MSc–project: **The Application of Neural Networks to Predict Skin Evolution After Burn Trauma**

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Burn injuries effect millions of people all over the world on a yearly basis. Often these injuries cause unaesthetic scars and/or skin contraction. In severe cases, skin contractions decrease the mobility of joints of the patients, which in turn may result in patient disability. In order to treat burn injuries, clinicians aim at the prevention of complications like contractions and unaesthetic scars. An important trigger for the occurrence of contractions is the motion of joints. This motion causes local strains and stresses in the damaged area. These local stresses and strains activate skin cells (fibroblasts) to differentiate into myofibroblasts, which are specialised in the production of the 'wrong type of collagen' and in exerting pulling forces on their immediate environment.

In order to optimise and to improve therapies, it is necessary to understand the underlying biological mechanisms. This insight is used to construct mathematical models, by which a quantification of the underlying biological mechanisms is obtained. The model relates several biological input parameters (such as cell division rates, skin stiffness, cell differentiation rate, ...) to output variables like the extent of contraction (scar volume) or residual strain energy. The model is based on a set of nonlinearly coupled partial differential equations of several types. Numerical approximations are obtained by the use of the finite element method. A source of major concern is the uncertainty in the values of the input parameters. This uncertainty is caused by poor documentation, or by measurement errors, or, more importantly, by patient-to-patient variations. One of the mayor challenges in modelling is the assessment of the impact of uncertainty on the output parameters.

In order to quantify the impact of uncertainty for each input variable, one may use the variation of the Z-statistic. However, this information is not of interest to clinicians. For clinicians, it is more interesting to predict the probability that, for instance, a contraction exceeds a certain threshold so that the patient's quality of life decreases. In order to obtain this information, clever Monte Carlo-based Bayesian sensitivity analyses are carried out. For this purpose, multiple (typically very many) finite element simulations need to be carried out. Since each finite element simulation is expensive from a computational point of view, such simulations aiming at estimating the probability of a 'severe contraction' are not feasible for clinicians. For this purpose, we propose to reproduce the finite element simulations by machine learning, in which a trained neural network is used to obtain the finite element results at very low computational cost.

This neural network helps clinicians get immediate access to finite element simulations and hence decision making on the basis of simulations (next to the clinician's own expertise) will be easier.

Machine learning is started by processing data that link the inputs to the outputs. One typically divides the data in three portions: the training set (the largest portion), the test set and the validation set. Neural networks consists of so-called *input and output layers*. These input and output layers contain *nodes* that need the values of the input parameters and nodes that generate the output values, respectively. Between the input and output layers, the *hidden layers* contain nodes that process information in terms of transferring their inputs into output through *activation functions*. The activation functions contain variables that determine the output of the nodes. The input and output layers use activation functions for the processing of information as well. The training of the neural network is based on the determination of the variables in the activation functions so that the difference between network generated outputs and desired outputs from the training set (based on finite elements) is minimised (typically in terms of a (weighted) least squares error). Typically, one uses the neural network error based on the test set to determine whether the topology (distribution of the nodes) of the neural network should be adjusted or not. Once the neural network is deemed 'optimal', then one uses the validation set to estimate the error and reliability of the obtained neural network.

The first steps towards the use of neural networks to reproduce the finite element simulations have been taken in [1]. In this work, the focus was on simulations in one spatial dimension. The current project will extend the class of simulations to higher spatial dimensionality so that the wound/scar geometry can be varied. It will be necessary to perform higher-dimensional finite element simulations (code is available), organise the data and determine a useful format of the data and search for the right neural network capacity (in terms of number of layers and nodes per layer), activation functions and training, testing and validation errors. If time permits, different neural network strategies such as autoencoder neural networks, which are suitable to filter out insignificant data, or the use of physics-based neural networks will be studied.

In this international collaboration, supervision will be done Alexander Heinlein (TU-Delft), Ginger Egberts (TU-Delft / UHasselt) and Fred Vermolen (UHasselt). More information can be obtained by contacting

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References

[1] M. Schaaphok. A Fast Neural Network-Based Computational Framework for the Prediction of Skin Contraction. MSc-thesis, Delft University of Technology, The Netherlands, https://repository.tudelft.nl/