## Cell Mechanics, Structure, and Function Are Regulated by the Stiffness of the Three-Dimensional Microenvironment

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## Supplementary information

For the neo-Hookean model, the energy function is given by,

$$U = C_1 (\lambda_1^2 + \lambda_2^2 + \lambda_3^2 - 3)$$
(Eq. A1)

The Cauchy stress at direction 1 is given by,

$$\sigma_1 = \lambda_1 \frac{dU}{d\lambda_1} - p = 2C_1 \lambda_1^2 - p \tag{Eq. A2}$$

For uni-axial test, the stretch ratios  $\lambda_i$  is given by,

$$\lambda_1 = \lambda$$
,  $\lambda_2 = \lambda_3 = \lambda^{-\frac{1}{2}}$ ,  $\sigma_2 = \sigma_3 = 0$  (Eq. A3)

$$\sigma_1 = 2C_1(\lambda_1^2 - \lambda_3^2)$$
 (Eq. A4)

$$\sigma_1 = 2C_1(\lambda^2 - \lambda^{-1}) = 2C_1(\lambda^2 - \lambda^{-1})$$
(Eq. A5)

$$\lambda^2 = 1 + 2e$$
, where e is the Green strain. (Eq. A6)

In the case of infinitesimal strain, it gives,

$$\sigma_1 = 2C_1 \left\{ 1 + 2e - (1 + 2e)^{-\frac{1}{2}} \right\} = 2C_1 \left\{ 1 + 2e - \left\{ 1 - \frac{1}{2}2e + \frac{1}{2} \times \frac{1}{2} \times \frac{3}{2}(2e)^2 + \cdots \right\} \right\} = 6C_1 e$$
 (Eq. A7)

Therefore, 
$$E = 6C_1$$
 (Eq. A8)

For the Ogden model, the energy function is given by,

$$U = \sum_{i=1}^{n} \frac{2\mu_i}{\alpha_i^2} (\lambda_1^{\alpha_i} + \lambda_2^{\alpha_i} + \lambda_3^{\alpha_i} - 3)$$
(Eq. A9)

$$\sigma_1 = \sum_{i=1}^n \lambda_1 \frac{dU}{d\lambda_1} - p = \sum_{i=1}^n \frac{2\mu_i}{\alpha_i} \lambda_1^{\alpha_i} - p \tag{Eq. A10}$$

For the uniaxial test,

$$\sigma_1 = \sum_{i=1}^n \left( \frac{2\mu_i}{\alpha_i} \lambda_1^{\alpha_i} - \frac{2\mu_i}{\alpha_i} \lambda_3^{\alpha_i} \right) = \sum_{i=1}^n \left( \frac{2\mu_i}{\alpha_i} \lambda^{\alpha_i} - \frac{2\mu_i}{\alpha_i} \lambda_i^{-\frac{\alpha_i}{2}} \right)$$
(Eq. A11)

In the case of infinitesimal strain, it gives,

$$\sigma_{1} = \sum_{i=1}^{n} \frac{2\mu_{i}}{\alpha_{i}} \left\{ \left[ 1 + \alpha_{i}e + \frac{\alpha_{i}}{4} \left( \frac{\alpha_{i}}{2} - 1 \right) \times 4e^{2} + \cdots \right] - \left[ 1 - \frac{\alpha_{i}}{2}e + \frac{\alpha_{i}}{8} \left( \frac{\alpha_{i}}{4} + 1 \right) \times 4e^{2} + \cdots \right] \right\} \approx \sum_{i=1}^{n} \frac{2\mu_{i}}{\alpha_{i}} \left( \frac{3}{2} \alpha_{i}e \right) = 3\sum_{i=1}^{n} \mu_{i}e$$
(Eq. A12)

Therefore,

$$E = 3\sum \mu_i$$
(Eq. A13)