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Non-invasive real-time prediction of inner knee temperatures during therapeutic cooling

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ABSTRACT

The paper addresses the issue of non-invasive real-time prediction of hidden inner body temperature variables during therapeutic cooling or heating and proposes a solution that uses computer simulations and machine learning. The proposed approach is applied on a real-world problem in the domain of biomedicine – prediction of inner knee temperatures during therapeutic cooling (cryotherapy) after anterior cruciate ligament (ACL) reconstructive surgery. A validated simulation model of the cryotherapeutic treatment is used to generate a substantial amount of diverse data from different simulation scenarios. We apply machine learning methods on the simulated data to construct a predictive model that provides a prediction for the inner temperature variable based on other system variables whose measurement is more feasible, i.e. skin temperatures. First, we perform feature ranking using the RReliefF method. Next, based on the feature ranking results, we investigate the predictive performance and time/memory efficiency of several predictive modeling methods: linear regression, regression trees, model trees, and ensembles of regression and model trees. Results have shown that using only temperatures from skin sensors as input attributes gives excellent prediction for the temperature in the knee center. Moreover, satisfying predictive accuracy is also achieved using short history of temperatures from just two skin sensors (placed anterior and posterior to the knee) as input variables. The model trees perform the best with prediction error in the same range as the accuracy of the simulated data (0.1 °C). Furthermore, they satisfy the requirements for small memory size and real-time response. We successfully validate the best performing model tree with real data from in vivo temperature measurement from a patient undergoing cryotherapy after ACL reconstruction.

1. Introduction

Measurements in biomedicine are often difficult to perform because human subjects are involved. Many examples can be found, particularly in clinical procedures, where in vivo measurements are often not as accurate as desired [3], difficult, dangerous or even impossible to perform [46], especially if deep tissues or vital organs are in question [15,38]. Moreover, non-invasive medical procedures are emerging in the search for more reliable, less expensive, and risk-free medical technology for the future [31,34,40].

Computer simulations provide safe and inexpensive insight into physiological processes. In recent decades, computer simulations have significantly helped to better

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understand and solve a variety of problems in science. Advances in computer technology enable simulation of natural phenomena that cannot be subject to experiments in reality because of ecological, hazardous or financial obstructions [18]. With the use of computer simulation, it is possible to calculate, analyze, and visualize both stationary and time-dependent temperature fields in living biological tissues [11]. The temperature of the human tissue is an important factor in many fields of physiology [51], sports [14], cryotherapy [19], etc.

In the context of the issues addressed above, computer simulations can be useful to estimate an immeasurable variable or a variable difficult to be measured based on other variables of the system/process whose measurement is more feasible – a concept known as soft or virtual sensing [2]. In the case of biomedical systems, if the variable of interest cannot be measured because of the non-invasive nature of the system – hidden system variable, then we should measure other non-invasive variables that can be used to estimate the hidden one. However, simulations are usually resource- and time-consuming which is not acceptable in real-time systems [42]. We assume that real-time biomedical systems, for example, for the purpose of controlling the variable of interest, require a solution usually deployed on a mini on-board computer that cannot process large amount of data nor perform computationally demanding operations.

To this end, we use machine learning methods [20] to construct a predictive model that will provide a prediction for the hidden variable in a much shorter time with satisfying accuracy. Namely, we use simulation to generate a substantial amount of data for different input simulation parameters: capture the correlation between the hidden system variable and the non-invasive measurable ones. The data generated in this way is then used to construct a predictive model. There are two main advantages of using predictive models: (1) a predictive model can be used to simplify the simulation model and elucidate the most important correlations between the measurable (input) variables and non-measurable (output) variables, and (2) the predictive models are typically more efficient in terms of memory and computational complexity. Various machine learning techniques have proven to be adequate for extracting knowledge from data resulting from simulation models in various areas like medicine [5,10], ecology [9], social sciences [21], etc.

In this paper, we apply this approach on a real-world problem in the domain of biomedicine – non-invasive real-time prediction of inner knee temperature during cryotherapeutic treatment after anterior cruciate ligament (ACL) reconstructive surgery of a knee. It is known, mostly from empirical evidence, that cryotherapy following reconstruction contributes to reduced tissue edema, inflammation, hematoma formation and pain, reducing the need for pain medication and enabling faster rehabilitation [35]. Various cooling modalities are routinely used in postoperative treatment in orthopedics, traumatology, facial surgery, pain prevention in sport [11], etc. In a previous study, we have shown that computer-controlled cryotherapy with pre-programmed protocols in terms of heat extraction intensity and treatment time is more effective and controllable than a conventional cooling with gel-packs [29]. We measured in vivo temperatures of the inner and outer knee parts and assessed the effectiveness of both methods. Moreover, we confirmed delayed and less severe pain in patients with the computer-controlled cryotherapy. However, a lack of uniformity in patients' response to the cooling was confirmed, which raised the need for "smart" cooling devices, i.e. personalized cryotherapy. Different patients need different cooling protocols, depending on their constitution and regulatory systems, and on environmental conditions. A "smart" cooling device would be able to perform cooling adapted to the individual patient's response. Therefore, we propose an upgrade of the method for computer-controlled cryotherapy by introducing automatic control of the temperature inside the knee by changing the cooling temperature in the pad [28]. A few non-invasive temperature sensors on the knee surface, providing data about the actual heat transfer and the physiological response of the patient, should give a feedback for the process of control. To control the deep knee temperature successfully in an arbitrary knee without measuring it, we need to estimate the deep temperature from the non-invasively measured data using predictive models – the main goal of this paper. The light-weighted predictive models will then correspond to the mini architecture of the computer that controls the cryotherapy. Our previous work in the field of heat transfer in biological tissues forms the ground base for providing the simulated data [30].

The machine learning tasks that we address in this paper belong to the predictive modeling setting where the goal is to predict the value of one property of the examples (called a target attribute or output) using the values of the remaining properties (called descriptive or input attributes) [17]. Considering that the solution requires efficient predictive models, we investigate and evaluate several state-of-the-art machine learning methods. The machine learning methods that we will consider include simple methods, such as linear regression and regression trees, as well as more complex methods, such as model trees, and ensembles of regression and model trees. The simple methods will also provide efficient and understandable predictive models, i.e., with these models we will be able to infer the most important correlations between the input and output variables. The complex methods, on the other hand, will be black-box models and will offer state-of-the-art predictive power. The methods will be evaluated based on the predictive power and the time/memory efficiency of the models they construct. At the end, we will select the best performing method that can be further used, for example, for control of the hidden output variable in real-time. Moreover, we validate the best performing method with real data from in vivo temperature measurement from a patient undergoing cryotherapy after ACL reconstruction. Furthermore, we use methods for feature ranking to provide an ordered list of the input variables by their relevance or importance for the output/target variable [16]. We use these methods to investigate which input variables are sufficient for making a good prediction and to which extent we need to measure them in time. The expected benefit would be the reduction of the number of sensors and construction of even smaller and more efficient predictive models.

The rest of the paper is organized as follows. In Section 2, we present the background knowledge from computer