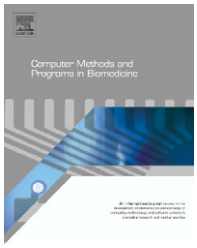
COMPUTER METHODS AND PROGRAMS IN BIOMEDICINE 86 (2007) 232–244

journal homepage: www.intl.elsevierhealth.com/journals/cmpb



Computational models of myocardial endomysial collagen arrangement

Benedetto Intrigila[a], *Igor Melatti*[b], *Alberto Tofani*[c,*], *Guido Macchiarelli*[d]

[a] *Dip. di Matematica Pura ed Applicata, Università di Roma "Tor Vergata", 00133 Roma, Italy*
[b] *Dip. di Informatica, Università di Roma "La Sapienza", 00198 Roma, Italy*
[c] *Dip. di Informatica, Università di L'Aquila, Coppito 67100, L'Aquila, Italy*
[d] *Dip. di Medicina Sperimentale, Università di L'Aquila, Coppito 67100, L'Aquila, Italy*

ARTICLE INFO

Article history:
Received 28 July 2006
Received in revised form
17 November 2006
Accepted 9 March 2007

Keywords:
Collagen
Endomysium
Heart mechanics
Modelling
Neural networks
Scanning electron microscopy

ABSTRACT

Collagen extracellular matrix is one of the factors related to high passive stiffness of cardiac muscle. However, the architecture and the mechanical aspects of the cardiac collagen matrix are not completely known.

In particular, endomysial collagen contribution to the passive mechanics of cardiac muscle as well as its micro anatomical arrangement is still a matter of debate.

In order to investigate mechanical and structural properties of endomysial collagen, we consider two *alternative* computational models of some specific aspects of the cardiac muscle.

These two models represent two different views of endomysial collagen distribution: (1) the traditional view and (2) a new view suggested by the data obtained from scanning electron microscopy (SEM) in NaOH macerated samples (a method for isolating collagen from the other tissue).

We model the myocardial tissue as a net of spring elements representing the cardiomyocytes together with the endomysial collagen distribution. Each element is a viscous elastic spring, characterized by an elastic and a viscous constant. We connect these springs to imitate the interconnections between collagen fibers. Then we apply to the net of springs some external forces of suitable magnitude and direction, obtaining an extension of the net itself. In our setting, the ratio *forces magnitude /net extension* is intended to model the *stress /strain ratio* of a microscopical portion of the myocardial tissue.

To solve the problem of the correct identification of the values of the different parameters involved, we use an *artificial neural network* approach. In particular, we use this technique to *learn*, given a distribution of external forces, the elastic constants of the springs needed to obtain a desired extension as an equilibrium position.

Our experimental findings show that, in the model of collagen distribution structured according to the new view, a given *stress /strain ratio* (of the net of springs, in the sense specified above) is obtained with much smaller (w.r.t. the other model, corresponding to the traditional view) elasticity constants of the springs.

This seems to indicate that by an appropriate structure, a given *stiffness* of the myocardial tissue can be obtained with endomysial collagen fibers of much smaller size.

* *Corresponding author*. Tel.: +39 0862 433252.
E-mail address: tofani@di.univaq.it (A. Tofani).
0169-2607/$ – see front matter © 2007 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.cmpb.2007.03.004

1. Introduction

The mechanical function of the heart depends crucially on its material properties. Therefore, according to [1], the objective of the cardiac mechanics research is the understanding of these properties, and how these properties (that relate also to the structure of the tissue) affect the pumping function of the intact heart.

In particular, high passive stiffness is one of the mechanical features that characterize the *cardiac muscle*. There are several studies concerning the components and the architectural aspects of the cardiac muscle responsible for this particular feature [2,3], in particular *cardiomyocytes* and *collagen matrix* have been proposed as candidates.

Cardiomyocyte architecture is widely described in the literature [4,5]; however, many researchers are investigating how the cardiomyocyte architecture is involved in regulating the electrical and mechanical behavior of the cardiac muscle [5,6].

On the other hand, the cardiac collagen matrix is composed by (1) *endomysial collagen* that connects *myocytes* and surrounds, in a mesh-like structure, the myocytes themselves and (2) *perimysial collagen* that groups myocytes together, running in parallel with *myofibrils* and linking itself to endomysial collagen [7–9].

In [9] a mathematical model of perimysial collagen is defined, to describe its role in myocardial mechanics during ventricular filling (*diastolic phase*) and identify the physical parameters characterizing perimysial collagen itself.

On the contrary, the endomysial collagen contribution to passive mechanics of the cardiac muscle is not yet fully understood. In particular, it is still a matter of debate its micro arrangement and how different micro arrangements could influence this mechanics [10,11].

To contribute to this discussion, we propose two computational models to investigate the mechanical and structural properties of endomysial collagen. To this goal, we need simplified computational models of some aspects of the cardiac muscle itself.

We start from the hypothesis that a healthy behavior of the cardiac muscle needs a limited thickness of the microscopical (i.e. endomysial) collagen fibers. This seems to be plausible considering that, as mentioned above, endomysial collagen connects and surrounds the myocytes, so that collagen fibers of excessive thickness could interfere with the normal mechanics of the myocytes themselves (both in the passive and active phase). Moreover, an increase in size of the collagen fibers has been observed in a number of heart disfunctions [7,12]. Finally, the morphological findings of [13,14] (see below) show an arrangement of the endomysial collagen based on very small fibers.

We set up two models:

- The first one is suggested by the mentioned morphological findings described in [13,14], obtained from scanning electron microscopy (SEM) in NaOH macerated samples (see Fig. 1).
- The second one is based on the traditional micro anatomical view of the endomysial collagen reported in [15].

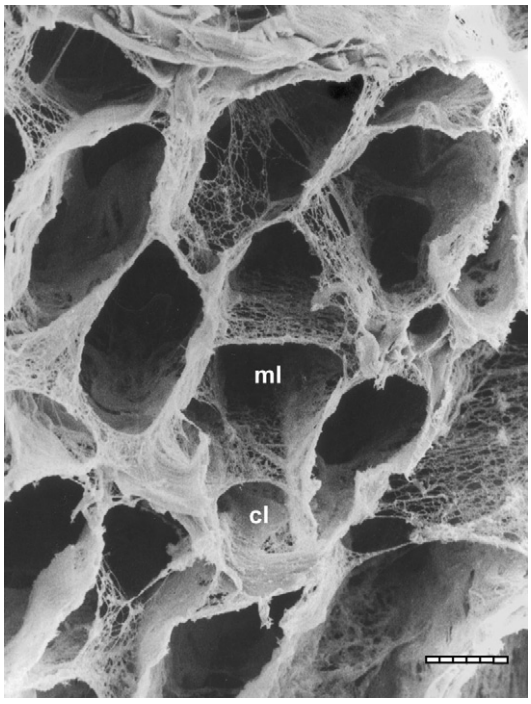


Fig. 1 – The endomysial collagen arrangement (ml: muscular lacunae, cl: capillary lacunae, bar = 10 μm). From [14] with permission.

We model the myocardial tissue as a net of spring elements (in the following simply "springs") representing the cardiomyocytes together with the endomysial collagen distribution. Each element is a viscous elastic spring, characterized by an elastic and a viscous constant. We connect these springs to imitate the interconnections between collagen fibers. Then we apply to the net of springs some external forces of suitable magnitude and direction, obtaining an extension of the net itself. In our setting, the ratio (*forces magnitude*)/(*net extension*) is intended to model the *stress/strain* ratio of a microscopical portion of the myocardial tissue.

Our starting point has been the hypothesis that if the net of springs is structured according to the new point of view of [13,14], then, to obtain a desired *stress/strain* value, in the sense specified above, we need much smaller elasticity constants of the springs than the ones obtained structuring the net according to the traditional point of view [15].

In order to understand whether this is the case, we organize our computational framework in such a way that it is able to *learn* the spring constants corresponding to a specified *stress /strain* value.

Moreover, to analyze the behavior of our nets from the *stress /strain* aspect, we need to consider the equilibrium positions only. Indeed, in the nets of springs that we consider, these equilibrium positions are independent from the viscous constant parameter of the springs (as we also verified by extensive computational experiments). This could be explained by the topology of our nets and the fact that we consider external forces that remain constant during the time period under consideration.