Journal of Biomechanics 47 (2014) 1537–1541

Contents lists available at ScienceDirect

Journal of Biomechanics

journal homepage: www.elsevier.com/locate/jbiomech
www.JBiomech.com

Short communication

A noninvasive approach to determine viscoelastic properties of an individual adherent cell under fluid flow

Jun Qiu [a,b], Andrew D. Baik [b], X. Lucas Lu [d], Elizabeth M.C. Hillman [c], Zhuo Zhuang [a], Cheng Dong [e], X. Edward Guo [b,*]

[a] School of Aerospace, Tsinghua University, Beijing, PR China
[b] Bone Bioengineering Laboratory, Columbia University, New York, NY 10027, USA
[c] Laboratory for Functional Optical Imaging, Department of Biomedical Engineering, Columbia University, New York, NY, USA
[d] Department of Mechanical Engineering, University of Delaware, Newark, DE, USA
[e] Department of Bioengineering, Pennsylvania State University, University Park, PA, USA

ARTICLE INFO

Article history:
Accepted 31 January 2014

Keywords:
Cell mechanical property
Viscoelastic
Fluid–structure interaction
Finite element method
Osteocyte

ABSTRACT

Mechanical properties of cells play an important role in their interaction with the extracellular matrix as well as the mechanotransduction process. Several *in vitro* techniques have been developed to determine the mechanical properties of cells, but none of them can measure the viscoelastic properties of an individual adherent cell in fluid flow non-invasively. In this study, techniques of fluid–structure interaction (FSI) finite element method and quasi-3-dimensional (quasi-3D) cell microscopy were innovatively applied to the frequently used flow chamber experiment, where an adherent cell was subjected to fluid flow. A new non-invasive approach, with cells at close to physiological conditions, was established to determine the viscoelastic properties of individual cells. The results showed an instantaneous modulus of osteocytes of 0.49 ± 0.11 kPa, an equilibrium modulus of 0.31 ± 0.044 kPa, and an apparent viscosity coefficient of 4.07 ± 1.23 kPa s. This new quantitative approach not only provides an excellent means to measure cell mechanical properties, but also may help to elucidate the mechanotransduction mechanisms for a variety of cells under fluid flow stimulation.

1. Introduction

One of the most common loading mechanism on cells such as osteocytes in bone is interstitial fluid shear resulting from tissue matrix deformation (Weinbaum et al., 1994). The fluid drag introduces strain inside the cell body, which may trigger the activation and transduction of biochemical signals, such as intracellular calcium signaling (Lu et al., 2012). In order to understand the spatial and temporal distributions of the stress/strain in a cell under fluid flow, knowledge of the constitutive material behavior and mechanical properties of the cell is necessary.

Several *in vitro* techniques have been developed to determine the viscoelastic mechanical properties of a variety of cells, such as micropipette aspiration, atomic force microscopy (AFM), magnetic tweezers, optical traps, and cytoindentation (Lim et al., 2006). However, these techniques are not ideal for determining the mechanical behaviors of cells under fluid flow, which is an important physiological loading mechanism on osteocytes.

In our previous studies, the 3D cell geometry of an osteocyte under fluid flow was recorded by a quasi-3D microscopy (Baik et al., 2010). The current study combines quasi-3D microcopy and a fluid–structure interaction (FSI) finite element method to simulate the viscoelastic creep behavior of osteocytes under steady flow. The objective of this study was to determine the viscoelastic properties of cells under fluid flow using this new approach.

2. Methods

2.1. Cell culture and shear flow experiments

MLO-Y4 osteocytic cells, a gift from Dr. Lynda Bonewald at the University of Missouri–Kansas City (Bonewald and Kato, 2002), are grown in α-modified Eagle's medium (α-MEM), with 5% fetal bovine serum and 5% calf serum. During experiments, cells were stained with Alexa Fluor 594 wheat germ agglutinin plasma membrane dye. A square glass micro-tube (width: 700 μm, height: 550 μm) was used as flow chamber. A laser cutter (Universal Laser Systems, Scottsdale, AZ) was used to cut glass slides (No. 1 thickness; Fisher Scientific,

* Corresponding author. Tel.: +1 212 854 6196; fax: +1 212 854 8725.
E-mail address: ed.guo@columbia.edu (X.E. Guo).

http://dx.doi.org/10.1016/j.jbiomech.2014.01.056
0021-9290

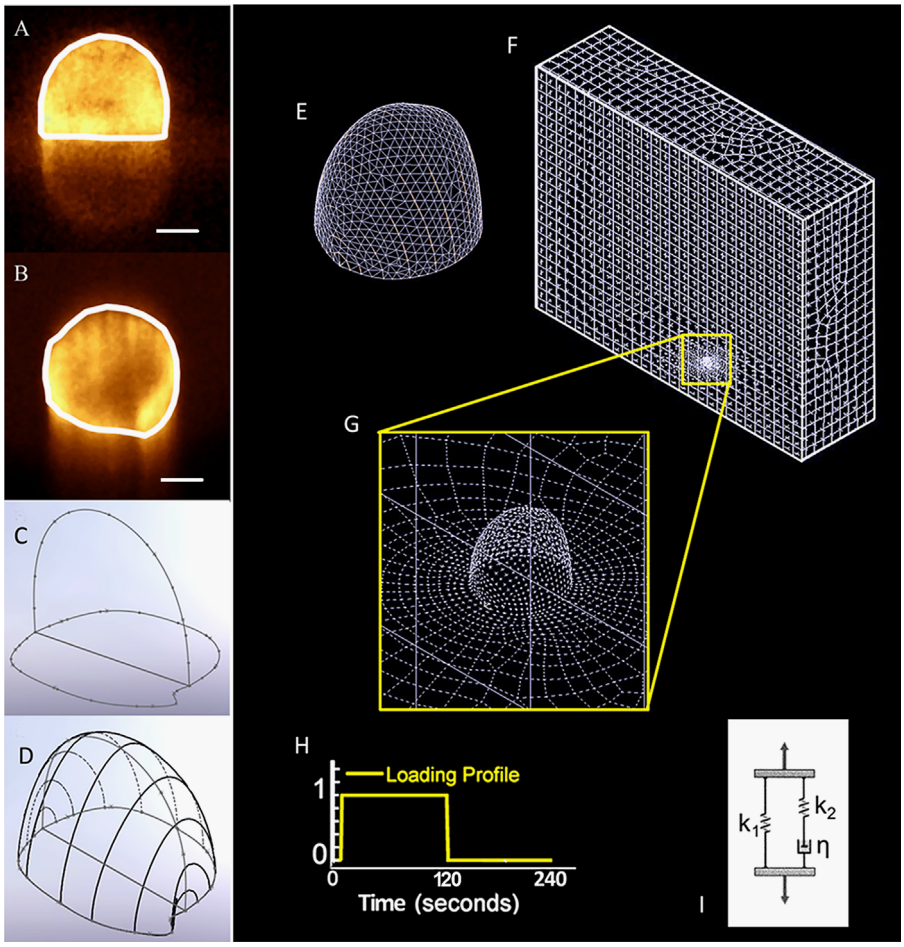

Fig. 1. 3D fluid–structure interaction FE model. ((A)–(D)) The process of 3D cell shape reconstruction. ((E) and (F)) The meshed model of cell and the fluid surrounding it. (G) The discrete elements with gradient size at the interface between cell and fluid. (H) The loading profile of inlet flow. (I) Standard linear solid model. Scale bar is 5 μm.

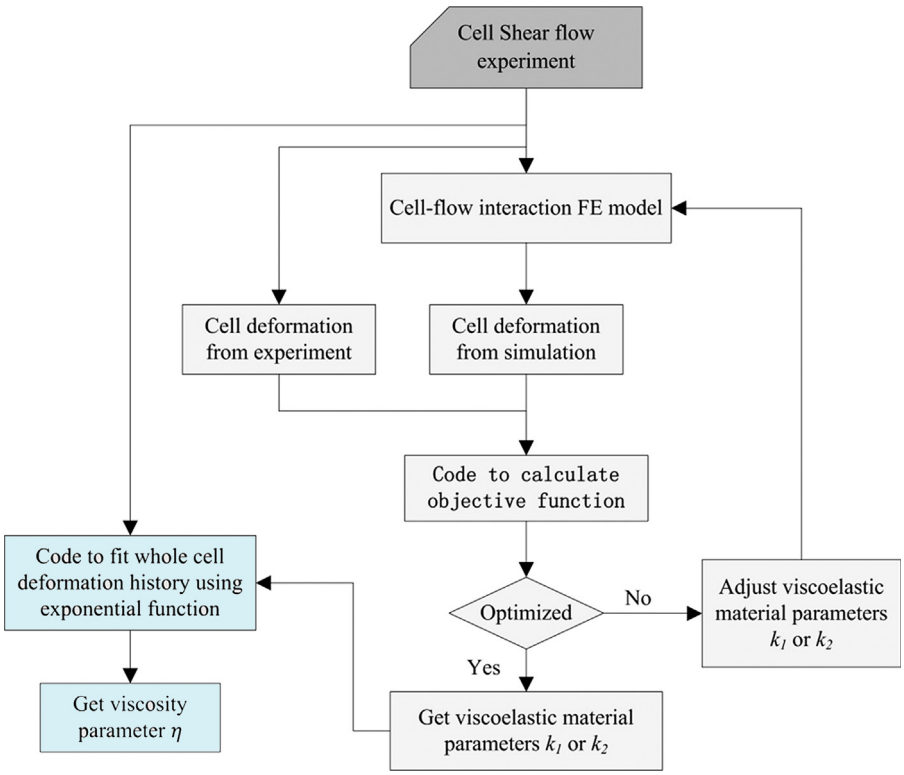

Fig. 2. Flow chart to obtain the three viscoelastic parameters of the cells. The section of light gray shows the process to optimize k_1 or k_2, and light blue section represents the process to obtain viscosity coefficient η. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)