4.4 Tensegrity model for the cytoskeleton

Why is the cell membrane model of the previous section not sufficient to charcterize cells like fibroblasts? What is the fundamental difference between a red blood cell and a fibroblast? Fibroblasts not only consist of a cell membrane but also have a nucleus and cytoskeletal filaments that are, as we have seen, relevant for locomotion and force generation. How do cells move? How do cells attach to surfaces? How are forces from outside the cell transmitted to the cell nucleus where they might influence gene expression? One of the most elegant but maybe also most controversial models in cell mechanics can help to explain these phenomena: the tensegrity model.

Tensegrity The term tensegrity was first coined by Buckminster Fuller to describe a structure in which continuous tension in its members forms the basis for structural integrity. Fuller most famously demonstrated the concept of tensegrity in architecture through the design of geodesic domes while his student, the artist Kenneth Snelson, applied the concept of tensegrity to creating sculptures that appear to defy gravity. Snelson's tensegrity sculptures are minimal in components and achieve their stability through dynamic distribution of tension and compression forces amongst their members to create internal balance. It was upon viewing Snelson's art that Donald Ingber became inspired by the sculpture's structural efficiency and dynamic force balance to adopt tensegrity as a paradigm upon which to analyze cell structure and mechanics. It has been 30 years since the premier appearance of the cellular tensegrity model. Although the model is still largely under discussion, empirical evidence suggests that the model may explain a wide variety of phenomena ranging from tumor growth to cell motility.

Tensegrity is an artificial term made up of the words tension and integrity. Tensegrity structures are well known in structural design for using a very special design concept: They are made of compressive trusses, in our case microtubules, tied together by tensile ropes, in our case actin and intermediate filaments. To better understand the interplay of these cytoskeletal filaments, we will ask ourselves the simple question: What is the effective Young's modulus of a cell under uniaxial tension? To explore this further, we consider one of the simplest tensegrity structures consisting of six microtubule trusses of equivalent length L_0, arranged in three pairs of two with an original truss distance s_0, and of 24 tensile actin and intermediate filament ropes of length l_0, as illustrated in figure 4.12. We will assume that the compressive trusses are perfectly rigid while the tensile ropes act as Gaussian chains or linear entropic springs [11]. Using simple

$$\circ \text{ kinematics} \quad l_0^2 = \left[\frac{L_0 - s_0}{2}\right]^2 + \left[\frac{s_0}{2}\right]^2 + \left[\frac{L_0}{2}\right]^2 \rightarrow l_0 = \frac{1}{2}\sqrt{[L_0 - s_0]^2 + s_0^2 + L_0^2} \tag{4.4.1}$$

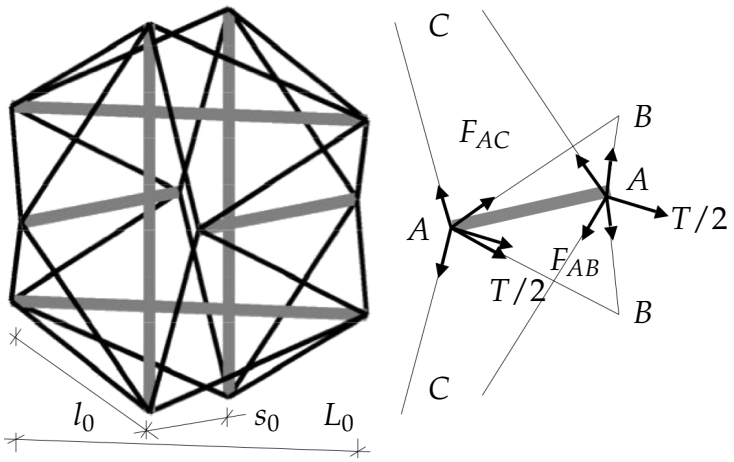

Figure 4.12: Kinematics of simple tensegrity cell model consisting of six compressive trusses (grey), in our analytical model assumed to be rigid, and 24 tensile ropes (black). In the original state, all trusses are of the same length L_0, the rope lengths are $l_0 = \sqrt{3/8}\,L_0$, and the distances between two parallel trusses are $s_0 = 1/2\,L_0$.

we can determine the length of all ropes l_0 with the help of Pythagoras. We can then draw a free body diagram for the truss A-A as illustrated in figure 4.12, right. Summing up all forces acting on this truss along the direction of uniaxial tension will give us the condition of

$$\circ \text{ equilibrium} \quad \sum F \doteq 0: \quad T + 4\,F_{AB}\left[\frac{L_0 - s_0}{2\,l_0}\right] - 4\,F_{AC}\left[\frac{s_0}{2\,l_0}\right] = 0, \tag{4.4.2}$$

where $[L_0 - s_0]/[2\,l_0]$ and $[s_0]/[2\,l_0]$ project the tensile rope forces F_{AB} and F_{AC} onto the direction of uniaxial tension in which we apply the force T. Since the ropes act as linear entropic springs, we can express their forces through the simple

$$\circ \text{ constitutive equation} \quad F = k\,[\,l - l_r\,], \tag{4.4.3}$$

where k is the spring constant, l is the current rope length, and l_r is the relaxed rope length assuming there would be no prestress in the ropes. For the special case with no externally applied tension $T = 0$, we obtain $s_0 = L_0\,/\,2$ from the equilibrium equation (4.4.2) and $l_0 = \sqrt{3\,/\,8}L_0$ from the kinematic equation (4.4.1). With all these preliminary considerations, we can again utilize the Hill condition similar to the previous section,

$$W^{\text{mac}} \doteq W^{\text{mic}} \qquad \text{or} \qquad \frac{\partial W^{\text{mac}}}{\partial s_x} \doteq \frac{\partial W^{\text{mic}}}{\partial s_x} \tag{4.4.4}$$

however now evaluated in a somewhat tricky way by taking its partial derivative with respect to the deformed parallel truss distance s_x. The macroscopic energy can be expressed as always and evaluated with the help of the chain rule.

$$W^{\text{mac}} = \frac{1}{2}\,\varepsilon\,E\,\varepsilon \qquad \text{thus} \qquad \frac{\partial W^{\text{mac}}}{\partial s_x} = \frac{\partial W^{\text{mac}}}{\partial \varepsilon}\,\frac{\partial \varepsilon}{\partial s_x} = E\,\varepsilon\,\frac{\partial \varepsilon}{\partial s_x} \tag{4.4.5}$$

Similar to the previous section, we can relate the macroscopic kinematics, i.e., the macroscopic strain ε in the direction of uniaxial tension, to the microscopic kinematics, i.e., the change in length $[s_x - s_0]$ scaled by the original length s_0.

$$\varepsilon = \frac{s_x - s_0}{s_0} \qquad \text{such that} \qquad \frac{\partial \varepsilon}{\partial s_x} = \frac{1}{s_0} \tag{4.4.6}$$

Now, we can look at the discrete microscopic free energy density, which is nothing but the tensile force T acting along the changing length $\int_{s_0}^{s_x} \mathrm{d}x$ scaled by the original solid volume of the tensegrity cell V_0.

$$W^{\text{mic}} = \frac{1}{V_0} \int_{s_0}^{s_x} T \, \mathrm{d}x \qquad \text{thus} \qquad \frac{\partial W^{\text{mic}}}{\partial s_x} = \frac{T}{V_0} \tag{4.4.7}$$

From the Hill condition (4.4.4), we obtain an expression for the macroscopic Young's modulus E in terms of the truss distance s_0, the tensile force T, the macroscopic strain ε, and the cell volume V_0.

$$\frac{\partial W^{\text{mac}}}{\partial s_x} \doteq \frac{\partial W^{\text{mic}}}{\partial s_x} \qquad \text{thus} \qquad E = \frac{s_0 \, T}{\varepsilon \, V_0} \tag{4.4.8}$$

We can further simplify this expression by plugging in the discrete values for the original cell volume $V_0 = 5\, L_0/16$, the distance of the parallel trusses $s_0 = l_0 \,/\, 2$, and the original rope length $l_0 = \sqrt{3/8}\; L_0$. We then obtain an expression for Young's modulus of the cell under uniaxial tension which we can further simplify for the case of small strains,

$$E = \frac{2\sqrt{3}}{5\sqrt{2} l_0} \frac{T}{s_x - s_0} \qquad \text{small strain} \qquad \underline{\underline{E_0 = 5.85 \, \frac{F_0}{l_0^2} \, \frac{1 + 4\,\varepsilon_0}{1 + 12 \varepsilon_0}}} \tag{4.4.9}$$

where $\varepsilon_0 = l_0/l_r - 1$ is prestrain in the ropes under resting conditions and $F_0 = k\,[l_0 - l_r]$ is the corresponding prestress of the ropes. We see that Young's modulus scales linearly with the prestress in the ropes F_0, and is inversely proportional to the initial rope length l_0^2.

Prestress Tensegrity models are an extremely elegant way to model prestress through the application of initial tension in the rope members. In fact, prestress is inherent to tensegrity structures in that tensegrity structures stabilize themselves through their own weight balanced by prestress. Prestress, very common to biological structures, is a design concept that we have adopted from nature, for example in the form of prestressed reinforced concrete bridges. We might ask ourselves: What is the order of magnitude of the prestress P in the cell? Even in the unloaded resting state, biological tissues and cells might be subjected to prestress in vivo. Let us assume that for our tensegrity model structure, the prestress generated by the ropes is approximately equal in all three spatial directions.

$$P \approx \tfrac{1}{3}\, \nu^{\text{actin}}\, \sigma^{\text{actin}} \tag{4.4.10}$$

Herein, ν^{actin} represents the volume fraction of actin filaments,

$$\nu^{\text{actin}} = \frac{V^{\text{actin}}}{V_0} = \frac{24 A^{\text{actin}} l_0}{[5\sqrt{2}]/[3\sqrt{3}] l_0^3} = \frac{24 A^{\text{actin}}}{1.3608 l_0^2} \tag{4.4.11}$$

and σ^{actin} is the stress acting on one actin filament with a typical cross section A^{actin}.

$$\sigma^{\text{actin}} = \frac{F_0}{A^{\text{actin}}} \tag{4.4.12}$$

The prestress can thus be approximated by

$$P \approx \frac{1}{3} \nu^{\text{actin}} \sigma^{\text{actin}} = \frac{1}{3} \frac{24\, A^{\text{actin}}}{1.3608 l_0^2} \frac{F_0}{A^{\text{actin}}} \qquad \rightarrow \qquad \underline{\underline{P \approx 5.85 \frac{F_0}{l_0^2} = E}} \tag{4.4.13}$$

What does that mean? According to the tensegrity model, the prestress P in a cell scales linearly with Young's modulus E. That is somewhat unexpected. Does it make sense? Let's look at cell experiments to validate this finding: measurements on human airway smooth muscle cells by Wang et al. [2001] who measured the relation between prestress P and shear modulus G, which, for the case of incompressibility, can be correlated to Young's modulus through $E = 3\,G$. The diagram in figure 4.13 demonstrates

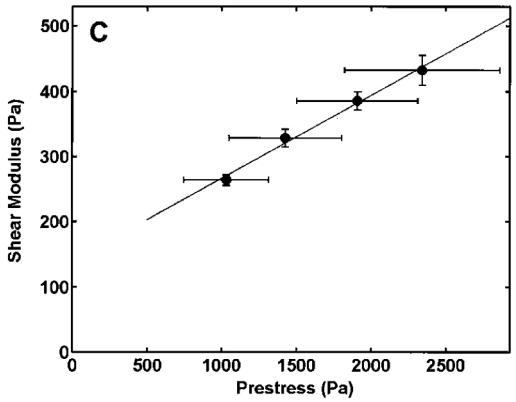

Figure 4.13: Plot of shear modulus as a function of prestress demonstrating a linear relationship, as predicted by a theoretical tensegrity model, adopted from [?]. The originally measured shear modulus G scales linearly with Young's modulus $E = 3\,G$ in the case of incompressiblity.

that the prestress P varies linearly with Young's modulus E. The E over P slope, however, is ≈ 0.4 rather than 1 as predicted by the tensegrity model. The large scatter in E values for different measuring techniques raises the question: What is the effective Young's modulus E of a cell? The cell is alive, and it is difficult to probe a cell without changing its Young's modulus.

And the take home message is... In their in vivo state, cells are subjected to prestress. This prestress is the net result of forces generated by active contractile forces in the actinomyosin apparatus balanced by forces from adhesion to surfaces. The tensegrity

model is a paradigm to characterize the equilibrium between these forces and prestress, however, it is only valid for particular loading scenarios. To incorporate a more complex filament arrangement, the nonlinear nature of the individual filaments, large deformations, and a discretely represented nucleus could be incorporated through the tensegrity concept. The cell model would then have to be solved for numerically, e.g., with the help of the finite element method.