

## **A thermodynamical model for stress-fiber organization in contractile cells**

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Citation: *Appl. Phys. Lett.* **100**, 013702 (2012); doi: 10.1063/1.3673551

View online: <https://doi.org/10.1063/1.3673551>

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*Journal of the Royal Society Interface* 8, 20110701. doi:10.1098/rsif.2011.0701

(Received 4 September 2011; accepted 5 December 2011; published online 4 January 2012)

Cell mechanical adaptivity to external stimuli is vital to many of its biological functions. A critical question is therefore to understand the formation and organization of the stress fibers from which

is the dependency of elastic modulus  $E_{\alpha}$  on the stretching frequency  $\omega$  to capture the viscoelasticity of SFs. Here, we describe SF stiffening with loading frequency  $\omega$  with a function  $E_{\alpha}(\omega)$  of the form<sup>23</sup>

$$E_{\alpha}(\omega) = E_{\alpha} + E_{\alpha v} \log(1 + 9\omega), \quad (4)$$

where  $E_{\alpha}$  and  $E_{\alpha v}$  characterize the static and dynamic stiffnesses of SFs at frequency  $\omega = 1$ , respectively. Without loss of generality, we assume here that cells are subjected to sinusoidal strain variation  $\varepsilon_{\alpha} = \bar{\varepsilon}_{\alpha} + \tilde{\varepsilon}_{\alpha} \cos(2\pi / \tau)$

Let us now turn to the case where cells are subjected to substrate deformation. Experimentally, SFs in contractile cells such as fibroblasts or myofibrils have been shown to preferably align in the direction of stretch for constant loading.<sup>11,27</sup> To replicate the constant substrate stretch condition, we impose a state of uniaxial strain  $\bar{\epsilon}_{11}$  to the substrate such that the angular stretch in a cell is written  $\epsilon_\alpha = \bar{\epsilon}_\alpha = \bar{\epsilon}_{11} \left( (1 + \nu) \cos^2(\alpha) - \nu \right)$ . This expression is then substituted in Eqs. (7) and (8) to derive the angular variation of SF density  $\phi_\alpha$ . As shown in Fig. 2, the model predicts a strong alignment of SFs in direction of stretch (Fig. 2(f)). However, once the critical strain is reached, SFs lose stability and start disassembling with stretch. This behavior can be understood by observing the curve corresponding to  $\omega = 0$  Hz in Fig. 1(a) where  $\phi_\alpha$  successively goes through assembling and disassembling phases (Fig. 2(d)) as strain increases and has been experimentally observed in myofibrils (Fig. 2(e)).<sup>11,28</sup>

In the case of cyclic stretch, the angular strain in a cell becomes  $\epsilon_\alpha = \bar{\epsilon}_\alpha + \tilde{\epsilon}_\alpha \cos(2\pi / \dots)$  with  $\tilde{\epsilon}_\alpha = \tilde{\epsilon}_{11} \left( (1 + \nu) \cos^2(\alpha) - \nu \right)$  and  $\tilde{\epsilon}_{11}$  the applied cyclic uniaxial strain. Conversely to the case of constant stretch, experimental observations have shown that SFs align in the direction of minimum stretch, i.e., at a 90° angle for a substrate's Poisson's ratio  $\nu = 0$  (no transverse compression)<sup>12</sup> or at a 60° angle for incompressible substrates ( $\nu = 0.5$ )<sup>13</sup> (Fig. 3). Indeed, introducing the cyclic stretch term  $\tilde{\epsilon}_\alpha$  and

