Microstructurally-based modeling of viscoelastic properties of cross-linked F-actin networks

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Introduction

Filamentous actin is one of the main constituents of the cytoskeleton and builds the densely cross-linked cell cortex. It is an initially isotropic, nonlinear viscoelastic network of biopolymers. We model this structure by means of a multiscalar elastic model together with a generalized Maxwell model for viscous contributions.

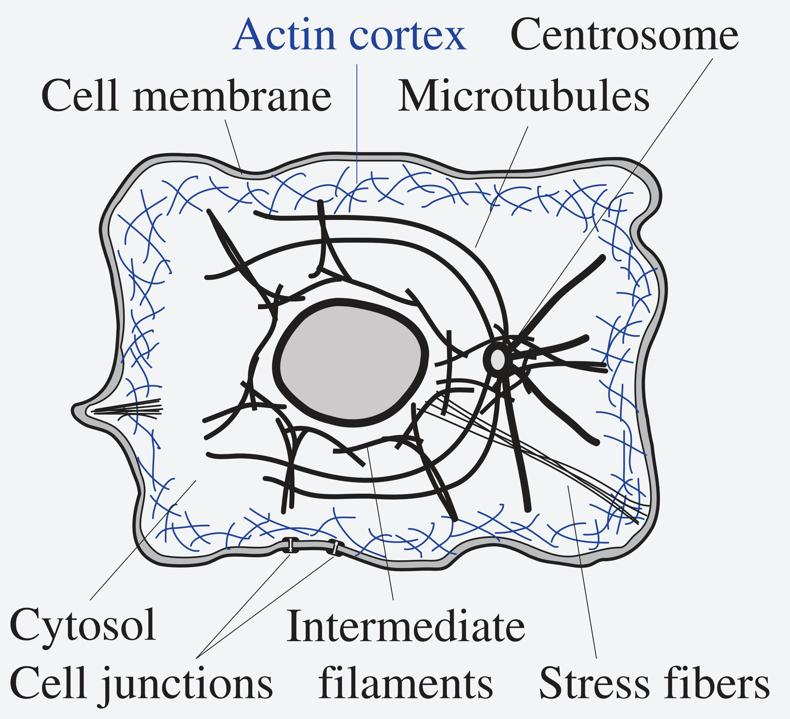

Fig. 1: Schematic of a typical cell with mechanically important components.

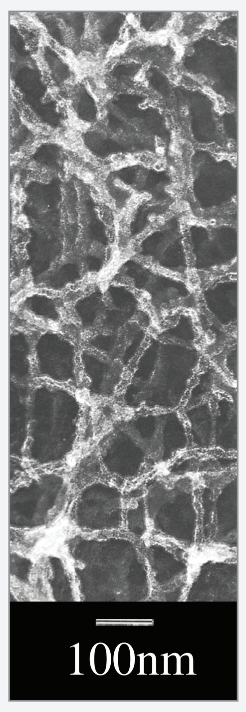

Fig. 2: In vitro *actin-filamin network. Modified from Niederman et al. (1983).*

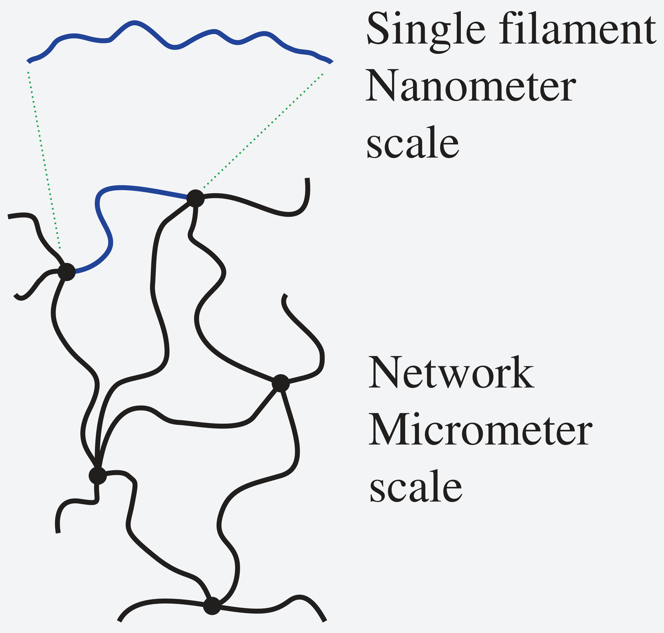

Fig. 3: Multiscale modeling.

We use the Jacobian $J = \det \mathbf{F}$ to split the deformation gradient $\mathbf{F}$ into volumetric and isochoric parts $\overline{\mathbf{F}} = J^{-1/3}\mathbf{F}$. This results in an additive decomposition of the Helmholtz free-energy density Ψ in terms of the isochoric right Cauchy-Green tensor $\overline{\mathbf{C}} = \overline{\mathbf{F}}^{\mathrm{T}}\overline{\mathbf{F}}$ and the internal variables $\overline{\boldsymbol{\Gamma}}_\nu$

$$\Psi(\mathbf{C}, \boldsymbol{\Gamma}_1, \ldots, \boldsymbol{\Gamma}_m) = \underbrace{\underbrace{\Psi^\infty_{\mathrm{vol}}(J)}_{\text{volumetric}} + \underbrace{\Psi^\infty_{\mathrm{iso}}(\overline{\mathbf{C}})}_{\text{isochoric}}}_{\text{elastic}} + \underbrace{\sum_{\nu=1}^{m} \Upsilon_{\mathrm{iso}\,\nu}(\overline{\mathbf{C}}, \overline{\boldsymbol{\Gamma}}_\nu)}_{\text{isochoric viscous}}.$$

From the above, the decomposition of the second Piola-Kirchhoff stress $\mathbf{S}$ follows with non-equilibrium stresses $\mathbf{Q}_\nu$, while the push-forward gives the Cauchy stress tensor $\boldsymbol{\sigma}$, i.e.

$$\mathbf{S} = \mathbf{S}^\infty_{\mathrm{vol}} + \mathbf{S}^\infty_{\mathrm{iso}} + \sum_{\nu=1}^{m} \mathbf{Q}_\nu, \qquad \boldsymbol{\sigma} = J^{-1}\mathbf{F}\mathbf{S}\mathbf{F}.$$

Elastic models

We use the multiscalar elastic model of Unterberger et al. (2011) as a basis.

Single filament model

The single filament is modeled as a worm-like chain according to Holzapfel and Ogden (2011). We use the shorthand notations

Bending stiffness

$$B_0 = k_{\mathrm{B}} T L_{\mathrm{p}},$$

Nondimensional force

$$f^\star = \frac{f L^2}{\pi^2 B_0},$$

Nondimensional parameter

$$\alpha = \frac{\pi^2 B_0}{\mu_0 L^2}.$$

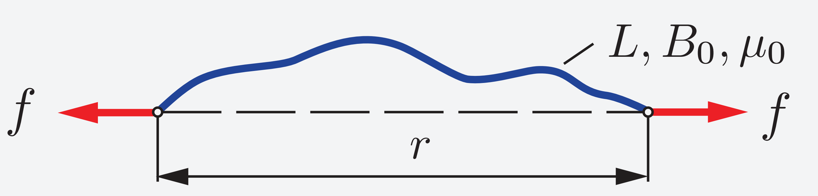

Fig. 4: Undulated filament chain pinned at the end points

Parameter	Symbol	Unit
Temperature	T	K
Persistence length	L_{p}	μm
Contour length	L	μm
End-to-end distance at zero f	r_0	μm
Stretch modulus	μ_0	nN
Effective extensional modulus	β	–

The relationship between tensile force f and end-to-end distance r is the basis for the strain-energy of a filament ψ_{f}

$$\boxed{\frac{r}{L} = 1 + \alpha f^\star - \frac{(1 + 2\alpha f^\star)(1 + \alpha f^\star)^\beta}{(1 + f^\star + \alpha f^{\star 2})^\beta}(1 - r_0/L), \qquad \psi'_{\mathrm{f}} = \lambda_0 r_0 f.}$$

Network model

Using the micro-sphere network model proposed by Miehe et al. (2004) we obtain a single homogenized stretch λ for one point in the material

$$\boxed{\lambda = \langle \overline{\lambda} \rangle_p = \left(\frac{1}{|\mathscr{S}|} \int_{\mathscr{S}} \overline{\lambda}^p \,\mathrm{d}A \right)^{1/p}.}$$

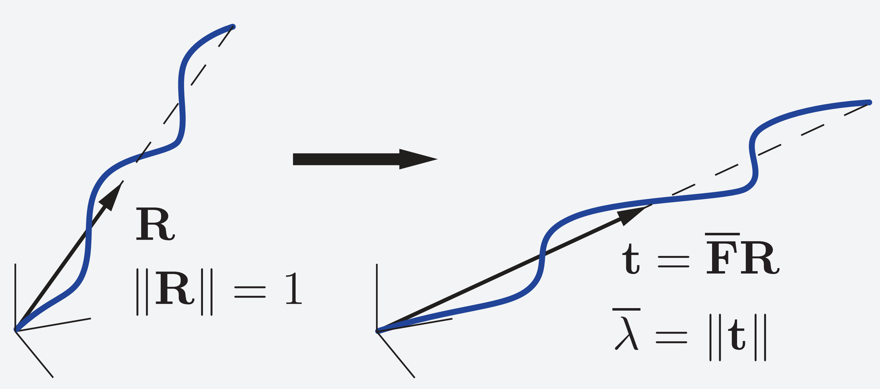

Fig. 5: Filament is stretched and rotated in space by the deformation gradient $\overline{\mathbf{F}}$.

The isochoric elastic strain-energy density of the continuum is then

$$\Psi^\infty_{\mathrm{iso}} = n\psi_{\mathrm{f}}(\lambda).$$

Parameter	Symbol	Unit
Filament density	n	μm^{-3}
Initial stretch	λ_0	–
Averaging parameter	p	–

The fourth order tensor $\mathbb{P} = \mathbb{I} - \mathbf{C}^{-1} \otimes \mathbf{C}$ furnishes the deviatoric projection in the reference configuration. Nonlinear continuum mechanics yields

$$\boxed{\mathbf{S}^\infty_{\mathrm{iso}} = J^{-2/3} n \psi'_{\mathrm{f}} \lambda^{1-p} \mathbb{P} : \mathbf{H}, \qquad \mathbf{H} = \langle \overline{\lambda}^{p-2} \mathbf{R} \otimes \mathbf{R} \rangle.}$$

Viscous contributions

Viscous effects are considered utilizing a generalized Maxwell model as described by Holzapfel (1996). Additionally to the elastic part, we consider m Maxwell elements with the evolution equation

$$\boxed{\dot{\mathbf{Q}}_\nu + \frac{\mathbf{Q}_\nu}{\tau_\nu} = \theta_\nu \dot{\mathbf{S}}^\infty_{\mathrm{iso}},}$$

and the inital condition

$$\mathbf{Q}^{0^+}_\nu = (J^{-2/3}\mathbb{P} : \widetilde{\mathbf{Q}}_\nu)|_{t=0^+}.$$

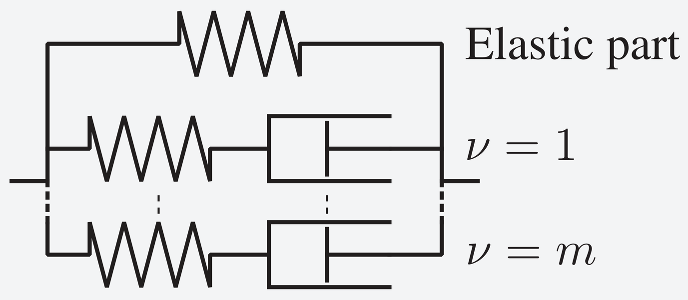

Fig. 6: Generalized Maxwell model

Parameter	Symbol	Unit
Relaxation times	τ_ν	s
Free-energy parameters	θ_ν	–

The solution gives a convolution integral

$$\mathbf{Q}_\nu = \exp(-t_n/\tau_\nu)\mathbf{Q}^{0^+}_\nu + \int_{t=0^+}^{t=t_n} \exp[-(t_n - t)/\tau_\nu]\theta_\nu \dot{\mathbf{S}}^\infty_{\mathrm{iso}}(t)\,\mathrm{d}t,$$

which can be treated numerically by means of the midpoint rule.

Results

We used experimental data from *in vitro* reconstituted actin networks obtained from bulk rheology. Heavy meromyosin in its rigid state served as cross-linking protein.

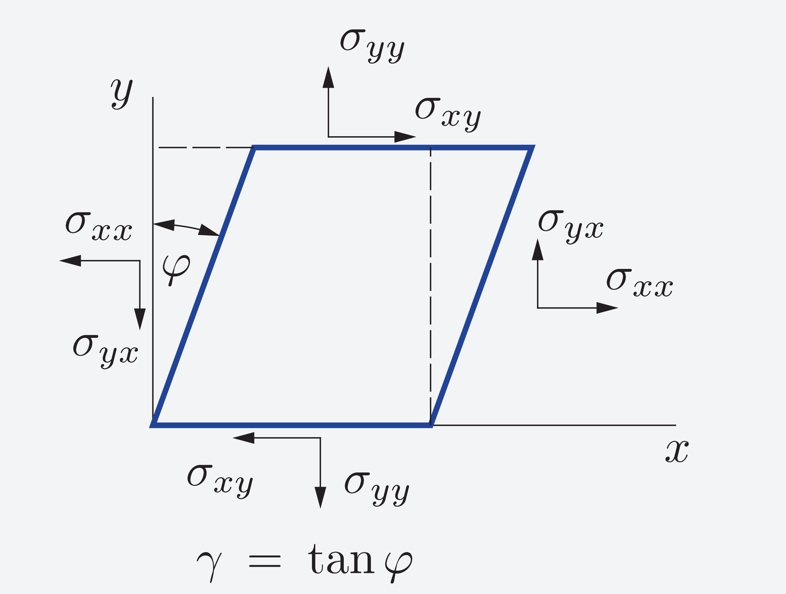

Fig. 7: The experiments were conducted with parallel plate geometry in oscillatory mode. The deformation mode is approximated by simple shear.

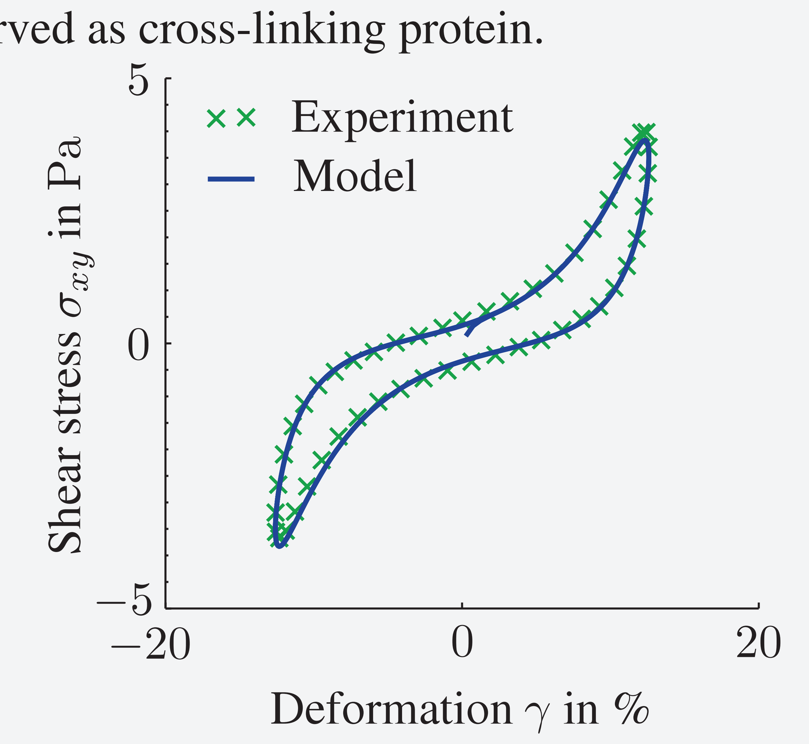

Fig. 8: Fit of one-element Maxwell model to large amplitude oscillation shear experiment.

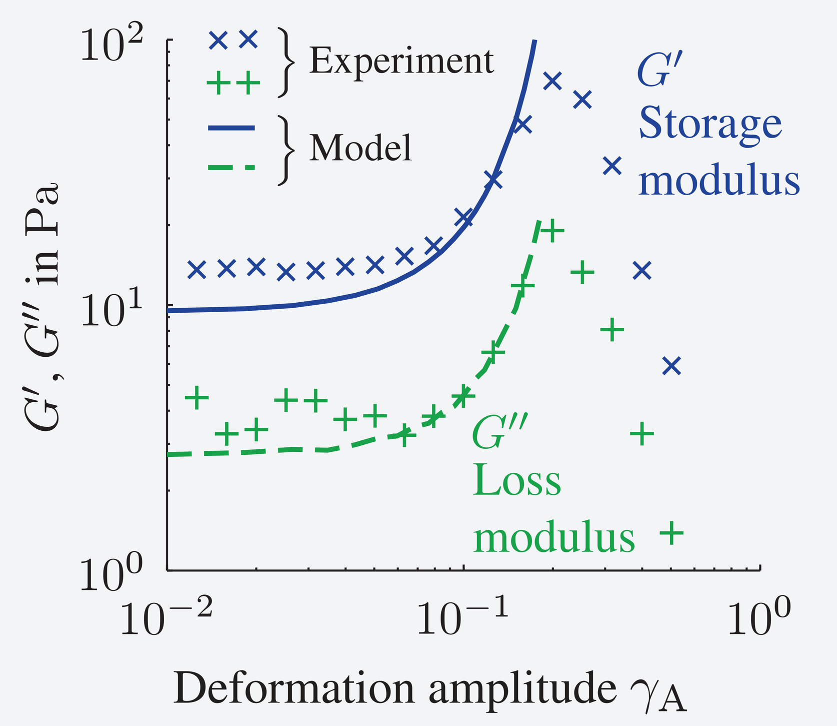

Fig. 9: Same model as in Figure 8 compared to data from amplitude sweep experiment.

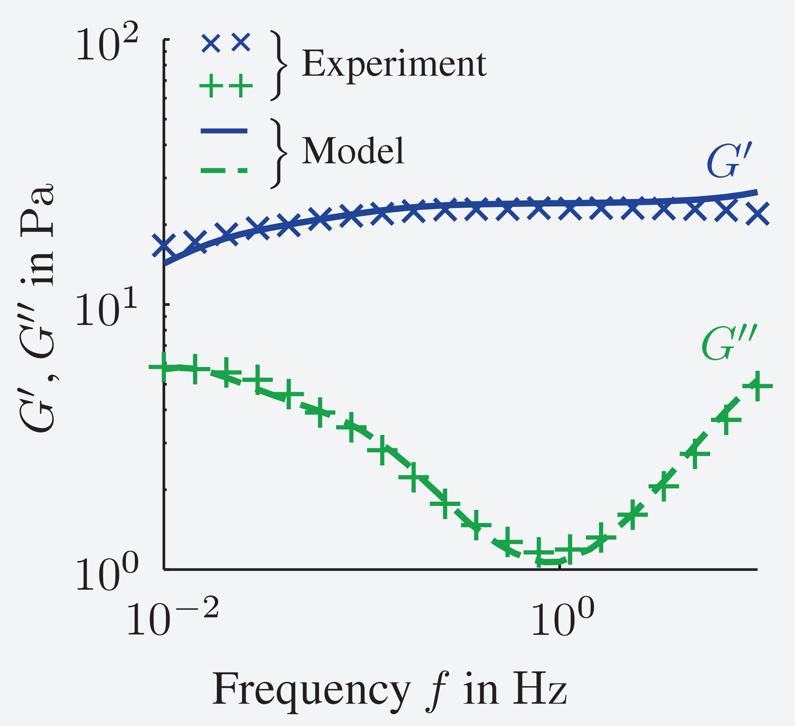

Fig. 10: Frequency sweep: a three-element generalized Maxwell model is needed to capture a large velocity range.

Conclusions

Isotropically cross-linked actin networks are well described by the proposed microstructurally-based nonlinear viscoelastic model. We obtained an excellent fit to the stress-strain data of the large amplitude oscillation shear experiment with a single Maxwell element. Storage and loss modulus comply with the experiment for a large range of deformation amplitudes. To achieve good agreement for different deformation velocities, i.e. oscillation frequencies, we need to increase the number of Maxwell elements. The elastic material parameters are not affected within this process.

Finally, the proposed model can be easily implemented into any finite element code, e.g., FEAP, to solve more complex boundary-value problems.

References and acknowledgment

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We want to acknowledge the experimental work of Christine Semmrich and Andreas R. Bausch from TU München.