A Theoretical Description of Elastic Pillar Substrates in Biophysical Experiments


Arrays of elastic pillars are used in biophysical experiments as sensors for traction forces. The evaluation of the forces can be complicated if they are coupled to the pillar displacements over large distances. This is the case if many of the pillars are interconnected by elastic linkages as, for example, in fiber networks that are grown on top of pillars. To calculate the traction forces in such a network, we developed a set of nonlinear inhomogeneous equations relating the forces in the linking elements to the resulting pillar deflections. We chose a homogeneous, activated two-dimensional network of cytoskeletal actin filaments to illustrate that a pillar substrate is generally not a force sensor but a force-gradient sensor. In homogeneous networks the forces acting along the filaments can be approximated by analyzing only pillar deflections in the edge zones of the substrate and by integration over the corresponding force gradients.

Introduction

Mechanical forces are central to the functioning of living cells. They are a means for cells to sense, modify or interact with the environment. Processes, such as cell adhesion, locomotion, invasion or tissue formation, rely on the generation and transmission of cellular forces. To quantify these forces, the elastic substrate method was first introduced by Harris et al.,[1] who used a continuous polymer film to infer the cellular traction forces from the wrinkles created in the film. Later studies improved the resolution of this method by increasing the elastic compliance of the substrate.[2] To measure substrate deformations within an area as small as a single focal adhesion site (1–10 µm²), micropatterned elastic substrates were fabricated with different surface morphologies, such as pits, flat pads and tips of submicron dimensions.[3]

In spite of this experimental progress, it remains a difficult theoretical task to obtain the traction forces that produce the displacements of the substrate. Within the framework of linear elastic theory, the elastic substrate can be approximated as a semi-infinite medium. Its equilibrium displacement field is related to the field of surface forces by the corresponding Green’s tensor of an elastic, isotropic halfspace.[4] The “inverse problem” of evaluating the forces from the displacements requires inversion of the Green’s tensor, which is mathematically an underdetermined problem. To obtain a conservative, stable solution, one therefore has to apply regularization schemes, that is, to introduce meaningful constraints. This approach, although computationally intensive, has been used successfully to calculate the traction forces exerted by a cell on an elastic substrate.[5–7]

To facilitate the quantification of cellular forces, elastic substrates with discretized surface morphologies were developed leading to arrays of micropillars with aspect ratios of up to 20. Pillar substrates of this kind are used as micromechanical sensors to evaluate cellular forces exerted at focal adhesion sites,[8,9] to measure the bending modulus of single filaments by flicker spectroscopy and to grow freely suspended actin networks on top of them.[10] There are several advantages of pillar substrates over continuous substrates. First, pillar compliances and geometries can be controlled for individual regions of the substrate or even for individual pillars, which allows the effects of anisotropy and inhomogeneities to be studied locally and in a controlled fashion. Second, surface interactions are minimized, which facilitates the study of two-dimensional polymer networks and thin films. Third, if the pillars are deflected independently of each other, as can be the case in cell adhesion experiments (Figure 1), the force acting on a pillar is simply given by the product of the deflection of the top and the bending stiffness of that pillar. However, if the pillars do not deform independently, the situation is much more complicated because pillar deflections and forces are coupled over large distances. For example, this is the case for fiber networks grown on pillars as seen in Figure 2. The fluorescence micrograph provides a top view on a quasi-two-dimensional (2D)
network of actin filaments that are bound to the tops of a pillar substrate by inactivated myosin-II motor proteins and cross-linked by the actin-binding protein filamin. Activation of this type of network, for example, by activating the myosin motor proteins or by using active myosin-II proteins as a cross-linker, would lead to contraction of only some filaments (the ones that bind to a myosin protein) but the field of induced pillar displacements would percolate through the entire cluster of interconnected pillars.

Herein, we develop a combined description of strains in a fiber network of arbitrary geometry on top of a pillar substrate. We assume that the fibers initially bridge the pillars in a strain-free, and hence force-free, fashion. Subsequently, all fibers are assumed to be subjected to a treatment that causes them to shorten. In a biophysical experiment, for example, this is expected to occur when a network of biopolymers is subjected to activated motor proteins or to some chemical or thermal treatment. If the fibers were bridging infinitely compliant pillars, they would experience a relative contraction \( \varepsilon^0 \) leading to pillar deflections that are large enough to restore the force-free state of the fibers. If the fibers are attached to real pillars with non-zero bending stiffnesses, however, the pillars resist the contraction of bridging fibers, which leads to residual axial forces in the fibers. In our analysis we take the prestrain \( \varepsilon^0 \) to be positive and assume that it generates purely lateral deflections of the pillar heads. The position of a fiber is described by the concatenated 4D vector \( \mathbf{r} = (\mathbf{r}_1, \mathbf{r}_2) \) consisting of the 2D position vectors \( \mathbf{r}_1 \) and \( \mathbf{r}_2 \) of two pillar heads 1 and 2 that are attached to either end of the fiber (Figure 3). Likewise, \( \mathbf{u} = (\mathbf{u}_1, \mathbf{u}_2) \) and \( \mathbf{F} = (\mathbf{F}_1, \mathbf{F}_2) \) denote the 4D vectors of displacements of, and forces on, the pillars, respectively. Furthermore, \( \mathbf{c} = (\mathbf{c}_1, \mathbf{c}_2) \) is the concatenated vector of unit orientation vectors \( \mathbf{c}_1, \mathbf{c}_2 \) pointing inward along the fiber axis at pillars 1 and 2 (Figure 3). There are four possible contributions to \( \mathbf{F} \) that are explained below.

1. Contribution due to Prestrain

A prestrain \( \varepsilon^0 \) of the fiber leads to forces on the pillar heads that are directed parallel to the fiber axis and point inward as shown in Equation (1):

\[
\begin{pmatrix}
\mathbf{F}_1 \\
\mathbf{F}_2
\end{pmatrix} = \varepsilon^0 \mathbf{E} A \begin{pmatrix}
\mathbf{c}_1 \\
\mathbf{c}_2
\end{pmatrix}
\]
Here \( E \) and \( A \) denote Young’s modulus and the cross-sectional area of the fiber.

### 2. Contribution due to Elastic Deformation of the Fiber

As depicted in Figure 3, displacements \( \Delta u \) of pillars 1, 2 yield a relative elongation along the fiber axis that is given by the expression in Equation (2):

\[
\frac{\Delta l}{l_0} = \frac{\Delta u}{l_0} - \frac{\epsilon_1 u_1 + \epsilon_2 u_2}{a} = \frac{\epsilon_1 u_1 + \epsilon_2 u_2}{a}
\]

where \( l_0 \) is the length of the initially unstrained fiber. The second expression in Equation (2) is a vector representation of the relative elongation and the third one is the equivalent matrix representation with \( T \) denoting the transpose of a vector. The forces on the pillars due to this elongation are as given in Equation (3), where \( C \) is a \( 4 \times 4 \) matrix consisting of the \( 2 \times 2 \) submatrices \( \epsilon_1 \epsilon_2 \):

\[
\begin{bmatrix}
E_1 \\
E_2
\end{bmatrix} = \frac{E_0}{l_0^2} \begin{bmatrix}
\epsilon_1 t_1^T \\
\epsilon_2 t_2^T
\end{bmatrix} u_2 = \frac{E_0}{l_0^2} \begin{bmatrix}
-\epsilon_1 t_1^T \\
\epsilon_2 t_2^T
\end{bmatrix} u_2
\]

### 3. Contribution due to Geometric Deformation of the Fiber

A fiber of length \( l_0 \) experiencing an axial force \( F_a \) and a rotation \( \alpha \) (Figure 4), acts as a lever that exerts torques on the end points of its arms. The magnitudes of these torques is defined as in Equation (4):

\[
M = \frac{P}{2} |F_a| = \frac{P}{2} E_0 \sin \alpha = \frac{P}{2} |F_a| |u_1| = \frac{P}{2} |F_a| |u_2|
\]

with the \( 2 \times 2 \) submatrices defined as in Equation (9):

\[
k_{2 \times 2} = \begin{bmatrix}
-\epsilon_2 & \epsilon_1 \\
\epsilon_2 & -\epsilon_1
\end{bmatrix} l_0 + \frac{|F_a|}{P} I_2
\]

where \( \Delta l = u_2 - u_1 \). Here \( F_a \) is the vertical component of \( F_a \) and \( u_1, u_2 \) are the vertical components of \( u_1, u_2 \), respectively (Figure 4), which can be expressed as follows in Equations (5a–c):

\[
\begin{align*}
\epsilon_1 u_1 &= u_1 - u_1 \epsilon_1 = \left[ I_2 - \epsilon_1 \right] u_1 \\
\epsilon_2 u_2 &= u_1 - u_2 \epsilon_2 = \left[ I_2 - \epsilon_2 \right] u_2 \\
\epsilon_1 u_1 &= \left[ I_2 - \epsilon_2 \right] u_1
\end{align*}
\]

In Equations (5a) and (5b) \( \epsilon_1 u_1 \) and \( \epsilon_2 u_2 \) are the parallel components of \( u_1 \) and \( u_2 \) respectively to restore the initial horizontal orientation of the fiber. The resulting forces on the pillar heads are given by Equation (6):

\[
\begin{bmatrix}
E_1 \\
E_2
\end{bmatrix} = \frac{E_0}{l_0^2} \begin{bmatrix}
\frac{u_1}{l_1} - \frac{u_2}{l_2} \\
\frac{u_1}{l_1} - \frac{u_2}{l_2}
\end{bmatrix}
\]

It is obvious from Equation (6) that the forces on the pillars due to a purely geometric deformation of the fiber depend only on the axial force \( F_a \) in the fiber but not on its elastic properties.

### 4. Contribution due to Pillar Bending

Bending of the two pillars with bending stiffness \( b \) exerts restoring forces on the pillar heads given in Equation (7):

\[
\begin{bmatrix}
F_{1a} \\
F_{2a}
\end{bmatrix} = -b \begin{bmatrix}
\sin \\
\cos
\end{bmatrix}
\]

Adding up all force contributions for two pillar heads 1 and 2 interconnected by a fiber and demanding that the net forces be zero, yields the following system of four inhomogeneous equations (Eq. (8)):

\[
\begin{bmatrix}
-\frac{k_{2 \times 2}}{l_0} & \frac{k_{2 \times 2}}{l_0} \\
\frac{k_{2 \times 2}}{l_0} & -\frac{k_{2 \times 2}}{l_0}
\end{bmatrix} \begin{bmatrix}
\frac{F_{1a}}{l_1} \\
\frac{F_{1a}}{l_1}
\end{bmatrix} + \frac{P}{l_0} \begin{bmatrix}
\epsilon_1 \\
\epsilon_2
\end{bmatrix} = -c\phi E_0 \begin{bmatrix}
\epsilon_1 \\
\epsilon_2
\end{bmatrix}
\]

where \( \frac{k_{2 \times 2}}{l_0} = \frac{P}{l_0} \begin{bmatrix}
0 & 0 \\
0 & 0
\end{bmatrix} \end{bmatrix} \begin{bmatrix}
\epsilon_1 \\
\epsilon_2
\end{bmatrix} + \frac{P}{l_0} I_2
\]

\[
k_{2 \times 2} = \begin{bmatrix}
-\epsilon_2 & \epsilon_1 \\
\epsilon_2 & -\epsilon_1
\end{bmatrix} l_0 + \frac{|F_a|}{P} I_2
\]
For an array with $n$ pillars the elemental stiffness matrices $k_{s_{x}x}$ have to be assembled into the global stiffness matrix $K_{2nx2n}$ of the whole fiber network such that the kinematic relations between two pillars and their interconnecting fiber are correctly reproduced. For a fiber $f$ bridging pillars $i$ and $j$, the total displacement vector of all $n$ pillar heads is given in Equation (10):

\[
\begin{pmatrix}
u_{ix}, & u_{ix}, & \cdots, & u_{ix}, & u_{ix}, & \cdots, & u_{ix}, & \cdots, & u_{ix}
\end{pmatrix}
\begin{pmatrix}
2i-1 & 2i \ \text{positions} (2i-1), 2i \ \text{positions} (2i-1), 2i
\end{pmatrix}
\] (10)

In this case the element matrices $k(\theta)_{f_{x}x_{2}}$ for fiber $f$ have to be assembled in rows/columns $(2i-1),2i/(2i-1),2i$, respectively [Eq. (11)]:

\[
K_{2nx2n} =
\begin{bmatrix}
2i-1 & 2i & \cdots & 2j-1 & 2j & \cdots & 2i-1 & 2i & \cdots & 2j-1 & 2j
\end{bmatrix}
\begin{bmatrix}
k(\theta)_{f_{x}x_{2}} & \cdots & k(\theta)_{f_{x}x_{2}} & \cdots & k(\theta)_{f_{x}x_{2}} & \cdots & k(\theta)_{f_{x}x_{2}} & \cdots & k(\theta)_{f_{x}x_{2}} & \cdots & k(\theta)_{f_{x}x_{2}}
\end{bmatrix}
\] (11)

The generalization of Equation (8) thus leads to a system of $2n$ inhomogeneous equations that are generally nonlinear in the pillar displacements [Eq. (12)]:

\[
\begin{bmatrix}
u_{ix}, & u_{ix}, & \cdots, & u_{ix}, & u_{ix}, & \cdots, & u_{ix}, & \cdots, & u_{ix}
\end{pmatrix}
\begin{pmatrix}
-e_{0}^{\theta f_{x}} & E_{f_{x}} \ A_{j} \ e_{\theta f_{x}} & \cdots & -e_{0}^{\theta f_{x}} & E_{f_{x}} \ A_{j} \ e_{\theta f_{x}} & \cdots & -e_{0}^{\theta f_{x}} & E_{f_{x}} \ A_{j} \ e_{\theta f_{x}} & \cdots & -e_{0}^{\theta f_{x}} & E_{f_{x}} \ A_{j} \ e_{\theta f_{x}}
\end{pmatrix}
\] (12)

Here $e_{0}^{\phi}$, $E_{f_{x}}$, $A_{j}$ denote the prestrain, Young’s modulus and the cross section of fiber $f$ connecting to pillar $j$. Likewise, $e_{\phi}$ is the unit orientation vector of this fiber as defined at the beginning of this section and $l_{mx2n}$ is the $(2n \times 2n)$-dimensional unit matrix. The sums on the right-hand side run over all fibers that connect to pillars $1, 2, \ldots, n$, respectively.

Equation (12) allows evaluation of the displacements of the pillar heads given the elastic and geometric properties of the individual fibers and the geometry of the entire fiber network. Once the displacements are known, the force acting along any fiber $f$ that connects any two pillars $i$ and $j$ can be evaluated as shown in Equation (13):

\[
F_{f} = \left( e_{0}^{\phi} + \frac{(u_i - u_j) e_{\phi}}{l_{f}} \right) E_{f_{x}} A_{j}
\] (13)

Simulation of a Homogeneous Actin Network

As the simplest possible example of the interaction between activated fibers and elastic pillars, we consider a regular pillar substrate of $11 \times 11$ equally spaced pillars and a regular network of actin filaments adhering to the pillar heads. Both, the substrate and the network are chosen to have the same quadratic geometry, that is, only nearest-neighbor pillars are connected by a filament, and all filaments have the same initial length and are subjected to a compressive prestrain $e_{0}^{\phi}$ as defined at the beginning of this section. This highly ordered arrangement of homogeneously strained actin filaments does not correspond to a realistic filament network that is subject to fluctuations and local inhomogeneities, but it is a clear and simple example to demonstrate the fundamental mechanical relations between a strained network and an elastic pillar substrate. Using Equation (12), we calculate the resulting pillar displacements by performing a singular value decomposition of matrix $K_{12}$. Subsequently, we evaluate the forces acting along the filaments with Equation (13). To this end, the filaments are modeled as elastic springs with a Young’s modulus and a cross-section corresponding to the values of filamentous actin: $E = 2 \text{ GPa}$ and $A = 50 \text{ nm}^2$ (corresponding to a radius of $4 \text{ nm}$). All filaments are infinitely stiff with respect to bending and torsion. The initial filament length was set to $l = 10 \mu m$ in accord with the actin network in Figure 2. We use two different bending moduli to describe the elastic stiffness of the pillars. The first one, $b_{1} = 8700 \text{ pN} \mu m^{-1}$, corresponds to polydimethylsiloxane (PDMS) pillars with $E = 3 \text{ MPa}$, length $l = 16 \mu m$ and a circular cross-sectional radius $r = 1.5 \mu m$ (stiff case). Pillars of this type can be manufactured by photolithography and molding and can be applied in experiments similar to those shown in Figures 1 and 2. The second one, $b_{2} = 55.2 \text{ pN} \mu m^{-1}$, corresponds to hypothetical PDMS pillars with $l = 20 \mu m$ and $r = 0.5 \mu m$ (compliant case).

The calculated displacements for both sets of pillars are shown in Figures 5a and 5b where black crosses and circles indicate the initial and the displaced positions of the pillar heads, respectively. Because of the regular structure of the network and the uniform prestrain, the displacements are symmetric.
metrical with respect to the center pillar, which remains undeformed for symmetry reasons. All other pillars undergo deflections that are largest at the edges and decrease towards the center of the substrate. As expected, the nominal deflections are much larger in the compliant case. The decrease of deflections from the edge region towards the center, however, proceeds faster in the stiff case as can be seen in Figure 6. To estimate the amount of decrease, we subdivided the substrates into five concentric squares of pillars with decreasing size and decreasing distance to the center. For each such square, the contraction of its edge length due to a compressive prestrain $\varepsilon_0 = 0.1$ is plotted versus its distance from the center before contraction. The figures above the bars denote the numerical values of the edge contractions.

This is also evident from Figures 7a and 7b where the pillar displacements $\Delta x$ along the $x$ direction of the sixth row of pillars and the corresponding axial filament forces are plotted. This row can be chosen arbitrarily because the graphs of $\Delta x/\Delta y$ versus pillar number are identical for any row/column. Comparison of the two sets of pillar substrates shows once more that the decrease of pillar deflections towards the center is approximately constant from the edge towards the center.

Furthermore, it can be seen that the axial forces in the filaments increase with decreasing distance from the substrate center, that is, they behave opposite to the displacements. By contrast, the changes in the forces, $\Delta F_a$, behave in the same fashion as the displacements, that is, they are largest at the edges. Here, $\Delta F_a$ denotes the difference in axial forces between two adjacent filaments. To estimate the size of the edge zone over which pillar deflections and force gradients are significant, we define this zone as the edge region inside which $\Delta F_a$ drops to 30% of its maximum value. It can be seen in Figures 7a and 7b that this zone comprises two and three full interpillar spacings in the stiff and compliant substrates, respectively.

This result demonstrates once more that the edge zone over which $\Delta F_a$—and thus also the pillar deflections—decrease significantly is shorter in stiff pillar substrates than in compliant ones. In other words, in stiff substrates this decrease proceeds faster and therefore leads to a larger “edge effect”. Taken to-

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**Figure 6.** Edge effects in the stiff (black bars) and the compliant (gray bars) substrate. The substrates can be hypothetically subdivided into five concentric squares of pillars of decreasing size and decreasing distance to the center. For each such square, the contraction of its edge length due to a compressive prestrain $\varepsilon_0 = 0.1$ is plotted versus its distance from the center before contraction. The figures above the bars denote the numerical values of the edge contractions.

**Figure 7.** Calculated pillar displacements in the $x$ direction, $\Delta x$ (a), axial filament forces, $F_a$ (●), and changes in axial filament forces, $\Delta F_a$ (●), for the 11 pillars in the sixth row of Figure 5 and the actin filaments connecting them. The values of $F_a$ are plotted midway between two pillars, that is, at the site of the midpoint of the corresponding filament, while the force differences $\Delta F_a$ between adjacent filaments are plotted midway between these filaments, that is, at the site of the pillar between them. The dotted vertical line marks the width of the edge zone as defined in the Results Section. The bending modulus of the pillars is a) $b_1 = 8700 \text{pN}\text{mm}$ and b) $b_2 = 55.2 \text{pN}\text{mm}^{-1}$.
gether, the simulations show that in the stiff case nominal deflections are small but edge effects are large while in the compliant case the converse is true.

Discussion

Herein, we present a novel set of inhomogeneous equations of the force-displacement relationship in elastic pillar substrates. It allows quantitative analysis of the interaction between an elastic pillar substrate and a network of activated fibers anchored to the pillar heads. The theoretical description presented here applies to arbitrary geometries of the pillar substrate and of the fiber network and also to an arbitrary initial state of strain of the fibers. Thus the theory includes random networks as well as ordered networks and homogeneous as well as inhomogeneous states of strain. It is therefore a powerful tool to evaluate traction forces in fiber networks ranging from synthetic polymer networks to cytoskeletal fibers in living cells. Based on this theory, we evaluated the pillar displacements and filament forces in a homogeneously strained actin network on two pillar substrates with different bending moduli. The results illustrate that individual displacements of pillars are not indicative of absolute forces of the fibers that attach to the pillars. Instead they are indicative of the changes of these forces as a function of the distance from the center of the substrate. A pillar substrate is therefore strictly speaking not a force sensor but a force-gradient sensor. Consequently, the entire displacement field of connected pillars is required to uniquely evaluate the forces in a fiber network.

This observation has a direct impact on experiments that try to measure traction forces in cells adhering to pillar substrates. So far, these studies have explicitly assumed that the pillars deflect independently of each other.\[^8,9\] As mentioned in the introduction, this allows direct calculation of the total traction force exerted on a pillar from the deflection of that pillar. However, this procedure has two drawbacks. Firstly, without taking into account the topology of the cytoskeletal network, it is not possible to determine how the total force acting on a pillar is distributed over the filaments that connect to that pillar. Secondly, the assumption that pillars underneath an adhering cell deflect independently of each other only holds if there are no direct links between the pillars and also no cross-links between the filaments connecting to the pillars. This condition is rarely met in living cells where many focal adhesion sites are connected by bundles of actin fibers.\[^10\] Evaluation of the complex distribution of forces in the cytoskeleton therefore requires evaluation of the displacement field of all the pillars that are either directly or indirectly connected to each other. Subsequently, the traction forces along the cytoskeletal fibers attached to the pillars can be determined from Equation (13).

The computer simulations show that pillar displacements and force gradients are largest at the edges of the sample while the forces in the fibers are largest at the center. This situation is similar to that in a fiber-reinforced composite consisting of a stiff fiber embedded in compliant matrix material. Upon elastic deformation of the composite, load is transferred from the matrix to the fiber over limited zones at the fiber ends (shear lag zones) which leads to an axial force in the fiber that is at a maximum at the fiber midpoint.\[^16,17\] These edge zones also exist in homogeneously deformed, elastic pillar substrates and their size depends on the elastic properties of the fibers and the pillars. In stiff substrates the edge zones are rather small, that is, pillar deflections and force gradients decrease fast in these regions whereas in compliant substrates the decrease is more uniform across the width of the substrate. The reason is that stiff pillars only deflect significantly if large net forces act on them, which is the case for pillars along the edges but not for those in the interior of the substrate. This leads to significant stress relaxation in edge fibers but not in interior fibers and thus to an abrupt decrease in the difference of forces in adjacent fibers. These effects are also present in compliant pillar substrates but occur less abruptly because compliant pillars require smaller net forces to bend and thus deflect more uniformly.

In homogeneously deformed substrates with pronounced edge effects, forces in the fibers can therefore be efficiently evaluated by measuring only pillar displacements in the edge zones where they are largest, and thus also easiest to determine accurately. From the deflections in the edge zones one can then continue to calculate the force gradients in these zones and gain information about the interior axial forces by integration. Examples of this procedure are outlined in the Supporting Information.

In most experiments the pillar deflections are not homogeneous, either because the spacings or geometries of pillars are not identical everywhere in the substrate or because the topology or the prestrain is not identical everywhere in the network. In these cases, there can be large fluctuations in the force gradients in the interior substrate region. However, if the fibers are oriented predominantly along a few directions only, it is still possible to apply a fit method to estimate the forces in these directions.

The simulations also illustrate that compliant PDMS pillars with a hypothetical aspect ratio of 20 or larger should be sensitive to forces in the sub-nN regime. Since motor proteins operate in this regime (3–4 pN for a myosin-II protein\[^18\]), there is a high motivation to manufacture such highly compliant substrates to measure directly the force transfer of these proteins to a network of cytoskeletal filaments. This shows that simulations of the type presented here are useful guidelines for experiments because they predict the resolution of a sensor from its properties and from the initial forces in the fiber network.

Finally, it is emphasized that although pillar displacements need not be calculated in a computer simulation if they can be measured directly in experiments, it is still advantageous to run both procedures in parallel. A direct comparison of the measured and calculated pillar displacements can be used to tune the simulation by iteratively varying the input parameters such as the prestrain and the cross section of fibers to approximate the experimentally measured displacements. This procedure can elucidate details that are otherwise difficult to access in experiments alone, as for example the exact value of prestrain in a fiber or the question of whether a single fiber or a bundle of fibers interconnects two pillars.
Conclusions

We have developed an analytical description and a self-consistent numerical algorithm to evaluate the force field in a strain-ed fiber network that is suspended on a substrate of elastic pillars. The description is independent of the geometries of the substrate and the fiber network and applies to homogeneous as well as to inhomogeneous strains. It provides a theoretical basis for experiments aiming at the quantitative evaluation of forces in an activated biopolymeric network on a pillar substrate. Our simulations of homogeneously strained actin filament networks show that elastic pillar substrates are micromechanical sensors of force gradients of fibers rather than of the forces themselves. To evaluate the forces therefore requires the displacements of all interconnected pillars to be evaluated. A homogeneous strain in the fiber network creates a monotonic decrease of pillar displacements and force gradients from the edges towards the center of the substrate. This “edge effect” is more pronounced in stiff substrates than in compliant ones. Integration of large force gradients over these edge zones can be used to approximate the forces in the interior region of the substrate. Our results also show that PDMS pillars, for example, must have an aspect ratio of at least 20 to be sensitive to forces in the sub-nN regime. This result can therefore serve as a guideline to construct pillar substrates that are to be used to evaluate forces in biological networks such as the synthetic actin cortex in Figure 2.

Computational Methods

Solving Equation (12) for the pillar displacements $(\mathbf{u}_{ij})$ is complicated if the matrix $K_{mn}$ is singular, that is, if some rows or columns are linearly dependent. In this case, an exact solution either does not exist or it exists but is not unique. In the latter case, the method of singular value decomposition (SVD) presents a powerful tool for finding the solution space of the singular matrix. In our work, we have applied SVD to calculate the unknown displacements of pillars given the prestrain-induced forces acting on them (the right-hand side of Eq. 12). To this end, we used the NAG Fortran Library routine F04JGF\(^{[12]}\) that returns the minimal least-squares solution, that is, the solution vector with the smallest Euclidian length.

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