Master thesis : In silico model for Gel Aspiration-Ejection (GAE) process in the context of clinical peripheral nerve repair

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In silico model for Gel Aspiration-Ejection (GAE) process in the context of clinical peripheral nerve repair

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Damage caused to peripheral nerves is called peripheral nerve injury which affect about 300,000 people a year. Even if the peripheral nervous system has the ability to regenerate naturally, depending on the severity of the injury, this natural repair process is not efficient enough. In most cases, a complete recovery is prevented and leads to heavy consequences for the patient and for our society due to lifelong disabilities and refractory neuropathic pain. A promising peripheral nerve repair solution is the Engineered Neural Tissue (EngNT). Current active research and literature works focus on identifying the optimal design of EngNT constructs to promote peripheral nerve repair. However, the manufacturing methods to produce this optimal design are therefore an essential factor. They consists in preparing the collagen gel then stabilising it, by expelling most of the fluid from the matrix to provide the EngNT with the desired structure and properties. There are two recent promising stabilisation processes which are the Plastic Compression (PC) and the Gel Aspiration Ejection (GAE). They are used but have not been properly studied yet leading to a lack of control and process understanding. That is why, this research work tries to provide an answer in three steps on how to build a primary mathematical model to initiate the control of the stabilisation methods to target the production of the desired EngNT design. The first step is a background study to define the features to model. The second step identifies the mathematical model focus. Indeed, the combination of modelling and experiments is found to be a powerful tool to control the stabilisation methods. However, the current stage in this integrated approach is the implementation of a primary mathematical model which first needs a model focus. A dynamic analysis has been chosen to target the aspiration stage of the construct in the cannula during the GAE method. The third step implements the model and answers to its focus. The chosen model for this research shown that an important dissipation at the wall boundaries is present due to fluid friction during the aspiration stage of the GAE process. Excessive aspiration pressure involves high dissipation which leads to elastic failure of the construct in the cannula. In successful cases, the aspiration stage has not been found to be the origin of cell death while it might be the cause of cells' alignment on the top of the construct especially for small cannula diameters. Through the three steps and the model implementation, this research work highlights the potential of modelling for the control of stabilisation methods, opens the path for longer studies and provides a first understanding of the aspiration process in the GAE method.

Keywords: Gel aspiration ejection, plastic compression, engineered neural tissue, peripheral nerve injury, mathematical modelling, stabilisation, collagen gel

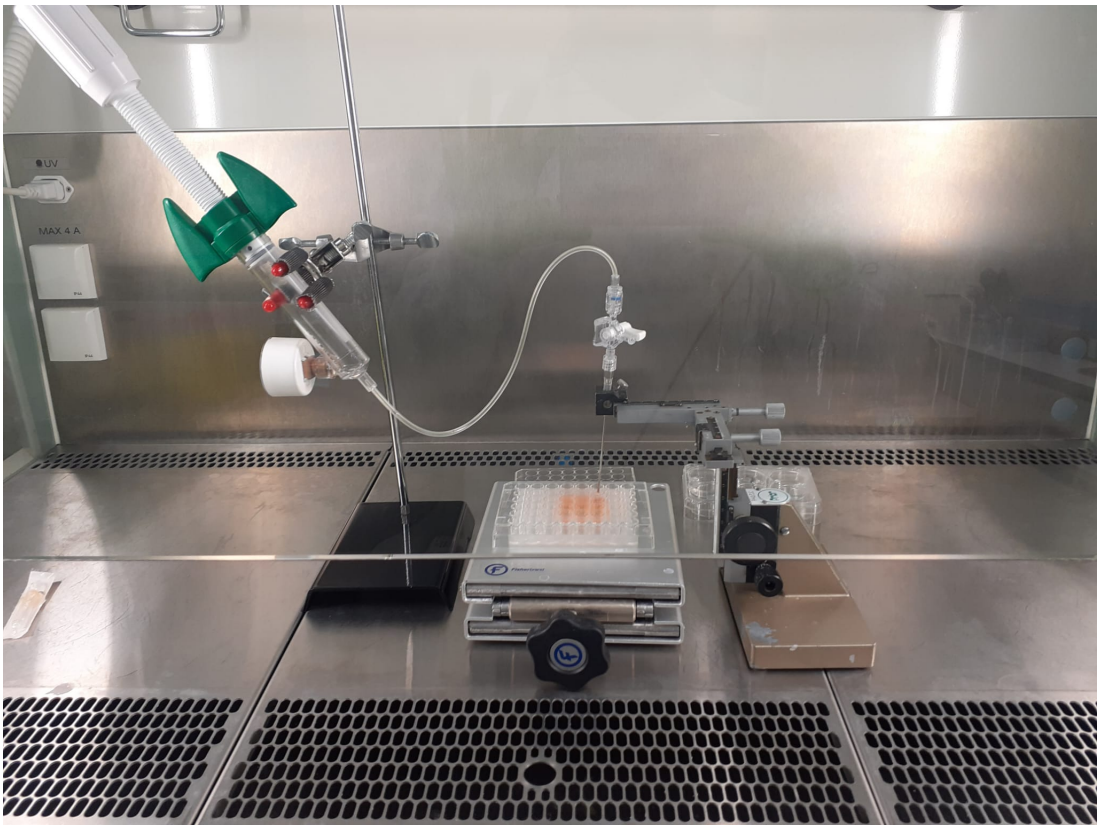

Figure 1: GAE experimental setup

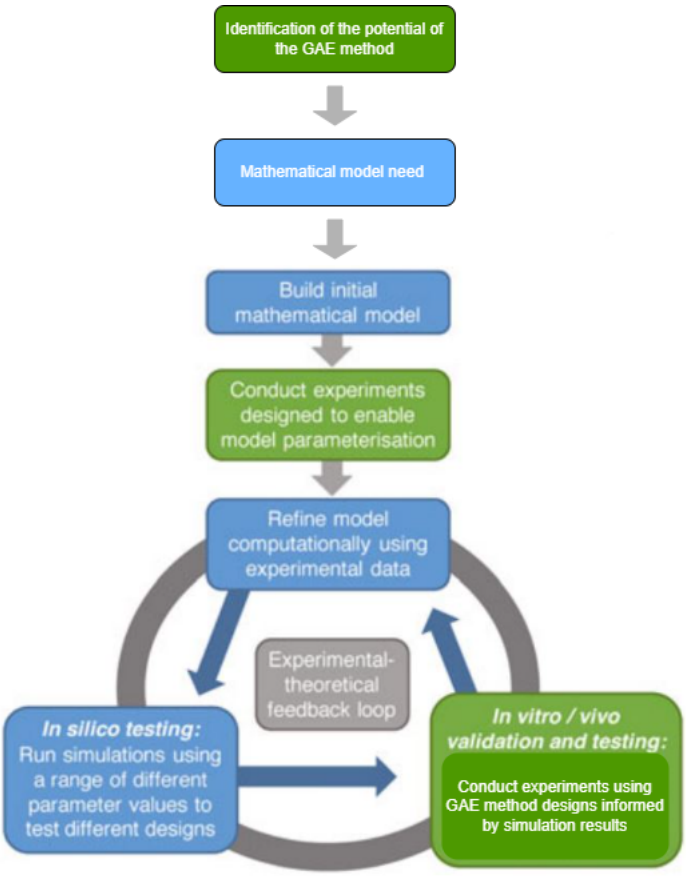

Figure 2: Experimental and theoretical integrated approach workflow

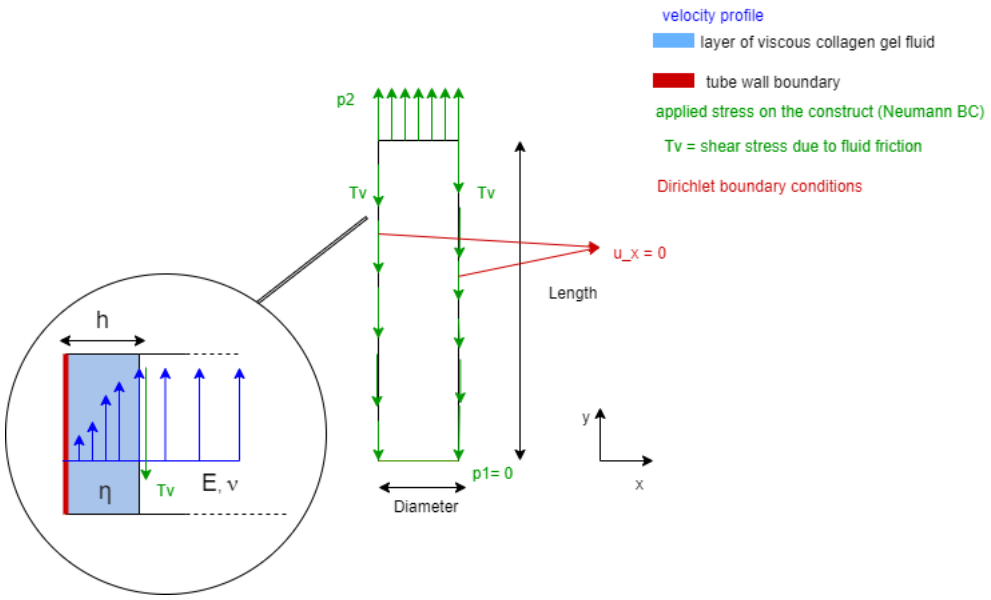

Figure 3: GAE process in silico representation

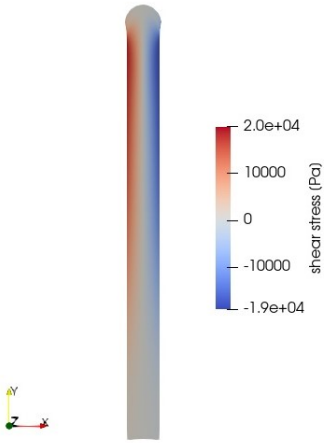

Figure 4: Shear stress distribution and deformation of the system with high aspiration pressure (10^5 Pa) over the 14G construct after 99 s of aspiration process

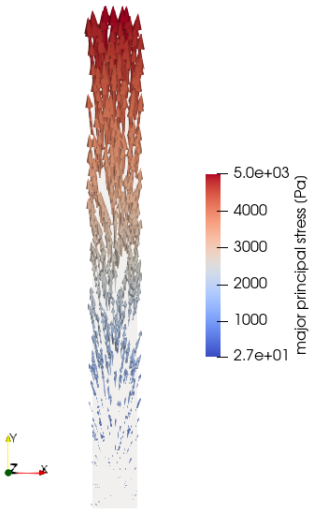

Figure 5: Maximum major principal stress field over the 16G construct after 270 s of successful aspiration process

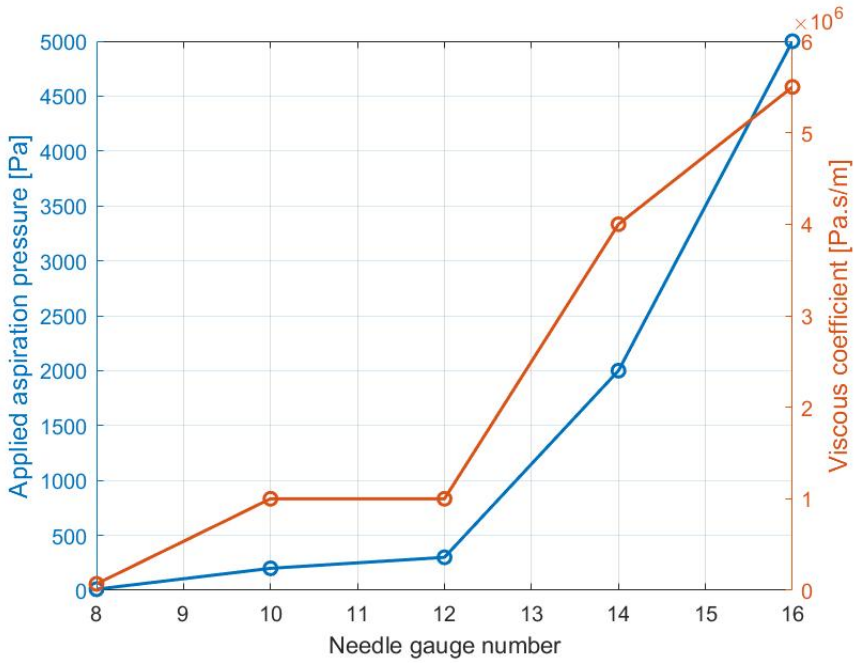

Figure 6: Applied aspiration pressure and viscous coefficient values to obtain a successful aspiration of the construct in the cannula for different needle gauge numbers