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Open forward and inverse problems in theoretical modeling of bone tissue adaptation

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ARTICLE INFO

Article history:
Received 22 October 2012
Received in revised form
15 April 2013
Accepted 11 May 2013
Available online 29 May 2013

Keywords:
Bone remodeling
Adaptation models
Finite element
Orthopedics
Review

ABSTRACT

Theoretical modeling of bone tissue adaptation started several decades ago. Many important problems have been addressed in this area of research during the last decades. However, many important questions remain unanswered. In this paper, an overview of open problems in theoretical modeling of bone tissue adaptation is presented. First, the principal elements of bone tissue adaptation models are defined and briefly reviewed. Based on these principal elements, four categories of open problems are identified. Two of these categories primarily include forward problems, while two others include inverse problems. In every one of the identified categories, important open problems are highlighted and their importance is discussed. It is shown that most of previous studies on the theoretical modeling of bone tissue adaptation have been focused on the problems of the first category and not much is done in three other categories. The paper tries to highlight these potentially important problems that have been so far largely overlooked and to inspire new avenues of research.

1. Introduction

The research on bone tissue adaptation dates back to the 19th century when Wolff observed that bone tissue adapts to the mechanical loads it experiences (Wolff's law) (Wolff et al., 1986). Since bone tissue adaptation has important practical consequences both in medicine and in physiology, many researchers have studied the mechanism of bone tissue adaptation since then and many important questions have been addressed. With the advent of computers and the imaging techniques in the late 20th century, computational modeling of the bone tissue adaptation process has also received significant attention. There are many reasons why researchers are interested in mathematically modeling the bone tissue adaptation process. One of the most important reasons is the predictive capacity of mathematical models. If one can establish a sufficiently accurate mathematical model of the bone tissue adaptation process, the model can be used to predict the response of bone tissue to any change in the mechanical loading of bones (macro-scale changes) and/or distribution of the mechanical loading within the tissue (micro-scale changes). For example, implantation of prostheses in total joint replacement surgeries changes the distribution of the mechanical loads experienced by the bone tissue that is close to the prosthesis (Peter et al., 2004; Prendergast, 1997; Skinner et al., 1994; Turner et al., 1997; Weinans et al., 2000). If the loading changes such that a part of the load that is normally transferred through a particular part of bone is shouldered by the prosthesis (stress-shielding), the relieved part of bone may start to weaken due to bone resorption. It is therefore important to be able to predict the response of bone tissue to the modified state of mechanical loading.

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1751-6161/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.jmbbm.2013.05.017

Due to the above-mentioned predictive capacity of models, theoretical models of bone tissue adaptation have been developed during last three decades (Cowin and Hegedus, 1976; Cowin and Nachlinger, 1978) and have been applied to study various problems in orthopedic biomechanics (Pettermann et al., 1997; Pioletti and Rakotomanana, 2004; Ramtani et al., 2004; Shefelbine et al., 2005; Skedros et al., 2003; Subbarayan and Bartel, 2000; Tanck et al., 2006). It is not the intention of this article to thoroughly review the theoretical models of bone tissue adaptation. The main purpose of this article is to review the main problems that have been addressed in the area of theoretical modeling of bone tissue adaptation and to categorize them (Sections 3–6). In order to do this, the principal elements that are used in bone tissue adaptation models are briefly presented in the next section. The focus of the paper will be on highlighting the major 'open' problems and the approaches that could be used for solving those problems. It could actually be argued that dichotomous separation of research into 'open' and 'solved' is unrealistic, as progress in solving important research problems is generally gradual. Categorizing the problems into distinct categories and identifying 'open' problems of every category are nevertheless useful approaches, because they help in organizing the currently available body of research and highlighting potentially important research problems that are currently overlooked. It is therefore hoped that this paper inspires new avenues of research in theoretical modeling of bone tissue adaptation.

2. Elements of the bone tissue adaptation models

Theoretical modeling of bone tissue adaptation often involves five principal elements (Table 1):

- bone tissue adaptation model;
- parameters of the bone tissue adaptation model;
- bone anatomy (shape);
- bone density distribution or trabecular architecture;
- loading (mostly musculoskeletal loading).

The bone tissue adaptation model and its parameters are very much related and one can argue that they are the same element, as too could bone shape and bone density distribution or trabecular architecture. However, it is useful to separate these related concepts to enable the categorization of the problems in the theoretical modeling of bone tissue adaptation based on which one of the elements is unknown and needs to be predicted from the other known elements. There is a sixth element, namely implant geometry and material properties, which will not be considered in the present article.

2.1. *Bone tissue adaptation model and its parameters*

The process of bone tissue adaptation is a complex and multi-aspect physiological process that is driven by inter-related effects of mechanical and biological stimuli. As a hierarchical and multi-scale process, bone tissue adaptation works at several spatial and temporal scales. Since 1970s (Carter et al., 1987, 1989; Cowin and Hegedus, 1976; Cowin and Nachlinger, 1978; Huiskes et al., 1987), there have been many attempts to explain this process through use of mathematical models. In general, the developed models can be divided into phenomenological and mechanistic models (Table 2).

Phenomenological models are not concerned about the detailed physiological mechanism that drives the bone tissue adaptation process. Therefore, they often require a small number of parameters and are relatively easy to implement in finite element codes. Due to their simplicity and their limited physiological underpinning, they appeared first in the literature (Carter et al., 1987, 1989; Cowin and Hegedus, 1976; Cowin and Nachlinger, 1978; Huiskes et al., 1987). As noted also by other researchers (Garcia-Aznar et al., 2005; Martínez-Reina et al., 2009), phenomenological models are either based on homeostasis, damage/repair or optimality assumptions. A more detailed description of certain examples of phenomenological models together with some of their mathematical derivations is presented in Appendix A (Supplementary material).

According to the homeostasis assumption, the bone tissue adaptation process tries to keep the level of certain

Table 1 – The different elements involved in the theoretical modeling of bone tissue adaptation. The related measurement techniques, the ease of measurement, and mathematical models are also mentioned in the table.

Modeling element	Quantified as	Measurement technique	Ease of measurement	Mathematical model
Tissue adaptation model	Mathematical functions and equations	NA	NA	It is a mathematical model.
Parameters of the adaptation model	Parameters with different dimensions	Various direct and indirect methods	Varies for different parameters	NA
Bone anatomy	3D surfaces, collection of points in space	Imaging techniques (CT, MRI)	Easy	Statistical shape models
Bone density distribution or trabecular architecture	Density distribution and bone texture parameters	CT, DEXA	Easy	Statistical shape and appearance models
Bone loading	Joint and muscle forces	Instrumented implants	Difficult to impossible	Musculoskeletal models
Implant properties	CAD surfaces, volumes, etc.	Not normally needed	NA	Not needed