Modelling Cross-Linking in Collagen Fibrils

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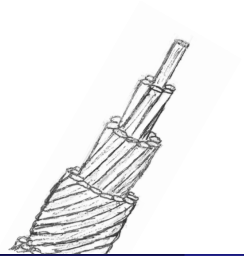
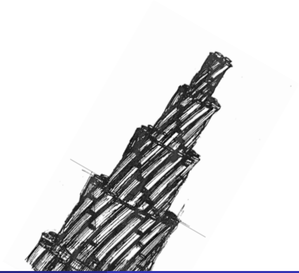




Collagen Fibrils

- Collagen fibrils are a principal structural component of many animal tissues such as tendons, bones, cartilage, and corneas.
- A fibril is a nematic liquid crystal composed of tropocollagen molecules oriented along a director field $\boldsymbol{n}$.

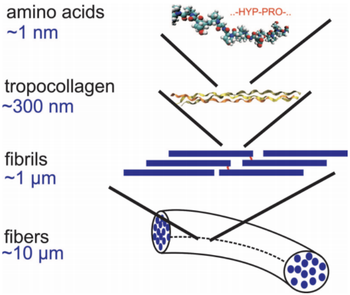


Figure: Buehler *et al.* *PNAS*, (2006).

Cross-linking

Collagen fibrils are held together by enzymatic cross-links (Lysyl Oxidase or LOX), spring-like molecules that connect two tropocollagen filaments at specific sites along their lengths.

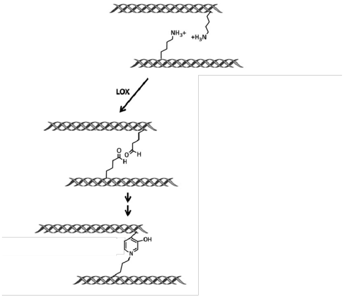


Figure: Perła-Kajan *et al. FASEB Journal*, (2016)

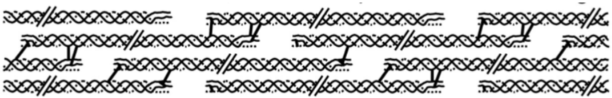


Figure: Kaku *et al. Journal of Prosthodontic Research*, (2014).

Question:

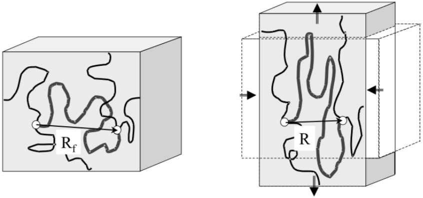
- How does the structure of a fibril determine its elastic properties?

Cross-links Modelled as Gaussian Springs

We model cross-links as entropic springs with end-to-end distance $\boldsymbol{R}$ following the distribution:

$$P(\boldsymbol{R}) = \left[\left(\frac{3}{2\pi L}\right)^3 \frac{1}{\mathrm{Det}[\underline{\underline{\boldsymbol{\ell}}}_0]}\right]^{1/2} \exp\left(-\frac{3}{2L}\boldsymbol{R}^\top \underline{\underline{\boldsymbol{\ell}}}_{\mathbf{0}}^{-\mathbf{1}}\boldsymbol{R}\right). \tag{1}$$

Here $\underline{\underline{\boldsymbol{\ell}}}_0$ is a tensor describing the structure of the fibril and its cross-links. We define $\zeta = \ell_{||}/\ell_\perp$ to be the anisotropy ratio.



[1] Warner, M., and Terentjev,E. M. "Nematic elastomers – a new state of matter?" *Progress in Polymer Science* (1996).

Free Energy

The free energy density for a cross-linked liquid crystal elastomer subjected to a strain field $\underline{\underline{\boldsymbol{\lambda}}}$ is:

$$\boxed{f_{\text{Cross-Link}} = \frac{1}{2}\rho k_B T \ \mathrm{Tr}(\underline{\underline{\boldsymbol{\ell}}}_0 \underline{\underline{\boldsymbol{\lambda}}}^\top \underline{\underline{\boldsymbol{\ell}}}^{-1} \underline{\underline{\boldsymbol{\lambda}}}).} \tag{2}$$

Here ρ is the (assumed to be constant) cross-linking density, and $\underline{\underline{\boldsymbol{\ell}}}$ is a tensor describing the post-strain fibril structure.

$$\text{Minimize } F = \frac{2}{R^2}\int_0^R r f dr \underset{\text{Numerically}}{\Longrightarrow} \begin{cases} \text{Post-strain fibril structure } \underline{\underline{\boldsymbol{\ell}}} \\ \text{Stress field } \underline{\underline{\boldsymbol{\sigma}}} \ \left(\sigma_{ij} = \frac{\partial F}{\partial \lambda_{ij}}\right) \end{cases}$$

$\underline{\underline{\boldsymbol{\ell}}}_0$: Double Twist Structure

Our ansatz:

$$\boldsymbol{n_0} = -\sin\psi(r)\hat{\boldsymbol{\phi}} + \cos\psi(r)\hat{\boldsymbol{z}}. \quad (3)$$

Then we have

$$\underline{\underline{\boldsymbol{\ell}}}_0 = \underline{\underline{\boldsymbol{\delta}}} + [\zeta - 1]\boldsymbol{n_0} \otimes \boldsymbol{n_0}. \quad (4)$$

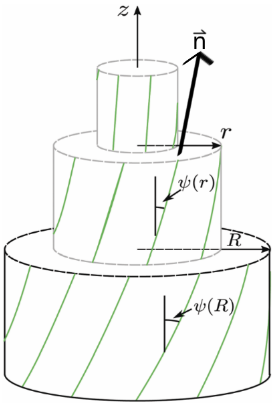


Figure: Cameron, Kreplak, and Rutenberg. *Soft Matter*, (2018).

$\underline{\underline{\ell}}_0$: Imposed Twist Phases

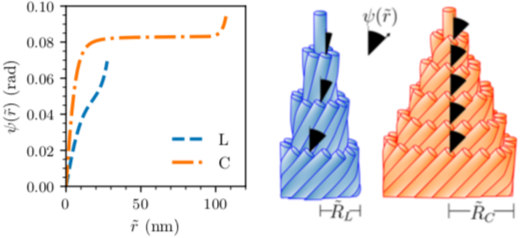


Figure: Cameron, Kreplak, and Rutenberg. *Unpublished,* (2019).

We consider two functional forms (phases) for $\psi(r)$:

- $\psi(r) = \alpha r$ (linear twist phase) (e.g. Tendon Fibrils),
- $\psi(r) = \beta \cdot \mathbb{1}_{[\frac{1}{10}R,R]}$ (constant twist phase) (e.g. Corneal Fibrils).

$\underline{\underline{\boldsymbol{\lambda}}}$: The Strain Field

We take as our strain tensor ($\boldsymbol{R} = \underline{\underline{\boldsymbol{\lambda}}}\boldsymbol{R_0}$) a volume-preserving longitudinal extension with a shear-twist around the fibril axis:

$$\underline{\underline{\boldsymbol{\lambda}}} = \begin{bmatrix} \frac{1}{\sqrt{\epsilon}} & 0 & 0 \\ 0 & \frac{1}{\sqrt{\epsilon}} & \kappa \\ 0 & 0 & \epsilon \end{bmatrix}. \tag{5}$$

Equilibrium Twist Angle

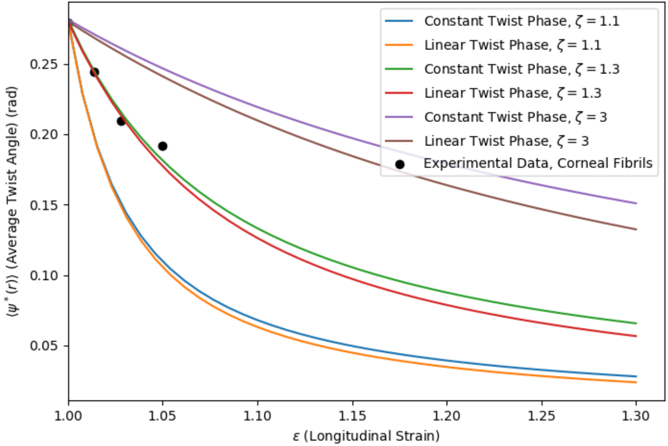


Figure: Data from Bell *et al.* *Acta Biomaterialia*, (2017).

Stress-Strain Curves

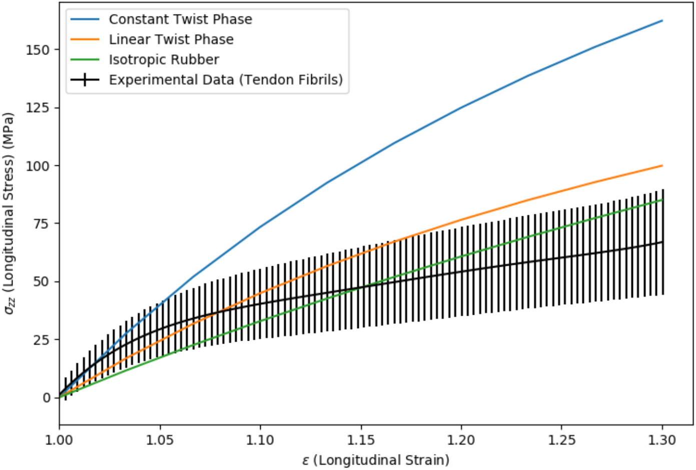


Figure: Data from Quigley, ..., and Kreplak. *Scientific Data,* (2018).

Thanks!

Form of the Anisotropy Tensor

$$
\begin{aligned}
\underline{\underline{\boldsymbol{\ell}}}_0 &= \ell_\perp \underline{\underline{\boldsymbol{\delta}}} + [\ell_\parallel - \ell_\perp]\boldsymbol{n_0} \otimes \boldsymbol{n_0} \\
&= \ell_\perp \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1+(\zeta-1)\sin^2\psi & (1-\zeta)\sin\psi\cos\psi \\ 0 & (1-\zeta)\sin\psi\cos\psi & 1+(\zeta-1)\cos^2\psi \end{bmatrix}, \\
&\text{where } \zeta = \ell_\parallel/\ell_\perp.
\end{aligned}
\tag{6}
$$

$$
\begin{aligned}
\underline{\underline{\boldsymbol{\ell}}}^{-1} &= 1/\ell_\perp \underline{\underline{\boldsymbol{\delta}}} + [1/\ell_\parallel - 1/\ell_\perp]\boldsymbol{n} \otimes \boldsymbol{n} \\
&= \ell_\perp^{-1} \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1+(\zeta^{-1}-1)\sin^2\psi^* & (1-\zeta^{-1})\sin\psi^*\cos\psi^* \\ 0 & (1-\zeta^{-1})\sin\psi^*\cos\psi^* & 1+(\zeta^{-1}-1)\cos^2\psi^* \end{bmatrix},
\end{aligned}
$$

where ψ^* is the post-strain twist angle.

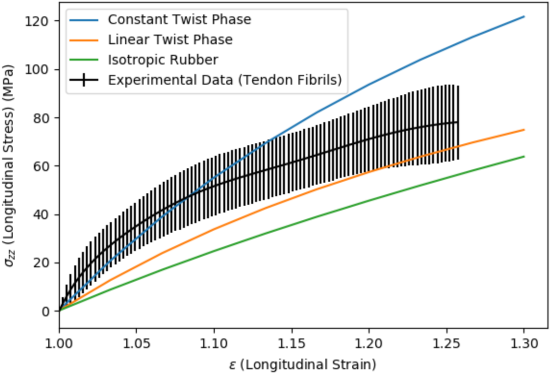
Frank Free Energy

The Frank free energy describes the energy contributions from the spatial arrangement of the tropocollagen filaments inside the fibril. For our double-twist director field $\boldsymbol{n}(\psi)$, the Frank free energy density is:

$$
\begin{aligned}
f_{\text{Frank}} = {} & \frac{1}{2} K_{22} \left(\frac{K_2}{K_{22}} - \psi' - \frac{\sin(2\psi)}{2r} \right)^2 \\
& + \frac{1}{2} K_{33} \frac{\sin^4(\psi)}{r^2} \\
& - \frac{1}{2} (K_{22} + K_{24}) \frac{1}{r} \frac{d}{dr} \left(\sin^2(\psi) \right).
\end{aligned} \tag{7}
$$

Here $K_2, K_{22}, K_{24}, K_{33}$ are the standard Frank elastic constants.

More Stress Strain Curves



Experimental Data

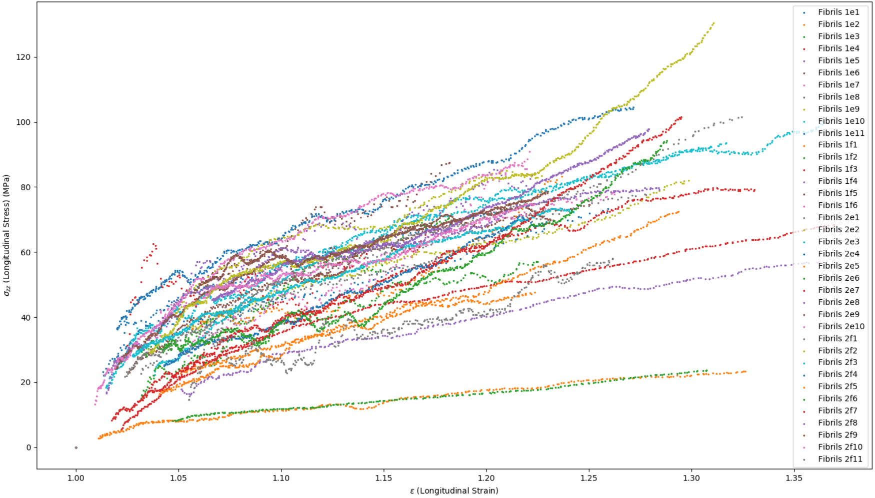


Figure: Data from Quigley, ..., and Kreplak. *Scientific Data,* (2018).