



# EX-VIVO LAYER-BY-LAYER ANALYSIS OF MECHANICS AND MICROSTRUCTURE OF FACIAL AND MAMMARY DERMIS

## A MECHANISTIC VIEW ON THE AGEING HUMAN SKIN

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Lynch et al, 2021, Sci. Rep. <https://www.nature.com/articles/s41598-022-04767-1>

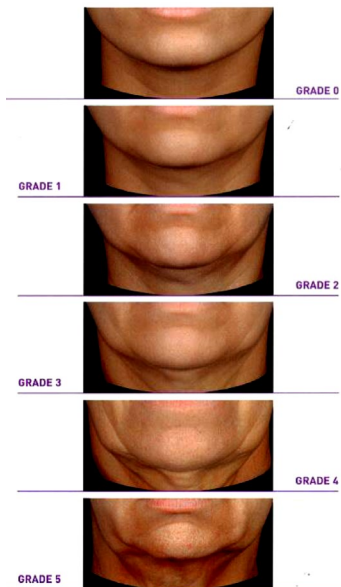
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ADVANCED  
RESEARCH



# CONTEXT AND INCENTIVE



From **perceived** age-related changes

*Wrinkles*  
*Firmness loss*  
*« Plumpness » loss*

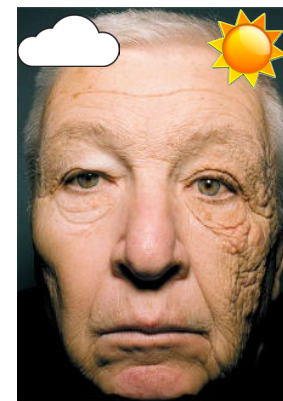
To the **mechanics** behind them



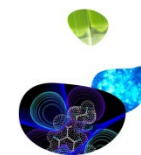
To the **microstructural** causes



To **actives and energy treatments**



**Characterize age-related changes in HUMAN skin mechanics, in particular in the FACE area: What, Where, When  
→ To determine relevant microstructural TARGETS**





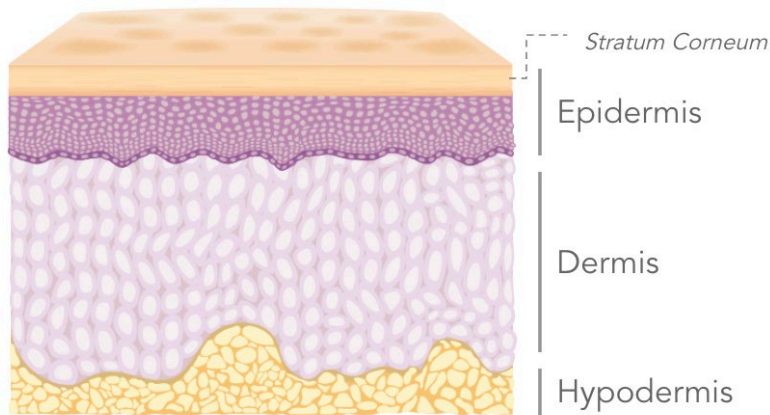
# SKIN BIOMECHANICS



**Stiff / soft** = how much resistance the material opposes to a deformation

**Modulus** = the material stiffness reported to its thickness

**Elastic** = how easily the material bounces back once the deformation is removed

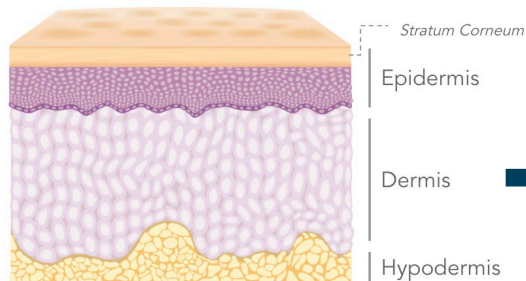


- **Each layer have their own mechanical properties**
  - SC is extremely stiff & very thin
  - Viable epidermis is very soft in comparison
  - **Dermis** is relatively stiff, and (visco)elastic  
= **Main contributor** to overall mechanics
  - Hypodermis is soft
- **Mechanical properties are:**
  - Intimately linked with microstructure
  - Highly dependent on mechanical test  
(e.g. direction, speed, location)
- **Skin layers are binded together** & influence each other through **biological + mechanical** signaling





# THE DERMIS



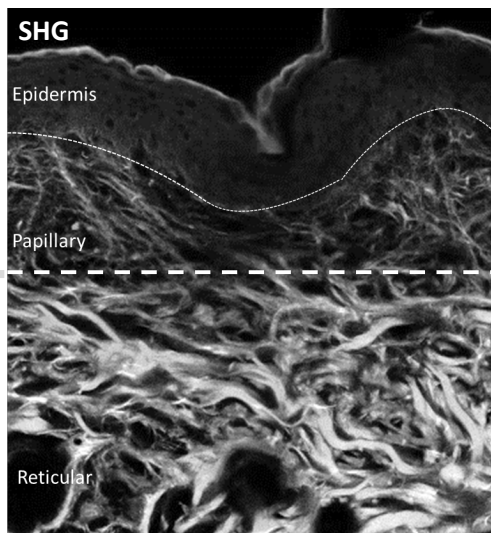
## Composite structure:

Collagen fibres, mainly type I

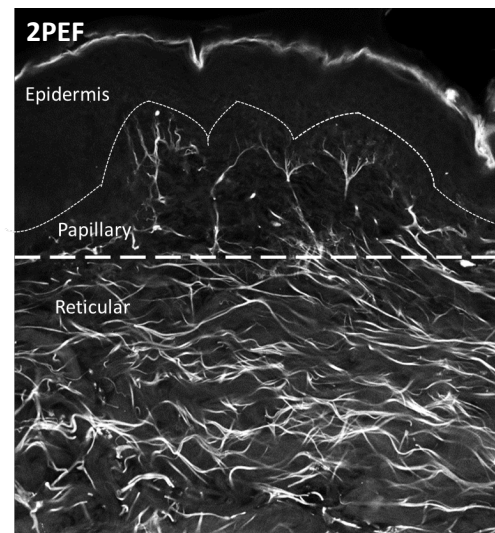
+ Elastin/Fibrillin fibres

+ Host matrix: water, glycoaminoglycans...

## Collagen fibres



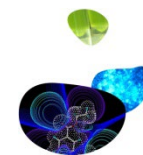
## Elastin/Fibrillin fibres



Two sublayers:

Papillary dermis

Reticular dermis

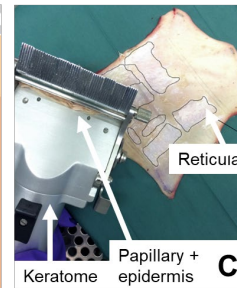
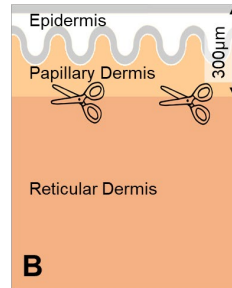
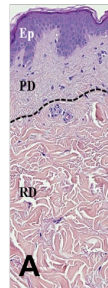
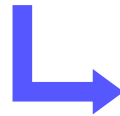
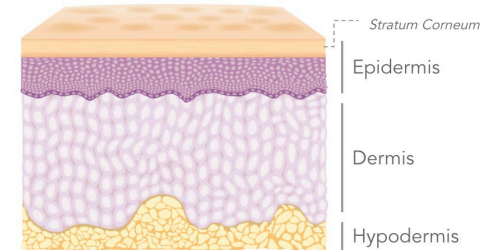




# EX VIVO SAMPLES

Ex vivo skin, from **mammary** + **lifting** surgeries → full thickness + layer-by-layer dermis

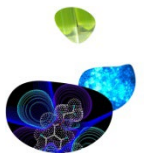
Age Group	Mammary photoprotected	Cheek photoexposed
18-40	6	0
40-60	8	8
60-80	3	12



+



Chemical de-epidermisation





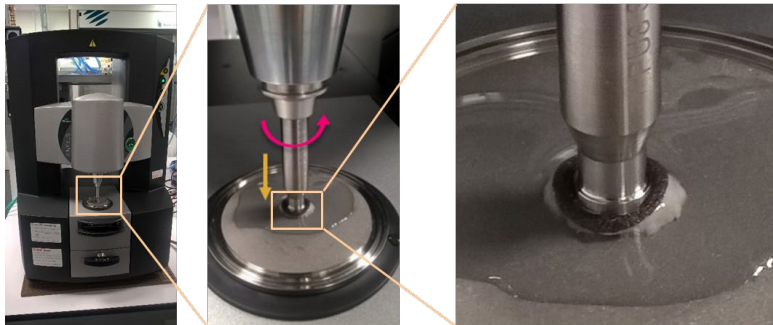
# MECHANICAL CHARACTERIZATION

## Using a reometer

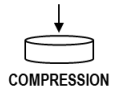
### 1. Stiffness and elasticity in small deformation in shear



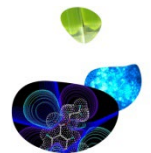
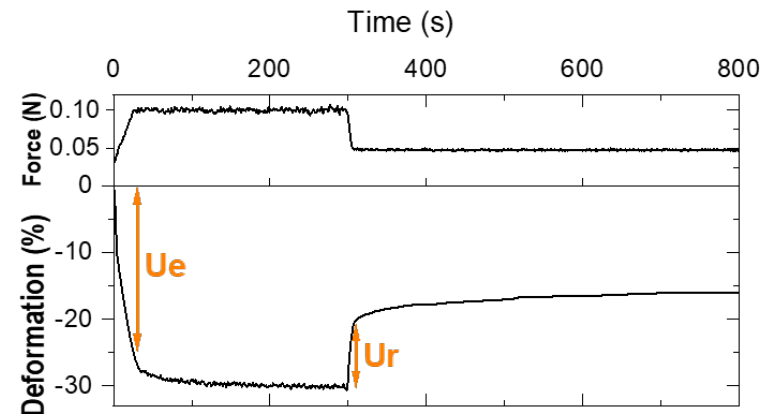
Amplitude sweep from 0.01% to 0.1%



### 2. Elasticity in large deformation in compression: $U_r/U_e$

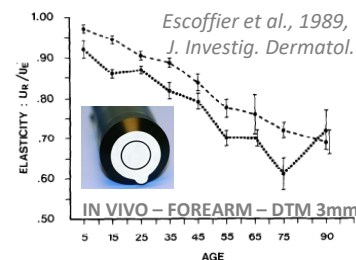
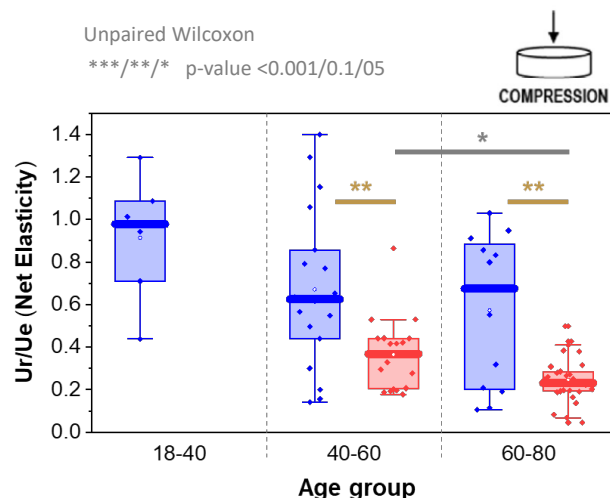
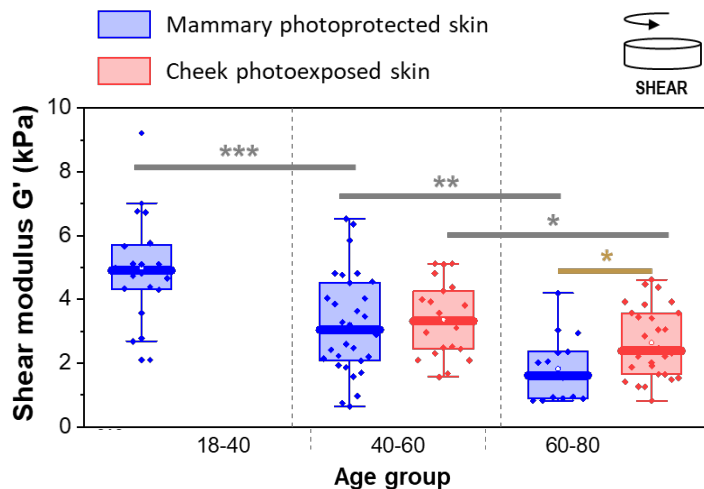


Creep-and-recovery response,  
0.1N compression, 300s creep, 500s recovery





# AGEING SKIN MECHANICS

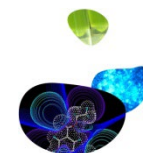
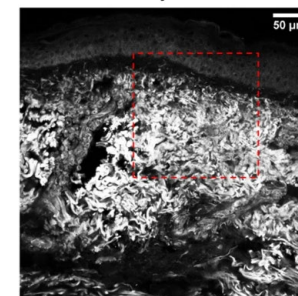


- Very significant age-related **decrease in stiffness** at small deformations
- **Loss in elasticity** with age
- Photoexpositon : Increase in stiffness in aged skin (elastosis?) + loss in elasticity



**Key to explain age-related changes in perception?  
Protection & Early intervention are essential**

**Aged Cheek Skin  
79 y.o.**

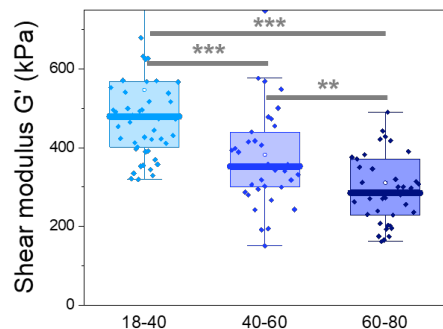




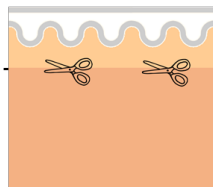
# AGEING ONSET

Unpaired Wilcoxon

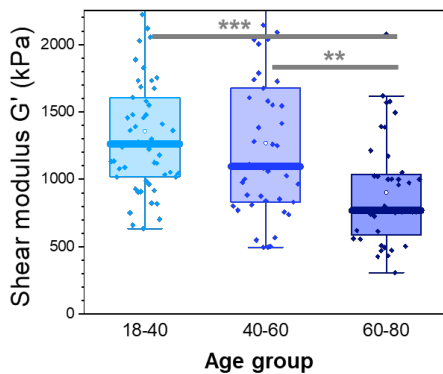
\*\*\*/\*\*/\* p-value <0.001/0.1/05



Papillary dermis side



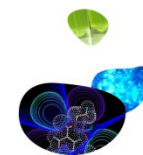
Reticular dermis side



- Reticular layer  $\approx$  3 times stiffer than papillary
- Decrease in stiffness with age on both layers
- **Earlier onset in the papillary, superficial layer of the dermis, around 40yo**



**Informs on where and when cosmetics should act to be effective on age-related disorders**

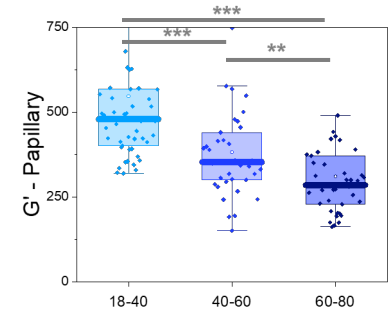






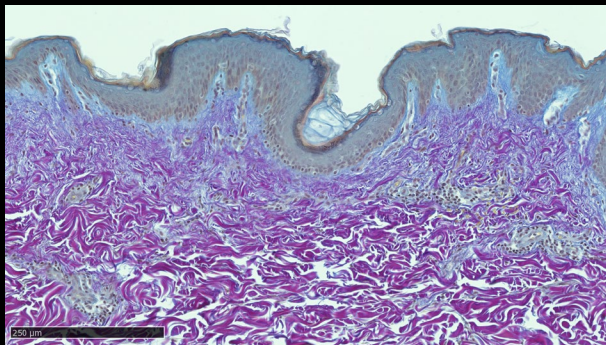
# ASSOCIATED MICROSTRUCTURAL CHANGES

- Collagen was found to be **more degraded with age, structurally and qualitatively**
- The **onset is earlier in the papillary**, superficial layer of the dermis
- The degradation was a lot worse in **photoexposed skin**



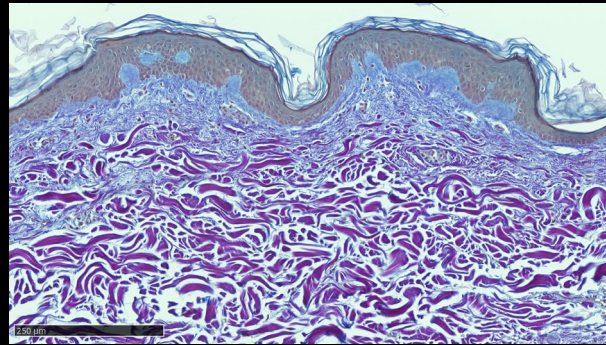
Young Mammary Skin

20 y.o.



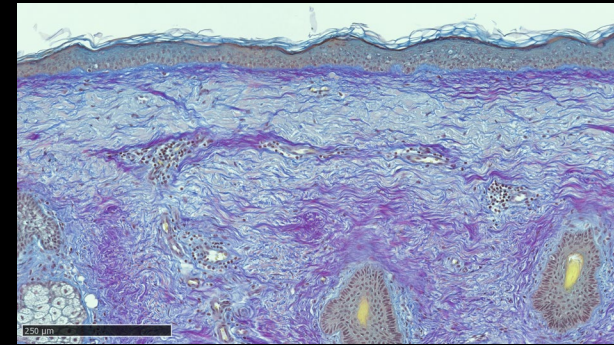
Aged Mammary Skin

65 y.o.



Aged Cheek Skin

70 y.o.



Herovici **Purple = Mature**  
**Blue = Immature / Degraded**



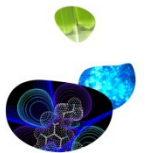
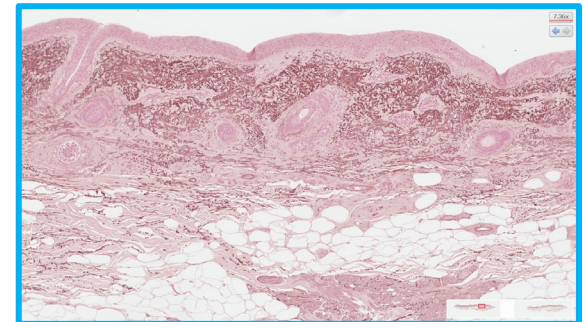
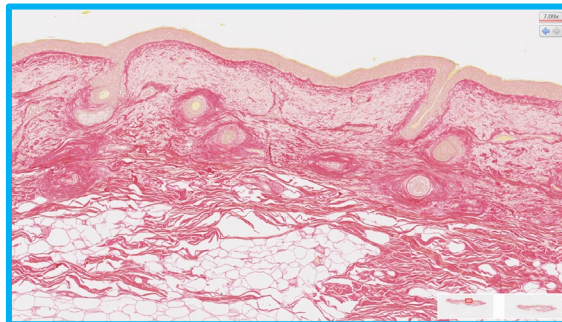
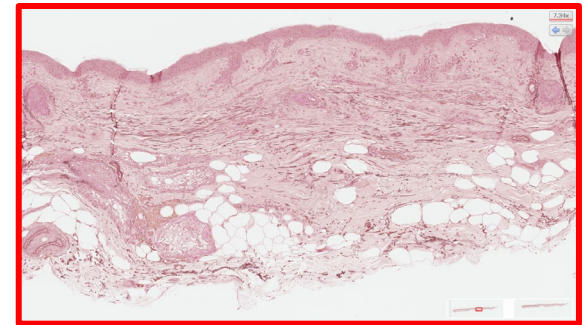
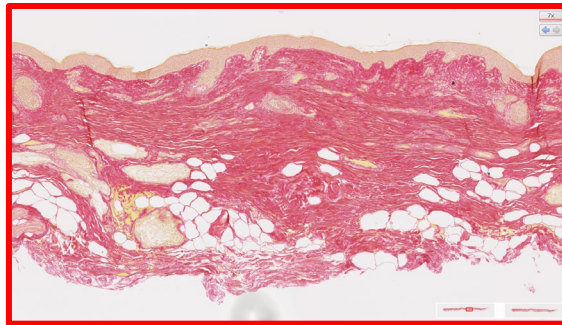
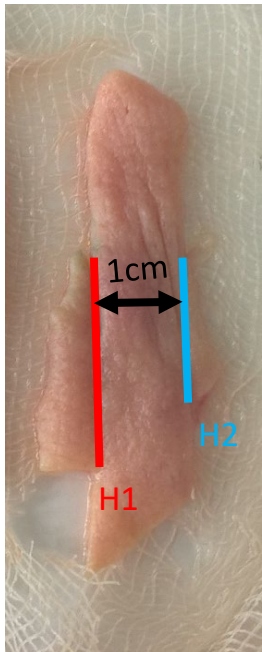


# ASSOCIATED MICROSTRUCTURAL CHANGES

- **Extreme spatial variability** in the microstructure on cheek: impact on **perception**?

Sirius Red = Collagen

Orcein = Elastin

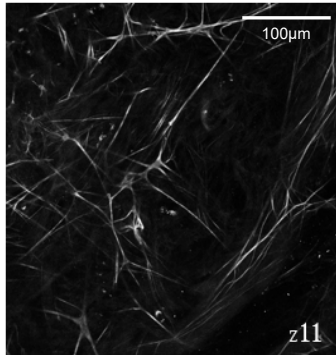




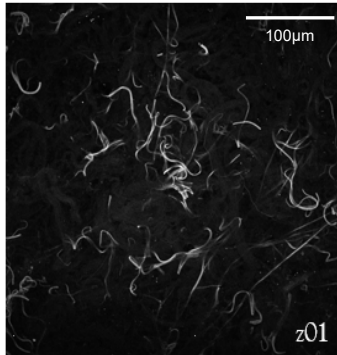
# ELASTIN & DERMIS MECHANICS

- Important clues about the probable role of elastin fibres in skin mechanics

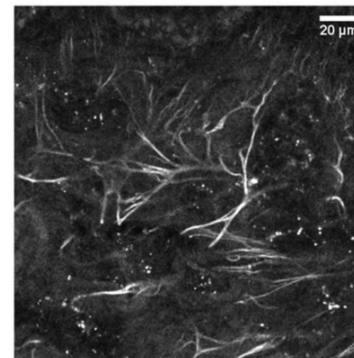
**Under tension**  
deep in tissue



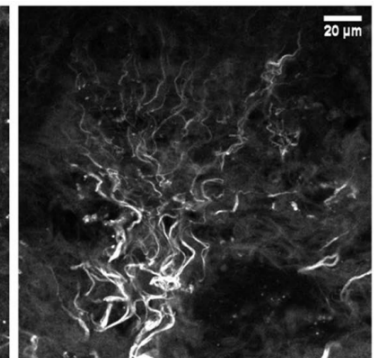
**Relaxed when cut**



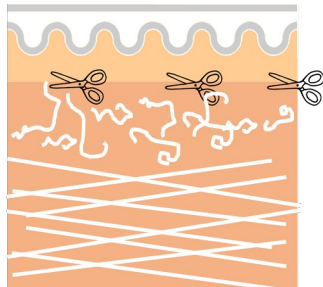
**Young Mammary Skin**  
19 y.o.



**Aged Mammary Skin**  
66 y.o.

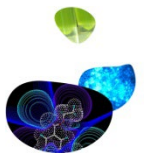


2PEF = Elastin, cells, hairs...



**Stretched**  $\perp$  to surface  
in young skin

Gradually **more**  
**fragmented + wavy** with age



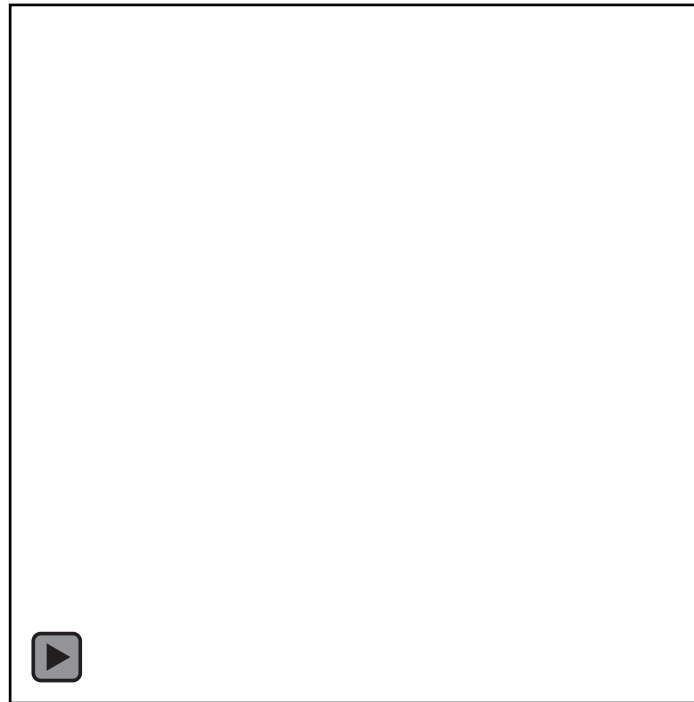


# ELASTIN & DERMIS MECHANICS

- Important clues about the probable **role of elastin fibres in skin mechanics**

Elastin fibres have much larger typical length scale than collagen fibres

→ Potential to impact on a **large scale**

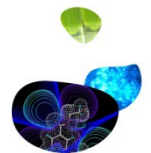


Optically-clarified dermis  
≈ 2mm deep stack

**SHG signal = Collagen**

**2PEF signal = Elastin, cells, hairs...**

500  $\mu$ m



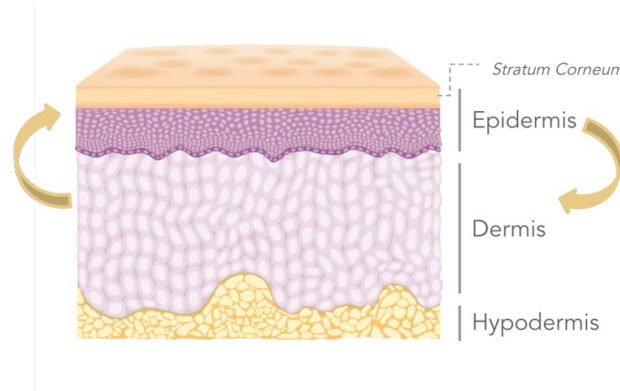


# INTERLAYER MECHANICAL CROSSTALK

## The papillary dermis softening with age could impact epidermal development

Possible factor in Dermal-Epidermal Junction flattening

- decreased nutrient supply to epidermis
- **decreased epidermal quality**
- **degraded perception of skin quality**

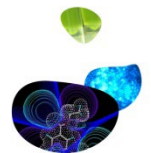
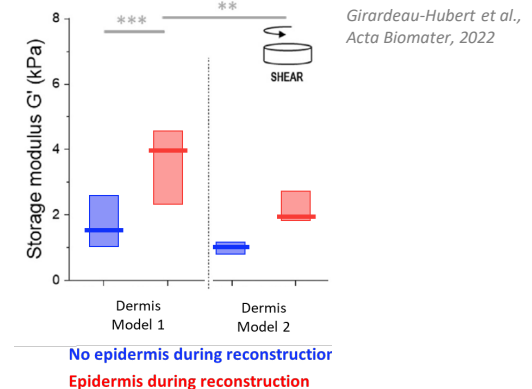


➔ **Skin layers strongly influence each other through biological + mechanical signaling**

- ➔ **Possible opportunities to**
- Improve **deep layers** through cosmetic treatment of superficial layers
  - **Stop vicious cycle or even trigger virtuous cycle?**

## In return, epidermal quality could impact dermis stiffness

Epidermal presence lead to stiffer dermis in VITRO skin models,

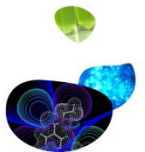




# CONCLUSION & PERSPECTIVES

- Very significant **age-related changes** in ex vivo human skin mechanics were observed
  - **Loss in stiffness** in small deformations
  - **Loss in elasticity**
- These changes were quantified in terms of
  - **Localisation** of onset: superficial dermis
  - **Age of onset**: around 40 y.o. for superficial dermis
  - Link with **photoexposition**And qualitatively linked with **microstructural changes**

- **Possible opportunities to**
  - Improve **deep layers** through cosmetic treatment of the superficial layers
  - **Stop viscous cycle or even trigger virtuous cycle?**
- Future work should aim at **expliciting the interlayer crosstalk**, both biological & mechanical to find new avenues for innovative anti-ageing treatments





# L'ORÉAL

Recherche & Innovation

