simple flow of time and progression into greater age. A major physiological change associated with ageing is a reduction in cell proliferative capacity which leads to cellular senescence and alters the biosynthetic activity of skin derived cells. It is widely accepted that DNA damage and chromosomes' telomere shortening [11, 53-55] are the two main triggers of ageing. Genetics determines the rate of skin ageing by controlling essential factors such as immunochemistry, cell biochemistry and hormonal mechanisms. Intrinsic ageing takes place in combination with ***extrinsic*** ageing which is a biochemical process driven by of external factors, not directly associated with the genetic make-up of individuals. These factors can be split into three main types: **environmental** (e.g. ultraviolet radiations (UVR) from sunlight [56-58], UVR from sunbeds [59, 60], from chemical air pollution [61, 62] including that produced by the use of tobacco products [61, 63], temperature), **mechanical** (e.g. repetitive muscle actions leading to tissue plasticity such as squinting and frowning) and **lifestyle** (e.g. diet and sleep patterns) [64]. Extrinsic ageing due to UVR exposure is called **photoageing** [57, 58], a term which was first coined by Kligman [58] using the American English spelling "aging".

In popular culture, the intuitive description of what one often refers to as ageing of the skin is mostly due to the bio-structural alterations of the skin induced by extrinsic ageing. Indeed, a well "maintained" skin, in terms of appropriate diet and skin care, and protection from UVR, exhibits a "remarkable resilience" [1] to intrinsic ageing. Intrinsic ageing can only be observed in old age subjects, and its extent and magnitude is strongly dependent upon ethnicity, individuals, even within the same ethnic group, and body locations. It is also characterised by a very gradual evolution of the skin appearance over decades unlike extrinsic ageing which can take place over much shorter periods of time. Both intrinsic and extrinsic ageing typically operate in concert and influence each other [1]. For example, exogenous factors associated with a particular environment such as pro-oxidants and antioxidants have an impact on cell turnover through neuro-endocrine-immune biological response modifiers. While intrinsic ageing can be influenced by extrinsic ageing it could also be defined as a form of purely biological ageing, a process genetically determined and immutable [65].

Intrinsic ageing is characterised by drier, unblemished, smooth, stiffer and less elastic skin [1] with fine wrinkles, with occasional exaggerated expression lines [20, 66], epidermal and dermal atrophy as well as reduction in the population of mast cells [67].

Extrinsic skin ageing manifests as deep wrinkles and leathery appearance due to photo-damage, pigmented lesions, actinic keratosis and patchy hyperpigmentations [68, 69] (see **Figure 3**). The externally visible structural effects of extrinsic ageing on the skin can be viewed as exaggerated intrinsinc ageing effects. It is worth pointing out that UV exposure leads to additional photobiochemical effects which are not present in intrinsic ageing. Extrinsic ageing is most apparent on sun-exposed body locations such as the face, neck, chest and the dorsal surface of the arms [56]. It is estimated that 80% of the effects of facial skin ageing are due to chronic UV exposure.

A review of theories of skin ageing is out of the scope of the present paper but can be found in excellent review papers such as those by Gragnani et al. [69], Tobin [1] and Krutmann et al. [64]. There is strong evidence that the main factors involved in skin ageing are oxidative stress [accumulation of oxidative damage to cells during their life due to excessive production of reactive oxygen species (ROS)], cellular senescence and telomeres' shortening due to apoptosis, diet, genetics, UVR, smoking, pollution, intracellular signalling and skin lesions, age-related diseases, disorders and conditions of the skin, hormonal changes and the production of advanced glycation end products [69].

(a)

(b)

Figure 3. Skin of an 82 year-old Caucasian male subject, with no known skin conditions, highlighting the wrinkled and leathery appearance of both intrinsically and extrinsically aged skin, particularly when subjecting the skin to surface shear and torsion loads. (a) Left inner forearm and right hand; (b) close-up view of inner forearm skin clearly showing exaggerated glyphic patterns as compared to the skin of a younger subject. In (b), the skin was not subjected to any external mechanical load. Adapted and augmented from Limbert et al. [70].

4   Overview of microstructural and mechanical aspects of skin ageing

4.1   General observations on skin ageing

Skin thickness generally decreases with age [71]. It reaches a maximum value around the fourth decade for men and third decade for women after which there is a gradual decrease [71, 72]. An overall 0.7-0.8 mm decrease of thickness in older skin was measured by Pawlaczyk *et al.* [73]. Oriba et al. [74] found that, after 20 years of age, across all layers, skin thickness starts to diminish at a pace that increases with age. Between 30 and 80 years, unexposed skin can lose up to 50% of its thickness (**Figure 3**). This effect is accentuated in zones exposed to sunlight such as the face or neck where more drastic microstructural and biochemical alterations of skin take place as a result of photo-ageing. Individual skin layers follow different trends depending on body location as the interplay of intrinsic and extrinsic ageing factors and effects modulate thickness changes at local (i.e. microscopic) level. Departing from other observations reported in the literature, Diridollou *et al.* [75] found that after an initial increase during maturation (0-20 years), skin thickness remains constant to about the age of 60 when a decrease in thickness is initiated, the rate of which is higher in female subjects.

Besides decreased elastin and collagen content as well as their structural rearrangement, intrinsic ageing also has other consequences such as increase in trans-epidermal water loss, reduction in skin moisture content, diminished sebum production, arteriosclerosis of small and large vessels, thinning of vessel walls [76], reduction in mast cells [67], melanocytes, Langerhans's cells, Meissner cells, Merkel cells and Pacinian corpuscules [76, 77] and increase in skin surface pH [78] after 70 years of age [79].

It is generally accepted that skin ageing is associated with a noticable increase in *macroscopic* or *apparent* stiffness, see [12, 20, 80] and references therein, although some studies suggest otherwise [81]. An increase of skin elastic modulus of around 20% after the age of 70 has been reported [71, 72]. Xu and Lu [82] reported that Young's modulus of skin suddenly increases by about 50% at age 30. Similar qualitative observations were made by Alexander and Cook [46] who found that the stiffness of skin starts to increase from the age of 25 after which the rate of stiffening increases with age. In the literature, there is little agreement on the age of onset of skin stiffening and on the value of the ground state Young's modulus. This partly stems from the highly subject-specific nature of ageing, particularly with regards to external factors driving extrinsic ageing. Intrinsic skin extensibility (*i.e.* a standardised mean extensibility to account for varying skin thickness) was found to decrease with age [71, 72].

4.2   Ageing of the epidermis

Overall, there is a 6.4% per decade decrease in epidermal thickness and this rate is higher in women than men. Silver et al. [83] suggested that epidermal thickness is controlled by the balance of external and internal forces acting on and within this layer. This suggestion was supported by the fact that, in areas of skin under high levels of external loading, such as on the hands and feet, the epidermis thickens. Intrinsic ageing slows the turnover of keratinocytes and is also accompanied by a reduction in *stratum corneum* water content [84] because of alteration in lipid content of the epidermal barrier [85]. This factor leads to an increase in the stiffness of the *stratum corneum* which is inversely proportional to humidity level [86-88].

4.3   Effect on the dermal-epidermal junction (DEJ)

In intrinsic skin ageing, the dermal-epidermal junction (DEJ)⸺which can be loosely identified with the basal lamina separating the dermis from the epidermis⸺flattens out with a decrease of the density of papillae [89] (compare **Figure 1-a** and **Figure 1-b**). This leads to a reduction of up to 20% in epidermis thickness. It is thought that the evolution of the structure of the DEJ with age is due to the progressive degradation of the essential network of thin oxytalan fibres (mainly collagen type VII) anchoring the papillary dermis to the viable epidermis. During intrinsic ageing, these oxytalan fibres are progressively shortened and resorbed leading to the disappearance of dermal papillae and flattening of the DEJ. Skin exposed to UVR experiences an accelerated flattening of the DEJ when compared to sun protected skin [90]. Flattening of the DEJ leads to a reduction in the surface area available for nutritional exchange and metabolic by-products evacuation between the dermis and epidermis. Consequently, epidermal cell turnover is slowed down and there could be increased free radical damage (oxidation). In young skin, there is an essential network of thin oxytalan fibres (mainly collagen type VII) anchoring the papillary dermis to the viable epidermis.

4.4 Effects on the dermal matrix

Important differences between the dermis of young, intrinsically aged and photoaged skin pertain to the level of structural organisation of fibrillar collagen which conditions its mechanobiological interactions with fibroblasts through their integrin attachments [20]. In young skin, the fibrillar collagen meshwork is made of small thin bundles of tightly packed fibres in the papillary dermis. These bundles are thicker and more spaced in the reticular dermis [91, 92] (see **Figure 1**). Fibroblasts are in a state of mechanical tension through the alignment along collagen fibres, the effect of which promotes a healthy homeostatic state for normal collagen fibre synthesis. The ratio of type III to I collagen increases with age [93, 94] which leads to rebalancing of the mechano-structural properties of the dermal matrix. In intrinsically aged skin, there is significantly reduced collagen turnover, thinning of fibre bundles and disappearance of the meshwork [95]. These structural changes affect the mechanobiological interactions of fibroblasts with collagen fibres leading to collapsed fibroblasts [95-97].

The reported thinning of skin [71, 72] is induced by a reduction in dermis thickness which is itself caused by the loss of dermal collagen and elastin in elderly adults, typically, as a result of progressive slowing down of dermal matrix turnover [98]. This reduced turnover stems from the imbalance between synthesis and degradation with the latter increasingly dominating cell activity during the intrinsic ageing process. In intrinsically aged skin, there is significantly reduced collagen turnover, thinning of fibre bundles, disappearance of the meshwork and an increase in the collagen III to I ratio [95]. Lavker et al. [99] reported an increased density of the collagen network with age and explained it by the decrease in ground substance which effectively provides more space to collagen fibres to occupy. This has the effect of reducing thickness of the dermis, as has the compaction of the collagen and elastin fibre networks in the dermis.

The intrinsic ageing process is correlated with a reduction of the fibroblast population which has the effect of decreasing the production of collagen. This phenomenon is also paralleled by an increased expression of matrix metalloproteinases (MMP) as a result of intrinsic ageing. This class of enzymes has the ability to cleave ECM molecules [100]. Disruption of the homeostatic state between activation and inhibition of MMPs is a key ingredient in the pathophysiology of both intrinsic and extrinsic ageing.

Macroscopically, alterations of the collagen network manifest themselves as reduced dermal volume and strength. Additionally, aged collagen fibres undergo non-enzymatic Maillard reactions that cross-link molecules by glycation [101, 102] and lead to non-degradable abnormal fibres [91] which belong to the class of advanced glycation end products (AGEs).

Elastic fibres are highly compliant structural elements of the dermal matrix with the ability to stretch elastically to twice their original length [42]. In the dermis, their close structural intertwining with the collagen network is a key factor that can explain the unique resilience and recoil ability of skin. This is supported by studies in which correlation between degradation of elastic fibres, abnormal collagen synthesis and apparent stiffening of the dermis was established [12, 71]. Alexander and Cook [46] and Daly et al. [47] reported a decrease of the low strain range portion of the strain-stress curve of skin (see **section 2.2**, **Figure 2**). This implies that the onset of stiffening associated with recruitment of collagen fibres occurs at lower macroscopic strain. These authors attributed this result to the degradation of the elastic fibre network and the presence of amorphous elastin [46, 47]. Also, the slope of the linear portion of the strain-stress curve—which corresponds to what researchers report as Young's modulus of skin—tends to increase with age [46]. Here, it is relevant to highlight that, as for any non-linear material, the apparent Young's modulus is a macroscopic homogenised mechanical property of skin, which only makes sense and is only valid for a particular strain range. An increase in the Young's modulus of skin is evidence of stiffening of skin, at least at the scale of mechanical characterisation (i.e. macroscopic tensile test). Indeed, *apparent* stiffening of skin does not necessarily mean that a change in the mechanical properties of its microstructural building blocks (e.g. collagen fibres) has occurred. Daly *et al.* [47] noted that the final slope of the strain-stress curve of skin in tension remains constant with age while the stiffness of collagen remains constant, possibly due to the reduction in the collagen content in the dermal layer. These data point to potentially complex microstructural reorganisation of the collagen network [80] and that of elastin, the combined effect of which is translated into macroscopic stiffening of the skin. Escoffier *et al.* [71] and Reihsner *et al.* [45] report an increased collagen crosslinking with age, which, from a mechanical standpoint, would reduce any slippage between neighbouring fibres and, ultimately result in stiffening of Sthe collagen network [103]. This would support the observations of Batisse et al. [86] who reported a stiffening of the whole dermis with age.

As evidenced above, the mechanical interplay of elastin and collagen is crucial to characterise the mechanical effects of ageing. Elastin fibres lose their elasticity while collagen fibres tend to unravel. As a consequence, the skin loses its extensibility, becomes less resilient and more lax [104].

It has also been shown through image analysis that intrinsically aged skin features the same density of veins and arteries as young skin but their diameter is reduced. In photoaged skin, the dermal vasculature is progressively lost and the diameter of veins and arteries is also reduced [105].

Chronic exposure to UVR induces a significant and incomplete ECM degradation. In photoaged skin, there is a massive increase in collagen fibre degradation. Acute UV exposure activates a key transcription factor in cells which triggers an increase in MMP 1, 2, 3 and 9 synthesis and cell activity linked to a decrease in type I procollagen synthesis [106]. It has also been suggested that, via the inflammatory response associated with chronic UV exposure, immune cells could play a role in collagen network degradation [56, 106]. Chronic UV irradiation spanning many years alters the normal structural and mechanical characteristics of the skin and ultimately causes premature skin ageing and cancer [56, 107]. Acute exposure to UV radiation sources trigger photochemical reactions in the skin which can manifest as sunburn, inflammation, immunity suppression, modified pigmentation and dermal connective tissue damage [107]. Extrinsic ageing through UV exposure leads to a partial degradation of existing elastic fibres by fibroblast and neutrophil elastase from the inflammatory infiltrate [108]. This is accompanied by higher turnover of tropoelastin and abnormal synthesis of new fibres [109]. The combined effects of the lysis of existing elastic fibres and synthesis of abnormal and non-functional elastic constituents provokes the accumulation of an amorphous and dense elastotic material in the upper and mid-dermis (**Figure 1-b**). The process leading to this altered quality of dermal tissue is called actinic damage [107, 110] which, when superimposed on the loss of normal elastic fibres, has a drastic effect on the recoil capacity and resiliency of the dermal layer [111]. In photoageing, glycosaminoglycans which are key to skin hydration [112] are abnormally located on the elastotic material in the superficial dermis instead of being more uniformly distributed throughout the whole dermis. Moreover, hyaluronic acid and proteoglycans (versican and decorin) undergo structural alterations with age which lead to impairment of their water retention abilities [107].

5 Tribological implications of skin ageing

From **section 4**, where a brief review of the main effects of ageing on the structural and mechanical properties of skin was presented, it is clear that these alterations have the potential to significantly affect the tribological response of the skin across the life course. Here, particular biophysical properties associated with the tribological response of skin which are modulated by ageing, are identified and discussed. The effects of ageing on skin surface biochemistry and physics are out of the scope of the paper's focus (material and structural properties).

5.1 Skin surface topography

The geometrical characteristics of the skin surface are fundamental properties that condition its mechanical response in contact interactions. The skin is endowed with a natural surface topography present at birth, known as microrelief, which evolves over the life course and that is strongly affected by extrinsic ageing. This surface structure is made of furrows and ridges—also known as *sulcus cutis* or glyphic patterns—criss-crossing each other and thus delimiting polygonal regions with triangular, rectangular, square and trapezoidal shapes [113] (**Figure 4**). During ageing, these polygonal patterns lose their isotropic distribution and form preferred structural orientations which gives rise to anisotropic distributions [114-116]. The characteristics of skin microrelief can be classified according to the orientation and depth of featured lines into primary, secondary, tertiary and quaternary lines [114, 115, 117-120] (primary and secondary lines are indicated in **Figure 4**). These multiple hierarchical levels effectively induce a multiscale roughness which is fundamental for contact physics in general [121], and friction in particular [14, 122]. The primary lines are wide and deep (30 to 100 μm relative to the skin surface) while the secondary lines are narrower and shallower than the former (5 to 40 μm) [119]. The thin micro-topography that delineates the edges of corneocytes on the skin surface constitutes the tertiary lines while the thinner irregular bulges and trabecular networks on the corneocyte membrane itself define the quaternary lines [120]. As a result of both intrinsic and extrinsic ageing, primary lines can deepen to several hundreds of micrometres to form wrinkles (see **Figure 3**). In young skin, the grooves formed by the skin glyphic patterns are shallow and closely spaced while this trend is reversed in aged skin [123].
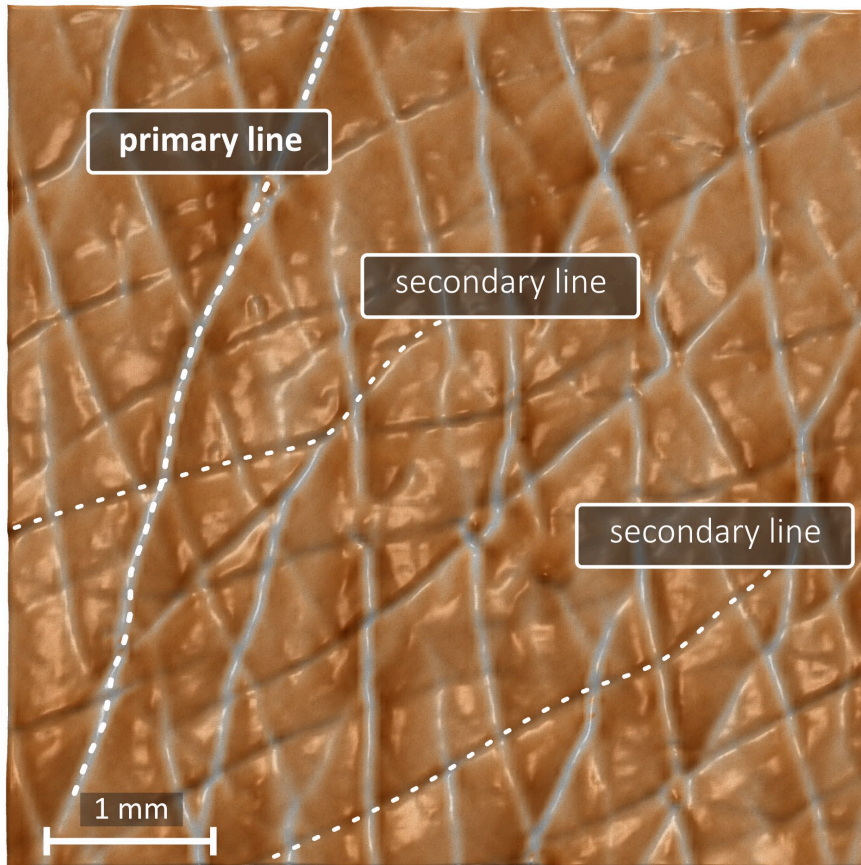
Figure 4. Computer-generated image representing the typical microrelief of human skin surface (ridges and furrows), reconstructed from laser scanning profilometry of a silicone replica of a human volar forearm skin patch (from a 40 year-old healthy Caucasian male subject). The profilometric acquisition was conducted using a Xyris 2000 TL (Taicaan Technologies, Southampton, UK) and featured a 400 x 400 grid of points that was fitted to a NURBS surface (XY spatial resolution: 25 μm). This followed standard skin profilometric characterisation using non-contact optical techniques [124, 125].

The ratio of mechanical properties to the thickness of each layer in multi-layer structures is critical in controlling the amplitude and wavelength of wrinkles induced by in-plane compression [126]. Surface instabilities including wrinkles, folds and cusps can not only be induced by compression in multi-layer assemblies but can also be produced as a result of differential surface or volumetric growth [127-129]. Thinning of the epidermis is an example of negative volumetric growth. In the clinical sense, skin wrinkles are defined as ageing-induced amplification of natural skin microrelief [130]. In the light of what is known about the physics of multi-layer assemblies [126] and reported experimental evidence in the skin science literature [80, 131], it is reasonable to infer that skin wrinkles are a by-product of alterations in the material and structural properties of its microstructural constituents caused by intrinsic and extrinsic ageing.

Other physiological changes not directly associated with the skin, and occurring during ageing play a role in controlling the emergence and characteristics of skin wrinkles. These phenomena include mechanobiological adaptation of skin's underlying anatomical structures including adipose tissues, muscles and bones, together with changes in the mechanical environment of the dermal tissue (e.g. relaxation and reorientation of tension along Langer lines [120]). Also, with age, the skin tends to lose its in-plane isotropy [132] because of the strong mechanical effects introduced by dermal collagen realignment arising in combination with collagen cross-linking and density alteration. The progressive mechanical decoupling between the epidermis and dermis through flattening of the DEJ, reduction in papillae density and degradation of oxytalan fibres is an important mechano-structural factor involved in modifying skin surface mechanics. At a mechanobiological level, an altered mechanical environment, implies altered mechanical cues sensed by cells (e.g. fibroblasts), which implies altered biochemical synthesis/degradation of skin elemental micro-constituents such as collagens and elastin.

It is straightforward to realise that the evolution of biomechanics of the ageing skin is a highly dynamic process with complex non-linear feedback loops [70, 80]. Ultimately, these mechano-structural variations modify the tribological response of the skin.

Temporary wrinkles, also called expression wrinkles are typically associated with macroscopic facial skin movement. They can be induced by facial muscular activation (e.g. smiling) or by mechanical actions on the skin surface such as twisting, shear or compression (**Figure 3-a**). At the length scale of skin microrelief, there also is another type of skin wrinkle, termed micro-wrinkles [113]. They could play a fundamental role in conditioning skin friction through finite deformation- and adhesion-induced resisting forces [14, 81, 122, 133]. Recently, Limbert and Kuhl [113] investigated the respective role of skin microrelief and that of material properties of an anatomically-based bi-layer finite element model of the skin on the geometrical characteristics of compression-induced wrinkles. The model featured a 20 μm thick *stratum corneum* and a 130 times thicker underlying substrate (**Figure 5**). Despite its low relative thickness (10 to 30 μm) compared to other skin layers, the *stratum corneum* was shown to be potentially a major contributor to the mechanics of the epidermis [14-16, 134]. This layer can stiffen by up to three orders of magnitude, in a matter of hours, when relative humidity levels drop from 100 to 0% [88, 135, 136]. In the context of compression-induced micro-wrinkles, stiffening or softening of *stratum corneum* would rebalance the stiffness ratio between *stratum corneum* and underlying layers (r, in **Figure 5**), leading to very different wrinkle morphologies. Similar effects would be observed if the mechanical and geometrical properties of the epidermis and/or dermis would vary, as is the case in skin ageing. Besides the geometry of skin microrelief for relatively low stiffness ratios r (up to 20), the key underlying physical mechanism at play that controls wrinkle characteristics is the competition between the bending energies of each structural layer [113, 126]. Large bending energies (i.e. stiffer and thinner layer) favour large wavelengths while low bending energies (i.e. softer and thicker layer) promote small wavelengths. Limbert and Kuhl [113] found that for moderate r values (≤100), secondary lines of skin microrelief can act as geometrical imperfections triggering wrinkle formation. As r increases, these imperfections (including those represented by primary lines) play a diminishing role on selecting wrinkle wavelength. Compressive and tensile principal strains also get progressively realigned along the direction normal to that of the applied compressive force. There is a clear correlation between the spatial frequency of wrinkles and r. The computational results were in very good agreement with analytical predictions for idealised neo-Hookean bi-layer structures [137].
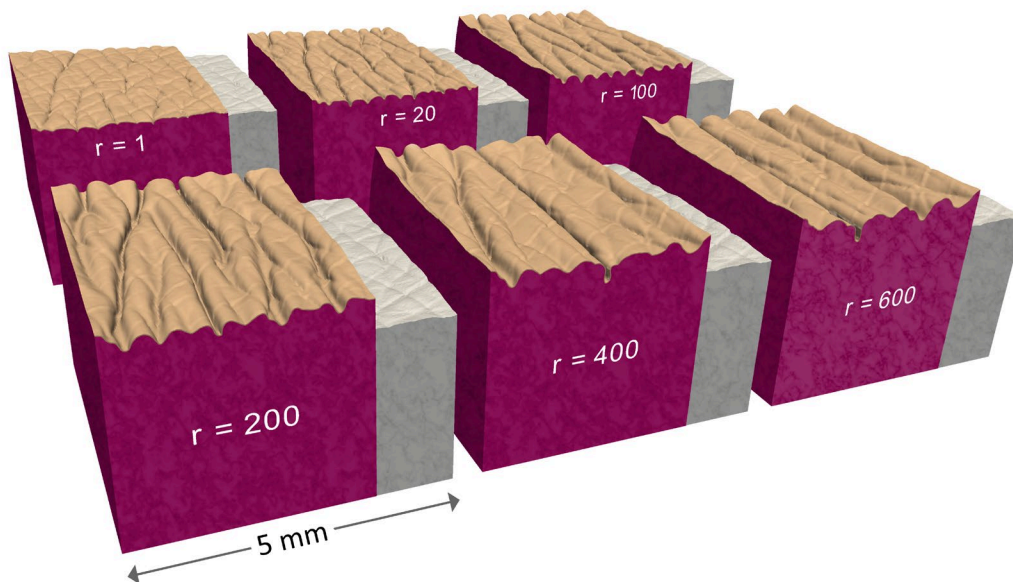

Figure 5. Structural deformations of an anatomically-based bi-layer finite element model of the skin upon application of a 25% in-plane compression as a function of the ratio of the ground state Young's modulus between the 20 μm thick *stratum corneum* and that of the underlying substrate representing the living epidermis and dermis. The ground state Young's modulus of the substrate was fixed at 0.6 MPa so that the ratios r = 1, 20, 100, 200, 400, 600 correspond respectively to a 0.6, 12, 60, 120, 240 and 360 MPa ground state Young's modulus for the *stratum corneum*. The deformed and undeformed geometries are respectively presented in light brown/magenta colour and grey colour. This original plot is adapted from the numerical study of Limbert and Kuhl on the emergence of skin micro-wrinkles [113, 138].

It is clear that, in the much more complex biophysical environment of *in vivo* skin compared to that of analytical and computational models of skin wrinkles, many additional factors would condition the formation and evolution of wrinkles, particularly across various length scales. Presence of hair, curvature of the skin surface and underlying layers, geometrical constraints around body openings (e.g. around the mouth) and joints (e.g. knee and elbow), and evolution of Langer lines with age are examples of such critical factors. In summary, from the simple viewpoint of mechanics, alterations of geometrical and mechanical properties of skin layers as a result of ageing and/or environmental conditions has the potential to significantly modify the topography and compliance of the skin surface through highly non-linear mechanisms involving surface instabilities [113] and structural folding [16]. In turn, these phenomena are critical factors underpinning the fundamental tribological response of the skin. These aspects are essential for many practical applications.

Alterations of the skin micro- and macro-topography have important consequences in applications where stable and long-term adhesion of external devices to the skin surface are sought, such as in medical adhesives [139, 140] and deformable electronics [141] for epidermal sensing and monitoring applications [142-144]. These latter applications are particularly relevant as evidenced by the growing widespread use of telemedicine for the elderly [145] which increasingly relies on ambulatory *in vivo* health monitoring systems.

The presence of hair over the skin is an important aspect of skin tribology as it directly influences frictional properties through the exposed hair surface, and because the hair-in-skin complex locally conditions the surface and bulk mechanical properties of the surrounding skin. There is evidence that hairs [34, 146], or perhaps, more precisely, the natural lubricating oily compounds (e.g. sebum) that coat their surface [35], lower the friction properties of skin. Compared to scalp hairs, beard hairs exhibit low emerging angles with respect to the skin surface [147]. In relation to ageing, the emergence of skin wrinkles and alterations of the structuro-mechanical properties of the skin, it is logical to expect that the frictional properties of skin arising from the presence of hair would be affected by age, body location and type of hair. Naturally, this would be modulated by the magnitude and direction of mechanical load applied to the skin surface. Influence of hair on skin friction is more important at low loads. It is well documented that there are significant ethno-specific differences of beard hair structure (length, diameter, cross-section shape), density and growth rate between ethnic groups, for example between Asian and Caucasian men [148]. Consideration of these differences together with differences in rate and effects of ageing in these two ethnicities would highlight potential distinct tribological responses of the ageing skin.

5.2 Skin friction is modulated by age-dependent mechanical and structural properties

A large number of engineered products that interact with, support or protect skin can actually cause discomfort to the user and even irritation or damage to the skin through excessive and/or ill-distributed load transmission (e.g. limb prostheses). Mechanics and friction are central to these problems [32, 35, 149]; friction is typically split into an adhesive and a deformation-induced component [14, 15, 122, 150]. Geometrical alterations of the the skin surface (e.g. wrinkles), particularly at the microscopic scale, is likely to modulate these effects [17, 35, 151, 152] via finite deformations and associated fluctuations in effective contact area. Geometrical effects on asperities (i.e. large structural deformations) alone can have a significant impact on the macroscopic frictional response of elastic contacts. This was demonstrated by Stupkiewicz *et al.* [153] in the context of a three-dimensional computational contact homogenisation study, and also by Leyva-Mendivil et al. [14, 15, 122] in two-dimensional computational studies focusing on skin micromechanics and friction. Leyva-Mendivil et al. [14] showed that the *macroscopic* coefficient of friction between the skin and a rigid slider moving across its surface is noticeably higher than the *local* coefficient of friction applied as an input parameter to the finite element analyses [14]. This underlined the fact that the deformation-induced component of skin friction could be significant—a finding also corroborated by Stupkiewicz et al. [153] and Masen [154]—unlike what had been widely assumed in the tribology community [30, 150, 155-157] where the dominant contributor to macroscopic friction is thought to result from adhesive forces.

5.3 Biophysical response of skin against a surface

If one adds the progressive degradation of skin biophysical properties and increased skin frailty as a result of ageing to ageing-induced variations in skin frictional properties, it is not difficult to imagine how the combination and interaction of these effects could result in higher probability of the elderly population to consistently experience skin injuries [9]. For instance, skin tears can simply happen when mildly rubbing an elderly skin against an angular or rough surface. Another very illustrative example of where an aged skin could be placed at a major disadvantage compared to the skin of a younger subject can be found in the consumer goods industry.

The mechanics of a razor sliding over the facial skin of a teenage boy and that of an elderly man with deeper wrinkles and micro-wrinkles, and stiffer, but more frail, skin are likely to exhibit very distinct tribological responses. Use of a shave preparation would introduce favourable lubrication properties but would also soften the *stratum coneum* (and also hair). If life expectancy continues to increase, current challenges in designing products adapted for the elderly population will have to be addressed so that satisfactory practical engineering solutions can be developed.

In the last few decades, unravelling and studying the biophysical mechanisms triggering skin injuries and those controlling their progression has become a very active area of research [9, 158]. Common experience and numerous scientific studies [159] have demonstrated that exposure of skin to cyclic mechanical loads, particular shear loads can result in skin lesions such as friction blisters [160]. These latter injuries are formed by fatigue damage and failure of the desmosomes which act as structural inter-cellular joints in the viable epidermis [161]. In such mechanical solicitation scenarios, the interfacial properties of the skin surface and counter surface (e.g. surface energy, topography of micro-asperities), as well as well as interfacial properties between skin layers, determine the level of traction skin experiences. It has been demonstrated that such traction is correlated with the likelihood of developing a skin injury [32].

Sustained pressure loads can result in skin and deep tissue damage (i.e. pressure ulcer), which is aggravated when augmented by interfacial shear [162-164] and an increased local temperature [32, 165]. Pressure ulcers are related to compression-induced ischaemia (i.e. reduction up to blocking of blood flow), and also, reperfusion of capillary blood flow when load is removed [166, 167]. Ischaemia disrupts nutrient supply and promotes the accumulation of waste products and build-up of acidity [167], which ultimately compromise tissue integrity. Wu et al. [168] showed that application of shear and compressive stresses to muscle cells is sufficient to induce cell death. It was reported by Goldstein and Sanders [169] that, in a pig model study, an interfacial shear up to 70 kPa could also result in skin breakdown. Excessive shear stresses experienced by living cells of the viable epidermis as a consequence of mechanical forces applied to the surface of the skin can ultimately lead to mechanical damage of their cytoskeleton and other basic cellular units, eventually leading to cell death as evidenced for muscle cells [168]. In turn, degradation of the supporting structural and biological constituents of the viable epidermis can compromise skin mechanical integrity and biological functions, thus increasing the probability of developing deeper tissue injuries (i.e. deep pressure ulcers) [170].

Epidemiological data indicate that, although occurring in all age groups [7, 167], pressure ulcers are clearly associated with ageing [7]. In the UK alone, as of 2004, pressure ulcers annually affected over 400,000 UK patients, with associated annual costs for the National Health Service (NHS) estimated to range from £1.4 to £2.1 billion, or 4% of its total expenditure [171]. In a large scale study conducted to estimate the level of resource and financial cost expanded by the NHS in managing wounds in 2012/2013, Guest et al. [172] found that the annual cost was £5.3 billion when accounting for co-morbidities, and between £4.5 and £5.1 billion after adjusting for co-morbidities.

These numbers are particularly significant considering that the average age of patients sampled was 69 years. The likelihood of these costs escalating as the population continues to age should be a cause for concern [10]. Scientists and engineers have an important role to play in improving existing devices and systems and also in coming up with novel innovative solutions. Any process, device or treatment that could reduce the effects of detrimental friction, shear and pressure, even in a small proportion, has the potential to save significant costs in terms of both staff time and required treatments as well as substantially reducing morbidity and improving quality of life.

The central theme running through the current paper is that decline in skin biophysical properties induced by ageing is a compounding factor in aggravating many skin diseases, conditions or dysfunctions, via physical processes associated with mechanobiology and tribology (**Figure 6**). When the skin interacts with external surfaces through contact, the risk of developing skin injuries depends on many factors which not only include the tribo-physical properties of these counteracting surfaces, but also the complete biophysical environment of the surface and bulk, that encompasses biological, chemical and physical processes. Properties governing these phenomena are dynamic and highly sensitive to changes in environmental conditions. An increase in relative humidity and/or temperature at the skin surface can trigger a cascade of biophysical processes, often spanning multiple length scales within the tissue. At the cellular level, increase humidity leads to swelling of corneocytes and plasticisation of the brick and mortar structure of *stratum corneum* [167]. In an experimental characterisation study, Takahashi et al. [173] concluded that breaking of hydrogen bonds in keratin by free water sorption in the *stratum corneum* is what causes its plasticisation.

These chemo-mechanical effects lead to softening of the skin surface, increasing surface conformity in contact interactions, and by so doing, increasing contact area and associated adhesive forces. Moreover, capillary forces also provide an additional contribution to adhesion-induced friction [150] between the skin and contacting materials. Higher friction leads to higher interfacial shear stress which, combined to supra-physiological temperature and softening of the *stratum corneum* [32, 167], are known to compromise skin integrity [31, 32]. These phenomena are not only central the study of mechanically-induced skin injuries, specifically skin tears, superficial pressure ulcers and friction blisters but are also of prime importance in incontinence. Incontinence associated with ageing—and the search for effective solutions [174, 175]—is likely to become an increasingly important factor in the prevalence of skin injuries as it also compromise mechanobiological skin functions [165, 176].
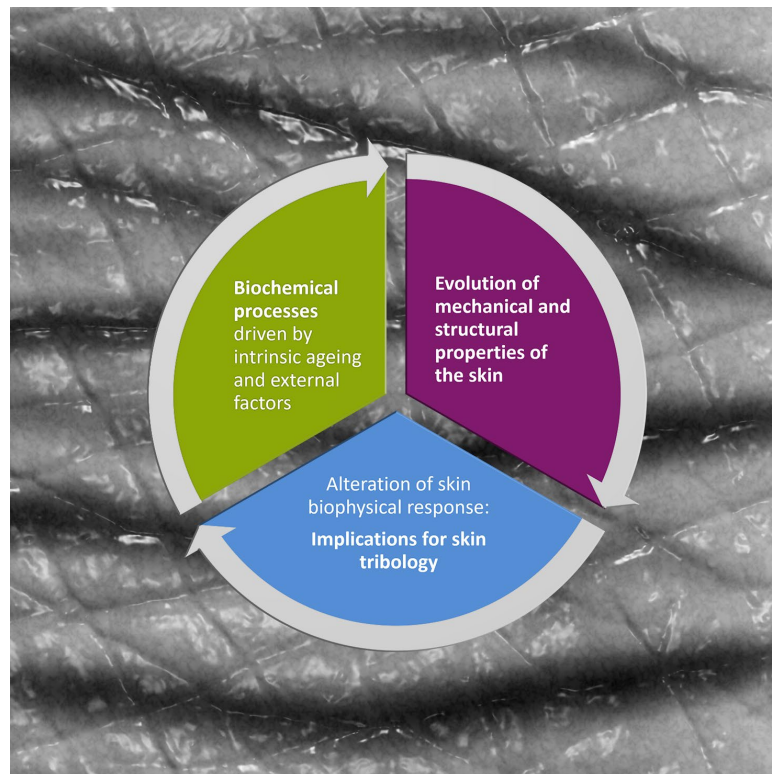

Figure 6. Simplified workflow diagram highlighting the dynamic nature of skin biophysical properties across the life course and their effects on skin tribology. Intrinsic and extrinsic ageing factors lead to a cascade of coupled biochemical processes which dynamically alter skin micro-constituents (e.g. collagen and elastin), leading to detrimental modifications of skin mechanical properties, across several length scales. Ultimately, these variations in properties affect the mechanical response, particularly at the surface, when the skin interacts with external devices.

Experimental studies have considered interfacial shear stress as a surrogate *in vivo* measure of the risk of developing skin injuries [162-164] but have not provided a quantitative insight into how these stresses are propagated from the external surface of the *stratum corneum* to the viable epidermis and dermis. In a two-dimensional image-based sensitivity finite element study Leyva-Mendivil et al [15] quantified the role of skin surface topography and internal layer microstructure, in terms of geometry and material properties, on the transmission and propagation of shear stresses within the skin. Three rigid discoidal slider sizes were considered (0.1, 0.25 and 0.5 mm). Although this study was purely computational it highlighted the fact that physics-based simulations of the mechanical response of skin against a surface (e.g. multi-asperity contact) must account for microstructural skin features if the objective is to gain a realistic and mechanistic understanding of frictional force generation and load transmission across the skin surface. These results have implications for a wide range of applications from basic discovery research in skin biology, prevention and treatment of pressure ulcers, friction-induced burns (e.g. like those occurring during airbag deployment) to personal care products and ergonomics. Again, any age-induced alterations of skin microstructure and material properties would lead to variations in skin's tribological response.

5.4 Skin sensing abilities

Tactile perceptual ability is known to decline with age [177-179]. As pointed out by Skedung et al. [178], besides physical dysfunction, the loss of tactile ability for the elderly also features an important emotional dimension, and both aspects will gain increasing importance as populations continue to age. As people age and aspire to remain active longer, it is likely that the role of skin-to-skin contact in intimate physical relationships will become an area of importance for many more individuals.

A recent parametric finite element study by Jobanputra [180] employed a simplified model that incorporated a multi-layered, linear elastic skin model and found that the flattening of the DEJ [65] and the susceptibility to tearing [9] may well be related: as the DEJ flattens, its ability to sustain both normal and shear stresses reduces. Furthermore, the flattening of the DEJ appears to redistribute these stresses away from the junction [180], which is the location of many mechanoreceptors. This result would suggest that changes in skin geometry may play an important part in the deterioration of tactical perception experienced by the elderly described by Skedung et al. [178]. Earlier, similar findings were obtained in a comparable three-dimensional finite element study conducted by Garcia-Martinez and Limbert [181] which was later extended [182]. These authors used age-dependent parametric DEJ, epidermis and dermis geometries in combination with neo-Hookean elasticity which is valid for finite deformations.

A precise mechanistic understanding of the already proven influence of physical properties such as surface roughness, texture anisotropy or elastic modulus on tactile perception remains to be established [178]. The basis of sensory tactile perception could be simply described as the conversion of a mechanical stimulus into a neural response which is interpreted by the brain. The skin contains sensory receptors—known as mechano-receptors—that can detect contact, tensile and compressive forces as well as vibrations [183]. The four main mechanoreceptors are Meissner's corpuscles, Ruffini's corpsuscules, Pacini's corpuscles and Merkel's discs [183]. Any physical stimulus sensed by these receptors is transformed into an electro-chemical signal triggering action potentials, transmitted through neuronal pathways to the central nervous system where the information is processed. In contact interactions, mechano-receptors relay haptic signals encoding the characteristics of the surface contacting the skin and the intensity/directionality of deformations [184]. Mechano-receptors are distributed throughout the dermis, and nociceptors (i.e. "pain sensors") throughout the epidermis [185, 186].

In a systematic experimental study using psychophysical testing, Skedung and colleagues investigated the role of physical surface characteristics of various grades of paper [184] and calibrated wrinkled polymeric surfaces [187] on tactile perception. It was shown that although the coefficient of friction induced by the finger sliding over a surface was dependent upon the surface characteristics, the applied load was unconsciously modulated by human participants to maintain a constant friction force [178, 184, 187]. In their recent experimental study investigating the mechanisms of tactile sensory deterioration in elderly subjects, Skedung et al. [178] suggested that, despite being correlated with reduced elasticity, moisture content and finger friction coefficient, the diminished tactile sensory perception is primarily explained by neural factors through age-related decline in receptor sensitivity, signal transmission or density. The contribution of the latter factor was also supported by experimental findings showing that, within the elderly cohort, those individuals with higher density of Meissner's corpuscles consistently outperformed those with lower density, in terms of tactile discrimination ability. Such a conclusion may be reconsidered in the light of new finer mechanical characterisation tests as, in this study, finger elasticity was measured using a Cutometer® MPA 580 (Courage and Khazaka, Köln, Germany) featuring a 2 mm aperture. Although measurements of this type are very useful in discriminating mechanical properties among particular groups [188], they are not directly related to physically-meaningful mechanical constitutive parameters. More subtle differences in the way mechano-receptors are triggered as a result of ageing-induced variations in skin microstructure and local (i.e. microscopic) material properties could be revealed by appropriate mechanical characterisation techniques. Recent work by Abdouni et al [189, 190] looked at experimentally characterising the influence of gender and age on the biophysical properties of the human finger, and also on touch gesture and tactile perception [190]. These authors found a positive correlation between age and Young's modulus (determined through indentation experiment), higher for women than for men. A negative correlation was observed between age and the arithmetic mean of surface roughness for female subjects while a positive correlation was found for male subjects. In a recent experimental study comparing the friction of human finger sliding on paper sheets in a cohort of 33 male and female subjects aged 20 to 80, Mabuchi et al. [191] observed that friction decreased with age. The authors suggested that water absorption was responsible for that finding as there was a positive correlation between skin moisture and coefficient of friction.

Although the ridge patterns of fingerprints, unique to each individual [192], do not evolve with age, the size of ridges and valleys can change due to mechanobiological effects of ageing and those associated with extrinsic mechanical and chemical factors such as in the case of particular manual activities over longer periods of time (brick-laying, washing up without protective gloves). As consequence of alteration of fingerprint ridge size and biophysical/biochemical properties of the skin associated with ageing [193], fingerprints left over a surface can reveal information about the age of individuals [194], for example, by lacking precise geometrical features compared to fingerprints left by younger individuals. This aspect is currently fuelling a large body of research in forensic sciences and biometrics.

From the few illustrative studies discussed in this section, it is clear that the biophysics of tactile perception is a rather complex system property involving a large number of independent and correlated factors. Mechanics is central to these physical phenomena so it is legitimate to consider possible links between degradation of geometrical and mechanical properties of skin microstructure and decline in haptic perception ability among the elderly.

The next stage in tactile, or simply contact, perception is the notion of discomfort which culminate as a pain sensation beyond a certain mechanical stimulus threshold. When the skin experiences excessive—and therefore potentially hazardous—deformations, nociceptors fire a "pain" signal, signalling to the brain to take action to supress that source of pain and prevent any initiation or further extension of damage; this is known as the withdrawal reflex [195]. In individuals with deficient neuronal pathways including comatose patients and those with paralysis or peripheral neuronal damage (e.g. diabetic patients), sensory perception of contact-related skin deformations is lacking or significantly diminished [15]. Disruption of sensory signals might lead these subjects to remain unaware of excessive mechanical stress on their tissues. Any prolonged position which involves contact pressure and shear at the surface of the skin has the potential to be seriously detrimental to an individual's skin integrity which can ultimately result in the initiation of superficial and deep pressure sores [170, 196, 197].

6   Perspective and conclusion

This focused review has highlighted selected examples of tribo-mechano-structural consequences of ageing on skin health and well-being. The intention was to raise awareness among the biotribology and biophysics research communities and point out high-impact and high-growth research areas. It is hoped that this article would be useful in that respect. Ageing of populations is an irreversible phenomenon and, in most Western countries, like the UK, the associated societal and technological challenges feature highly in the list of government priorities and that of research councils (e.g. UKRI, RCUK). Recognising the nature and extent of these challenges is a first step toward addressing them.

Beside what could be viewed as negative economical consequences of population ageing on welfare/healthcare services and governments, extension of life expectancy, combined with paradigm-shifting evolution in the social perception of age, has necessitated and created tremendous technological [198] and commercial opportunities [199]. This trend will continue to increase in the future and novel market segments associated with particular age groups, or categories within age groups (e.g. female and male), will emerge. Life expectancy in Western countries is expected to reach 100 years by the end of the century [198]. The repercussions of this unprecedented phenomenon for human history will be more significant for women, as they will spend as much as half of their life post-menopause, where skin function is drastically affected by low estrogen levels [1, 200]. In addition to cardiovascular and neurodegenerative diseases, Type 2 diabetes, certain types of cancer (e.g. breast cancer) and immunoscenescence [200], there are also gender-specific manifestations of ageing in skin, such as in tactile perception [189, 190].

There is now a large cohort of older people who are capable of, and want to remain, physically active well into their seventies. But consumer products for leisure, including sportswear, gardening products, walking shoes and wearables are designed primarily for younger people with intact, less fragile skin. It is common to see older people adapting products—for instance by always having to use gloves when using tools—to protect their skin from damage. It is of paramount importance to gain a more precise idea of the extent and scope of these issues in order to inform future research directions and to understand where benefit could be delivered. This recognises that skin fragility is not just an issue for those who are sick, for instance for those needing less abrasive incontinence or other products, but for the well to allow them to continue to enjoy an active lifestyle.

Similar considerations also extend to a wide range of other products from medical devices through personal care products to vehicle interior surfaces and consumer electronics. For many of these products the biophysical response of the skin, particularly for contact mechanics, is crucial in terms of comfort, performance and safety. It is therefore essential to engineer products that take into account altered biophysical characteristics of an aged skin, so to optimise their performance in terms of human factors. These aspects are embodied by the concept of inclusive design [201].

Moving research on skin biotribology forward, the goal should be to understand how age-related alterations of skin biophysics can be accounted for in the development of new or enhanced products that will improve health, quality of life, and enable the aged and ageing population to remain active longer. Particular research efforts should be devoted to gain a fundamental and quantitative insight into the mechanisms that drive and govern the ageing process. Unravelling the inherent complexity of the skin ageing process, firstly by identifying its biophysical drivers, underlying modulating factors and effects, and secondly, by gaining a mechanistic insight into their interplay, is a formidable challenge at both experimental and modelling levels. This stems from the fact that: (1) ageing is a multi-factorial problem which features multiple types of processes rooted in biology, chemistry and physics, and more particularly, mechanics; (2) these processes are non-linear and lead to complex non-linear feedback loops and (3) there is a significant intra-individual (primarily due to anatomical location and environmental exposure) and inter-individual (as a consequence of age, sex or genetics) variability. This complexity currently hinders our ability to develop a mechanistic understanding of ageing, and therefore, a rational basis to design prevention and treatment strategies against its mischievous effects. The provision of experimentally-based mathematical and computational models of skin ageing holds the promise of offering a rational quantitative basis to develop such solutions whilst also enabling and accelerating innovation, and alleviating the reliance on animal models through a better quantitative understanding of human ageing. One of the main challenges in developing, testing and validating biophysics-based model lies in the (limited) availability of relevant experimental data. Nowadays, it is almost a cliché to state that, because of complex technological demands induced by societal challenges (e.g. ageing), only inter- and multidisciplinary approaches integrating experimental characterisation, imaging, clinical observation and modelling from the outset, will have a real chance to deliver *predictive* tools [202] to account for skin ageing in the design of treatment solutions and products.

The multiscale aspects of tissue structure—both in length and time scales than span several orders of magnitude—coupled to evolution of cell/tissue biochemistry present significant technical challenges for experimenters and modellers alike. Models are only as good as the quality and statistical significance of the experimental data they are based on. Practical, economical and ethical reasons typically limit the scope and scale of physical characterisation experiments. These constraints are in direct conflict with many aspects of skin biology and biophysics, namely a large intra- and inter-individual variability of biophysical properties, a major sensitivity of the skin to internal and external environmental conditions, and the fact that the *in vivo* and *ex vivo* biophysical environments of the skin are fundamentally different. Intra-individual sources of variability include anatomical location and associated skin tension lines, health status and history, diet, age, sleep patterns, hormone and glucose levels while ambient temperature, humidity level, air pollution level, water quality and sun exposure are external factors modulating this variability. There are therefore formidable challenges in *representatively* characterising the skin hierarchical structure as well as its biotribological properties.

Probabilistic numerical techniques based on Bayesian inference [203] have been applied to soft tissue mechanics [204] and virtual skin surgery procedures [205, 206], whereby variability of constitutive parameters, loads or geometry is accounted for, and uncertainties arising from this variability, propagated through to the resulting statistical mechanical response. This type of approach can equally be applied to experimental data sets, expert knowledge (e.g. clinician's expert opinion, observations made by patients themselves) or data sets generated from parametric physics-based simulations, the objective being to infer (complex) system behaviour and unravel complex or hidden relationships between system input and output variables.

Computer realisation of Bayesian inference theory belongs to the broad class of machine learning techniques. These methods are currently making a big impact in the computational mechanics community [207, 208], as they go beyond mere data mining and machine learning. They also offer the possibility of creating and exploiting data-driven *model-free* simulations. These paradigm-shifting technological advances are to be closely monitored because they have the potential to make a huge impact in biophysics, skin science and biotribology, in the not so distant future.

Moreover, the question of how to best integrate multi-modality/multiscale imaging and characterisation data together with modelling techniques naturally arises. This is an area where, we think, significant research efforts should be expended. It is crucial to develop and seamlessly integrate modelling and experimental methods/methodologies, from the outset, so that data sets and models are well planned and optimised, featuring only needed input and response variables, thus avoiding the syndrome of "*post mortem* analysis" of data [209]. The focus should be on *relevant* and *useable* rather than *big* data.

It is also in our opinion that the marriage of biological soft matter physics, biology and tribology is long overdue. Many of the concepts, models, and characterisation techniques of tribology that have been introduced in the 19th Century during the Industrial Revolution, and developed further throughout the 20th Century to design metallic heavy machinery systems, continue to be sometimes inappropriately used in a biophysical context. For example, except in the ground state (i.e. in the close vicinity of the undeformed configuration), the notion of a constant Young's modulus or Poisson's ratio does not make any sense for non-linear structural materials undergoing finite deformations, even if they are assumed to feature isotropic mechanical properties. Similarly, contact mechanics is a branch of tribology which is particularly relevant for the physical response of skin but that has not really delivered *quantitative* and *mechanistic predictive* tools that generalise to a wide variety of conditions and tribo-systems in the context of biological soft matter tribology. At the moment, brute-force computational models [14, 153, 210] can partly address these questions but, should be improved to better account for the multiphysics and multiscale nature of problems, as well as for a better integration of internal and external parameter variability, for example by means of stochastic numerical techniques [211]. Besides featuring an extreme compliance, biological soft matter such as the skin, is inherently non-linear because of the non-linear mechanical behaviour of its microstructural constituents and/or complex geometrical, and often multiscale, arrangement of these elemental building blocks. Characterising and describing the mechanics of skin *in vivo* through predictive models is already in itself a tremendous technical challenge, let alone if the ambition also is to account for the coupling of mechanical phenomena to biochemical processes such as those arising during ageing of the skin.

In summary, it is hoped that a convincing case was put forward to explain why we should care about the tribology of the ageing skin and what, as inter- and multisciplinary scientific and engineering communities, we can do to enable discoveries, increase our understanding of the biophysical complexity of skin ageing, develop methods and methodologies to be more mechanistic and quantitative in our experimental protocols and modelling predictions, and, ultimately, enable and accelerate innovation in the pursuit of healthy ageing and well-being.

7 Acknowledgements

8 Conflicts of interest

None to declare.

9 References

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