

## Electromagnetic-Mechanical Stimulation on PC12 for Enhancement of Nerve Axonal Extension

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**Abstract :** In recently, electromagnetic and mechanical stimulations have been recognized as the effective extracellular environment stimulation technique to enhance the defected peripheral nerve tissue regeneration. In this study, we developed a new hybrid bioreactor by adopting 50 Hz uniform alternative current (AC) magnetic stimulation and 4% strain mechanical stimulation. The guide tube for nerve regeneration is mesh structured tube made of biodegradable polymer, such as polylactic acid (PLA). However, when neural damage is large, there is a possibility that peripheral nerve undergoes necrosis. So it is quite important to accelerate the nerve tissue regeneration by achieving enhancement of nerve axonal extension rate. Therefore, we try to design and fabricate the system that can simultaneously load the uniform AC magnetic field stimulation and the stretch stimulation to cells for enhancement of nerve axonal extension. Next, we evaluated systems performance and the effectiveness of each stimulation for rat adrenal pheochromocytoma cells (PC12). First, we designed and fabricated the uniform AC magnetic field system and the stretch stimulation system. For the AC magnetic stimulation system, we focused on the use of pole piece structure to carry out in-situ microscopic observation. We designed an optimum pole piece structure using the magnetic field finite element analyses and the response surface methodology. We fabricated the uniform AC magnetic field stimulation system as a bio-reactor by adopting analytically determined design specifications. We measured magnetic flux density that is generated by the uniform AC magnetic field stimulation system. We confirmed that measurement values show good agreement with analytical results, where the uniform magnetic field was observed. Second, we fabricated the cyclic stretch stimulation device under the conditions of particular strains, where the chamber was made of polyoxymethylene (POM). We measured strains in the PC12 cell culture region to confirm the uniform strain. We found slightly different values from the target strain. Finally, we concluded that these differences were allowable in this mechanical stimulation system. We evaluated the effectiveness of each stimulation to enhance the nerve axonal extension using PC12. We confirmed that the average axonal extension length of PC12 under the uniform AC magnetic stimulation was increased by 16 % at 96 h in our bio-reactor. We could not confirm that the axonal extension enhancement under the stretch stimulation condition, where we found the exfoliating of cells. Further, the hybrid stimulation enhanced the axonal extension. Because the magnetic stimulation inhibits the exfoliating of cells. Finally, we concluded that the enhancement of PC12 axonal extension is due to the magnetic stimulation rather than the mechanical stimulation. Finally, we confirmed that the effectiveness of the uniform AC magnetic field stimulation for the nerve axonal extension using PC12 cells.

**Keywords :** nerve cell PC12, axonal extension, nerve regeneration, electromagnetic-mechanical stimulation, bioreactor

**Conference Title :** ICBM 2018 : International Conference on Biomechanics

**Conference Location :** Madrid, Spain

**Conference Dates :** March 26-27, 2018