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Form-finding of complex tensegrity structures: application to cell cytoskeleton modelling

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Abstract

The ability to model the mechanical behaviour of the cell cytoskeleton as realistically as possible is a key point in understanding numerous biological mechanisms. Tensegrity systems have already demonstrated their pertinence for this purpose. However, the structures considered until now are based only on models with simplified geometry and topology compared to the true complexity of cytoskeleton architecture. The aim of this Note is to propose a form-finding method for generating nonregular tensegrity shapes of higher diversity and complexity. The process relies on the use of the dynamic relaxation method. Further improvements have made it possible to control the computed morphologies and to modify them to approach experimentally observed configurations. Various examples illustrate the use of the method and the results obtained for different cell typologies. ***To cite this article: H. Baudriller et al., C. R. Mecanique 334 (2006).***

Résumé

Recherche de forme des structures de tenségrité complexes : application à la modélisation du cytosquelette cellulaire. La capacité à modéliser de façon la plus réaliste possible le comportement mécanique du cytosquelette des cellules constitue un point essentiel dans la compréhension de nombreux mécanismes biologiques. Les systèmes de tenségrité ont à cet égard déjà démontré leur pertinence. Néanmoins, les structures considérées à ce jour reposent uniquement sur des modèles avec une géométrie et une topologie simplifiées au regard de la complexité réelle de l'architecture des cytosquelettes. Ces travaux ont ainsi pour objectif de proposer une méthode de recherche de forme permettant de générer des formes de tenségrité non régulières plus riches et complexes. Le procédé est fondé sur la méthode de relaxation dynamique. Les modifications apportées offrent la possibilité de contrôler les morphologies ainsi calculées pour se rapprocher de configurations expérimentalement observées. Plusieurs applications montrent la mise en œuvre du processus et les résultats obtenus s'agissant de différentes typologies de cellules. ***Pour citer cet article : H. Baudriller et al., C. R. Mecanique 334 (2006).***

Keywords: Biomechanics; Tensegrity; Nonregular shape; Cytoskeleton

Mots-clés : Biomécanique ; Tenségrité ; Forme non régulière ; Cytosquelette

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1. Context and objectives

One of the main goals of cell biomechanics is to clarify the relationship between the principal biological functions such as differentiation, gene expression or migration, and the state of stress and strain of living adherent cells. These parameters depend on the cell's mechanical behaviour, essentially relying on the behaviour of its cytoskeleton (CSK). Hence, numerous studies aim to propose mechanical structural models to provide a better understanding of the phenomena involved [1].

The CSK is a complex structure mainly composed of three networks of filamentous biopolymers in interaction with an extracellular matrix (ECM): actin filaments or microfilaments, microtubules and intermediate filaments (see Fig. 1). Several organizational principles can, however, be distinguished. The microfilaments are located throughout the entire volume of the cell, predominantly in the membrane cortex and basal fibres (i.e. the stress fibres). The microtubules generally irradiate from a specific point called the centrosome while the intermediate filaments envelop the nucleus and connect it to the cell membrane. Some components are also connected to particular zones of the membrane, which constitute the adhesion complexes, or focal points, allowing adhesion to the ECM and/or to neighbouring cells. However, beyond these principles, the observed network architectures (geometry and structural composition) are complex, irregular, vary from one cell to another, and change during the cell life. They can be observed experimentally using image techniques with video microscopy coupled to 3D reconstruction software.

Experimental observations have also highlighted the presence of internal forces within the CSK [2], mainly composed of traction and compression stresses which give the cell its necessary rigidity and stability.

Although the role played by each component is not fully elucidated, particularly in the case of intermediate filaments, it is now generally admitted that actin microfilaments undergo traction while microtubules are compressed [3]. These forces are due to two considerations. Firstly, it has been shown that the CSK components have initial stresses when no external load and no adherence to the ECM occur. This corresponds to an initial three-dimensional selfstress state. Secondly, after the cell spreading and adherence to the ECM, stress fibres appear in between anchoring zones. They correspond to a prestress state, mainly located close to the basal adhesion surface. The combination of these internal stresses, its distribution and intensity, has a direct influence on the cell behaviour and thus need to be taken into consideration when developing a pertinent mechanical model.

Several models have been proposed to evaluate the cell mechanical behaviour. Works based on approaches with finite elements [4], alveolar media [5] and soft glassy media [6] may be quoted. However, these methods do not provide a sufficiently realistic representation of CSK architecture and, more restrictively, fail to take into account the presence of initial stresses. As a result, models based on tensegrity systems have been proposed by different authors [7,8]. A tensegrity system is a spatial reticulate selfstressed structure composed of tensile elements (cables, Fig. 2) connected to compressive elements (bars). Such an approach allows an analogy between cables and microfilaments and between bars and microtubules. It makes it possible to take into consideration internal stresses in the elements due to a selfstress state and also to a prestress state for the components in interaction with the anchoring points. Experimental studies on living cells using magnetic twisting cytometry or optical tweezers have shown a good qualitative correlation between

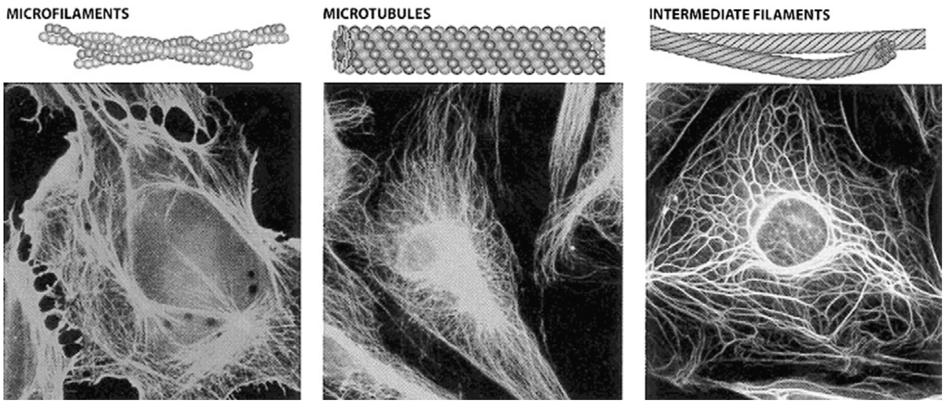

Fig. 1. Networks of CSK components [2].

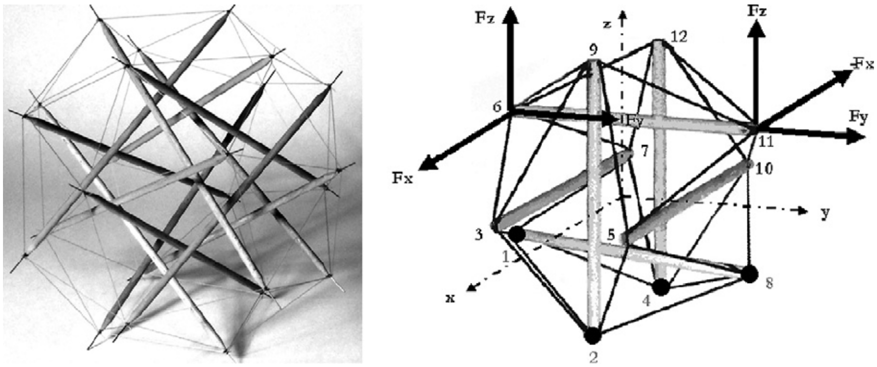

Fig. 2. Regular tensegrity systems (physical model and example of numerical simulation).

their mechanical behaviour and that numerically simulated by tensegrity [9]. However, we emphasize on the fact that tensegrity is just a model and that the CSK is definitively not a tensegrity structure.

Moreover, most of the studies using the tensegrity analogy were based on models with very simple CSK architecture compared to the biological complexity. Also, very few elements were considered (from 9 to 48 for cables and 3 to 12 for bars, see Fig. 2 left) and simplified geometries with regular shapes were used [10].

Our objective is therefore to show the possibility of designing more complex and diverse selfstressed tensegrity structures. These will comprise a higher number of nodes and elements and define non standard geometries and topologies. The aim is not to be 'as close as possible' to real observed biological CSK, but to get a little closer. These complex architectures may potentially contribute to the future definition of more pertinent models to study the mechanical behaviour of living cells.

Considering the level of structural complexity, tensegrity structures may be classified into three categories [11]:

- regular systems with identical length cables and identical length bars, as for the models represented in Fig. 2 (this category corresponds to all the models proposed by researchers until now);
- semi regular systems with a minimal number of different lengths, i.e., the fewest possible groups, a group being composed of identical components;
- nonregular systems characterized by no constraint on the lengths of the elements.

The design of a selfstressed tensegrity structure requires us to specify its topology, its geometry and the associated initial stresses. This self equilibrated configuration is determined by form-finding methods that can be classified into two categories. The first deals with the 'form controlled' methods based on a heuristic approach using experimentation and a trial and error process. The second relies on 'force controlled' methods and has been developed with theoretical considerations in order to meet the mechanical requirements of equilibrium. Different techniques have been proposed, initially based on static calculation, but currently using force density or dynamic relaxation methods [11,12].

The force density method has proven its efficiency in determining regular systems, even if the choice of density coefficients may be difficult: a unique combination of coefficients is indeed associated to each self equilibrated structure. As a result, an arbitrary or poorly adapted choice leads to the impossibility of converging to a solution. A multi parametered approach was therefore proposed to overcome this issue and to calculate shapes that are not only regular [13]. However, if such a possibility was successful for very simple systems with few groups of elements, it has proved inefficient for structures comprising several groups, especially nonregular systems. On the other hand, the dynamic relaxation method has all the advantages of being able to generate this type of structure. It controls the morphological evolution of an initial system by modifying the stiffness of one or several elements, or by prescribing a constant internal force.

The aim of this Note is thus to demonstrate the possibility of designing nonregular selfstressed tensegrity systems by using a numerical method based on the dynamic relaxation approach. The resulting selfstressed initial forces are independent from anchoring conditions to a support. At this stage, no prestress associated to the adherence to the ECM is indeed considered. Such a development may be envisaged but requires a detailed study on the cell spreading and adherence. The type and the role of attachments conditions have to be precise so as to define boundary specifications for the tensegrity systems. When determined, the prestress forces have next to be combined to the initial selfstress forces.

2. Form-finding of nonregular tensegrity shapes

2.1. The dynamic relaxation method

For a given tensegrity system geometry and an arbitrary distribution of initial stresses, the structure is unlikely to be self equilibrated. However, if certain values are imposed in accordance with the nature of the elements and with adapted relative intensities, the resulting out balanced forces will produce a movement in the system, possibly stabilizing it around a self equilibrated position. The shape obtained and its associated stresses thus define a self equilibrated configuration for the system according to the imposed values.

This position can be calculated by resolving the equations of dynamic. To do so, the dynamic relaxation method considers a structure without viscous damping and determines its successive movements until equilibrium is reached. In the case of a spatial reticulate system, the internal residual out balanced forces are evaluated at every node. Hence, for a node i in direction x and at time t, we have $R_t^{ix} = m_i \ddot{x}_t^i$ where R represents the residual force and m a fictitious nodal mass. The use of central finite difference writing gives $\ddot{x}_t = (x_{t+\Delta t} - 2x_t + x_{t-\Delta t})/(\Delta t^2)$ and $\dot{x}_t = (x_{t+\Delta t} - x_{t-\Delta t})/(2\Delta t)$. The m value and the time step Δt are coupled so as to ensure the convergence by $m_i = \lambda k_i \Delta t^2$. The parameter λ is constant for the whole structure [14], the 'nodal' rigidity $k_i = \sum(EA/L_u + N_t/L_t)$ is the sum of the linear and geometric stiffnesses of each element connected to node i. The length L_u is the unstrained length (unstressed) for an element of cross-section A with the assumed linear elastic behaviour of Young's modulus E. At time t, the element has a current length L_t and an internal normal force $N_t = EA(L_t - L_u)/L_u$. An important feature may be here put forward: this internal force can be fixed by the designer to an imposed value ($N_t = cste$), the elements concerned are then called 'active'.

The principle of the method is the following. From a given geometry with certain prescribed internal force values for the active elements, the nodal out balanced forces R are calculated, followed by the resulting speeds at the nodes and their new positions. Then, the out balanced forces are once again calculated and the system evolves accordingly. The dynamic relaxation method can ensure the convergence of the process by considering a 'kinetic' damping. This consists in calculating the kinetic energy of the system and checking whether a maximum has been reached. If so, the system is close to an equilibrium position. The nodal speeds are then set to zero and the process resumed. A sequence of decreasing energy peaks is generally obtained until final self equilibrium. The resulting geometry and stresses define the desired tensegrity structure.

2.2. Shape control strategies

Considering the complexity and diversity of the CSK networks, the process must allow the shape obtained to be modified from the same topology. Two methods can provide such control on the form.

The first relates to the choice of active elements and their interaction in the system. When an initial configuration is defined by the designer (geometry and topology) at $t = 0$, the internal forces in the elements are considered as nil, which also implies that their unstrained lengths are given by the initial form ($L_u = L_{t=0} = L_0$). Certain components are then chosen as active. A normal force is prescribed for each of them that will remain constant whatever the future evolution in the structure. These stresses create nodal out balanced forces and the system will possibly stabilize around an equilibrium position. The convergence of the process depends on the choice of active elements and on the compatibility of the imposed forces. The distribution of the prescribed tensions and/or compressions may not indeed be acceptable by the topology of the structure. To overcome this drawback, another option gives the designer more flexibility. This consists in modifying the unstrained lengths of several active elements. For instance, the unstrained length of a cable can be reduced at the beginning ($L_u < L_0$), or at a later step ($L_u < L_t$), hence creating a tension in this element and nodal residual forces. However, the intensity of the tension will not remain constant but will change according to the evolution of the geometry. This procedure is less restrictive than the first one in terms of convergence since it allows a kind of 'adaptation' of the internal force.

The second strategy deals with the non active (passive) elements and their rigidity EA. The ratio between the values for cable elements and bar elements acts on the system's morphological evolution. Since at the beginning a high ratio (1000) between these stiffnesses is considered, any change will allow modifying the obtained shape. More local evolutions are also possible by changing the rigidity of some components inside a zone to be geometrically modified. This technique generates lower shape variations compared to those obtained by playing on active elements. It is mainly used for small morphological adaptations, generally localised.

We point up that all these changing (tension or unstrained length for active elements, rigidity for some passive components) have no biological correspondence but should be only seen as mechanical/numerical ways to modify and control the resulting shape.

2.3. Methodology and implementation of the process

Designing a tensegrity system with a complex geometry requires being able to change its topology and shape in a friendly and quick way and also to go back and forth between two steps. A method was developed to modify at any time the number of nodes and elements, the values of tensions or unstrained lengths for active elements and of rigidity for passive elements. A real time processing works out the solution, if any, and the parameters are modified until a suitable architecture is obtained. Design and visualisation software using OpenGL interactive libraries has been thus implemented. Through a trial and error approach, the designer could thus generate the complex tensegrity structure, step-by-step.

A simple example is presented in Fig. 3. A system composed of three bars and nine cables is set up with arbitrary node positions (top left). From this topology, the bars are chosen as active and the same level of compression is imposed to them. The calculation converges to a regular form, well known by specialists since it corresponds to the simplest example of spatial tensegrity system (the 'simplex', top right). This structure is next perturbed by modifying the unstrained length of two cable elements. A nonregular shape is then obtained (bottom left, where all the compo-

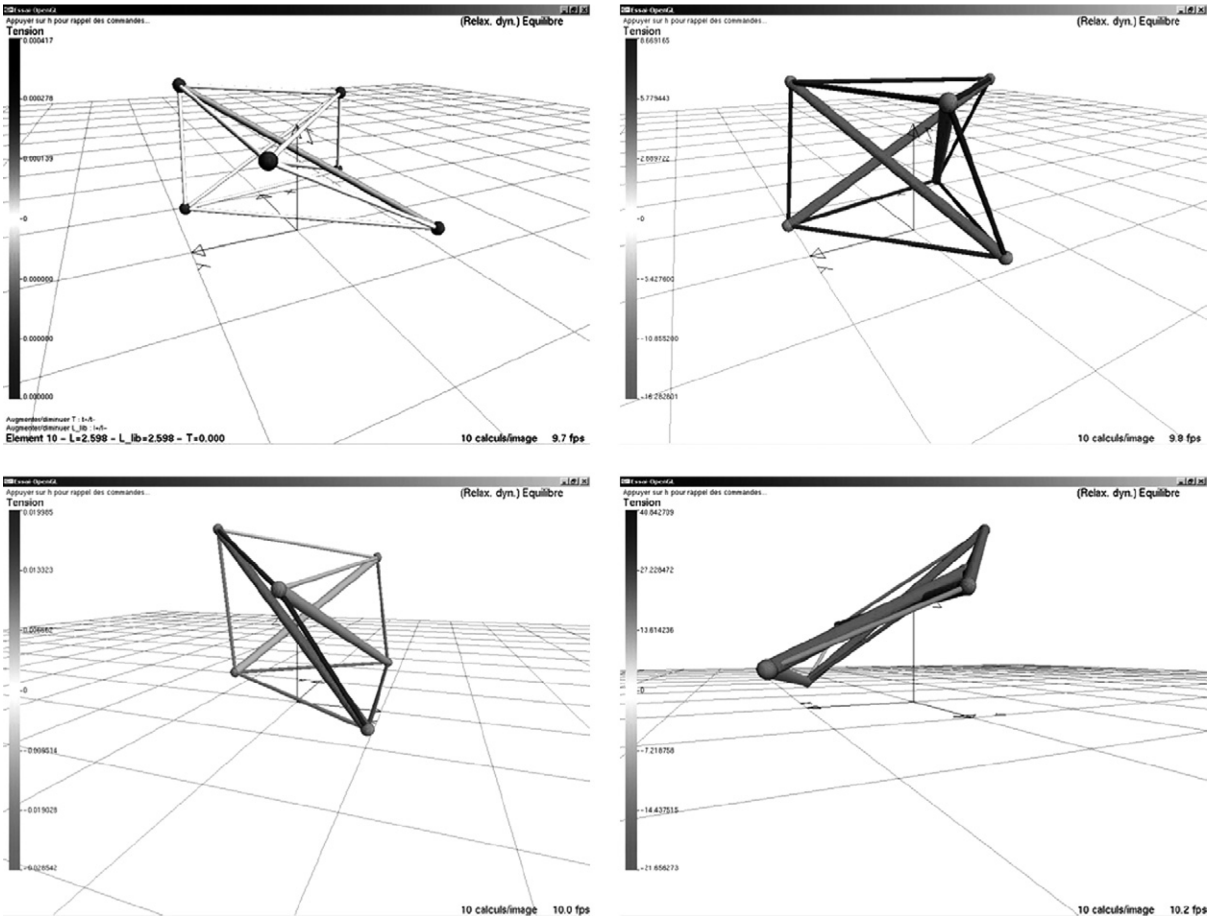

Fig. 3. Generation of a simple tensegrity structure.

nents have different lengths). If a constant tension is imposed with higher intensity in some cables belonging to the upper and lower layers, a plane configuration is reached (bottom right). This form is not satisfactory and it is necessary to go back. This example highlights the fact that, to control the evolution of the generated systems, the methodology has to be implemented interactively.

3. Application to the simulation of cytoskeleton typologies

The aim is to illustrate the possibility to designing nonregular tensegrity systems that can respect some basic principles of CSK organizations. Some 'primitive' tensegrity systems corresponding to various cellular configurations are thus presented.

The first case deals with an epithelial cell typology characterized by a star-shaped microtubular network whose origin (centrosome) is close to the cell center. It also has an actin network both cortical in the periphery and diffuse in the cytoplasm. Two complex tensegrity systems have been then generated and are presented in Fig. 4 in accordance with such principles. We note their nonregular and dissymmetric features. The first (top) has 35 nodes and 127 elements; the second 41 nodes and 143 components (bottom). The grey level indicates the intensity of the internal force of traction or compression. The elements were included progressively by way of interaction with the designer, who was able to modify the structure in real time by removing the unnecessary components (stress close to zero) or by adding those that equilibrate and stabilize the system. After calculation, the result can be visualized in term of geometry and stresses and the designer can again modify the topology or operate on active elements to change the system. It is, however, important to emphasize the degree of skill required in designing this kind of structure in such a way.

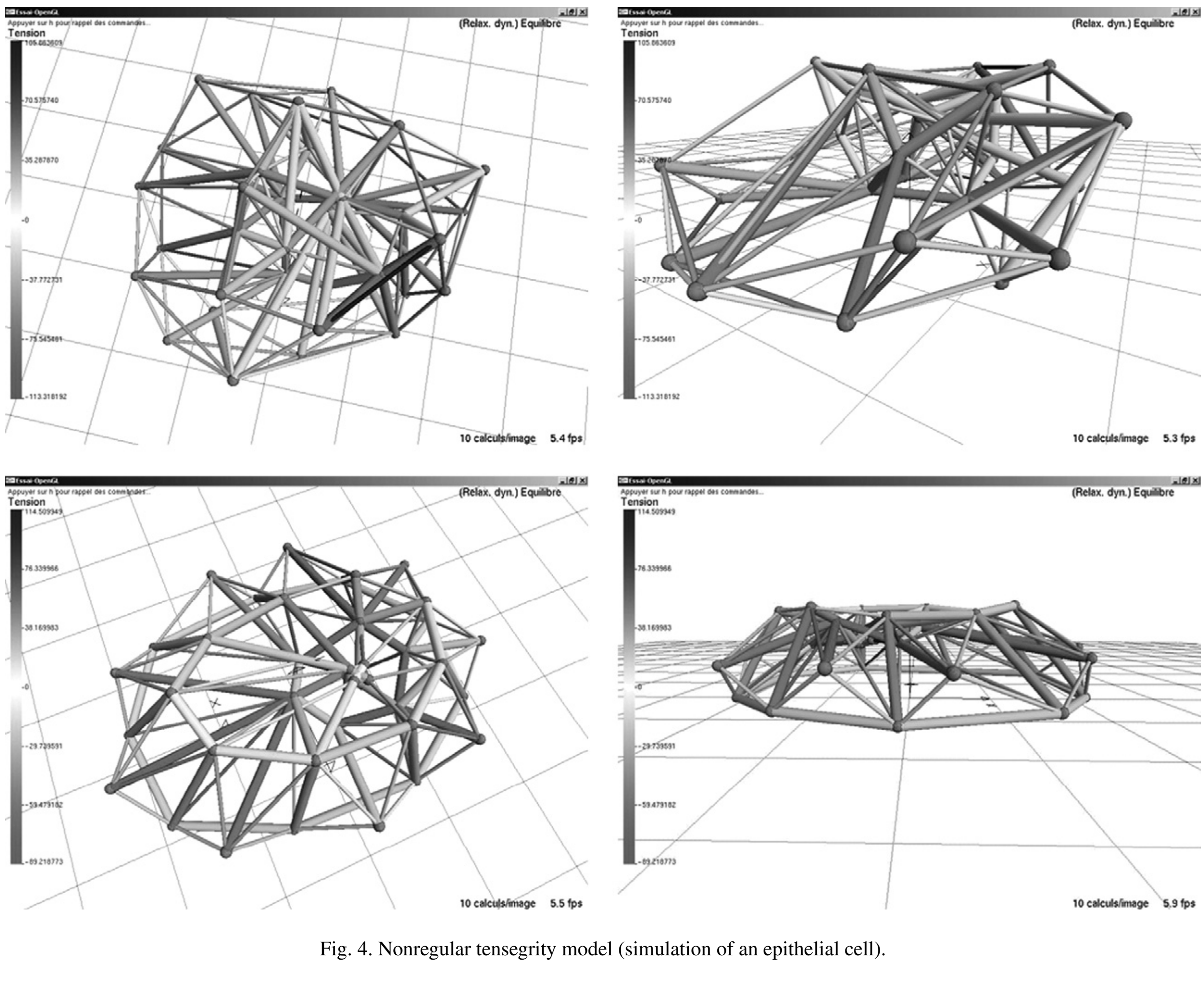

Fig. 4. Nonregular tensegrity model (simulation of an epithelial cell).

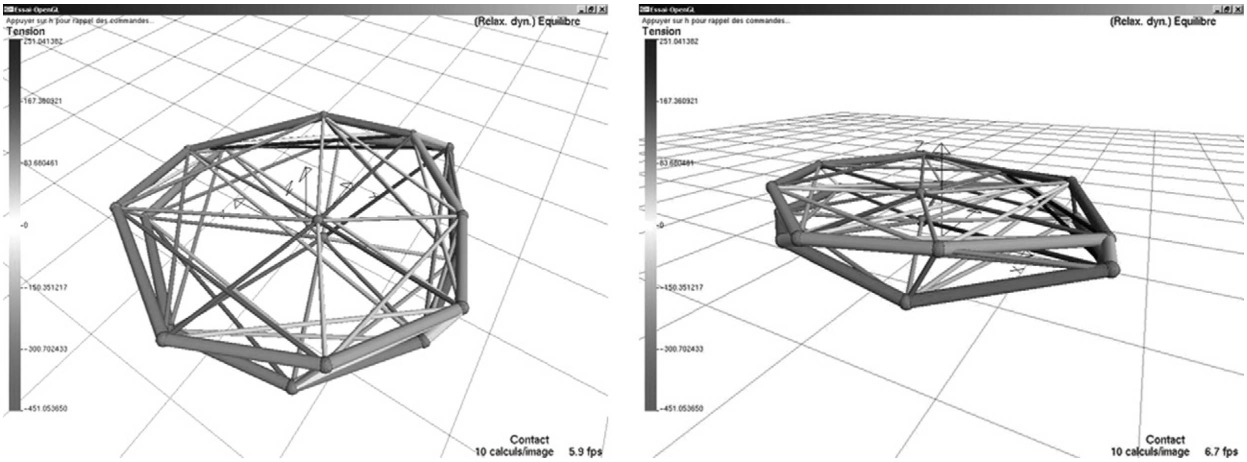

Fig. 5. Nonregular tensegrity model (simulation of a blood platelet).

The second application is related to a blood platelet cell typology. It has a peripheral microtubule net associated to a cortical and diffuse actin net; it is also characterized by a low thickness. A computed tensegrity model that respects these conditions is presented in Fig. 5.

4. Conclusion and perspectives

The purpose of this work is to propose a form-finding method devoted to the design of nonregular selfstressed tensegrity structures. The use of the dynamic relaxation method allows complex and various shapes to be created the evolution of which can be controlled by several mechanical parameters. The application of this process is related to the tensegrity simulation of cell cytoskeleton typologies. Several examples illustrate the potential of the method and its ability to generate structures that is able to respect some biological basic principle, in contrast with to the tensegrity models used until now. The main future development is related to the possibility to take into consideration prestress forces involved in the cell adherence to the extracellular matrix and, then, to analyse its mechanical behaviour when loaded or deformed.

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