

Microelectrode arrays and nerve tissue engineering for novel muscle stimulation

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Introduction

- Low level spinal cord injury in the lumbar spine causes motor neuron damage at the injury site [1]. Disrupting the connections between the spinal cord and lower body muscles leads to impaired function. Illustrated in figure 1.

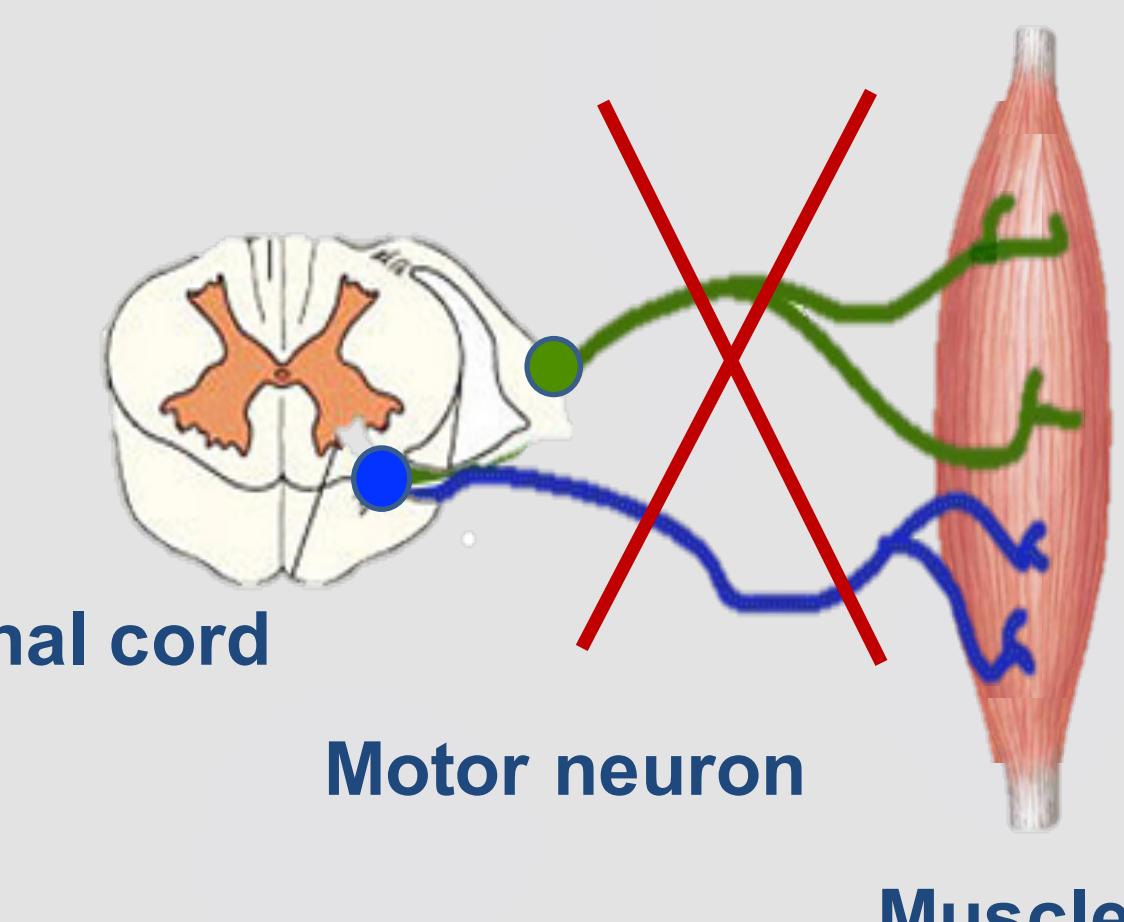


Figure 1. Schematic diagram showing motor neuron damage.

- Currently, the only way patients with denervated muscles can maintain their muscle bulk is via direct external stimulation. This is a crude, obtrusive method for muscle stimulation that requires large, long current pulses delivered with large electrodes in order to stimulate enough muscle [2].
- This work aims to develop a bio-hybrid device using engineered nerve tissue and microelectrode arrays to stimulate denervated muscle. Thus, providing a more practical method for muscle stimulation, particularly for those suffering from denervated muscles.

Aims

- To investigate how well NG108-15 cells grow motor neurons in artificial nerve tissue.
- To understand the development of the microelectrode array and how the microelectrode array could interface with the engineered nerve tissue.

Methods

a) Engineered nerve tissue

Engineered nerve tissue was manufactured as previously described [3]. Rat Schwann cell line SCL 4.1/F7 (Health Protection Agency, UK) and NG108-15 cell lines (Sigma, Aldrich) were grown in DMEM (Sigma) supplemented with penicillin and streptomycin (100 U/ml and 100 mg/ml, respectively; Sigma) and 10% v/v foetal calf serum (Sigma) was used throughout the study.

NG108-15 cells were co-cultured (50,000 cell density/gel) with the Schwann cell sheaths; positively stained for β III-tubulin (Sigma; 1:400 dilution) to allow neurite measurement (figure 5). The measurement was performed with ImageJ from images captured with a Zeiss microscope at 10X magnification.

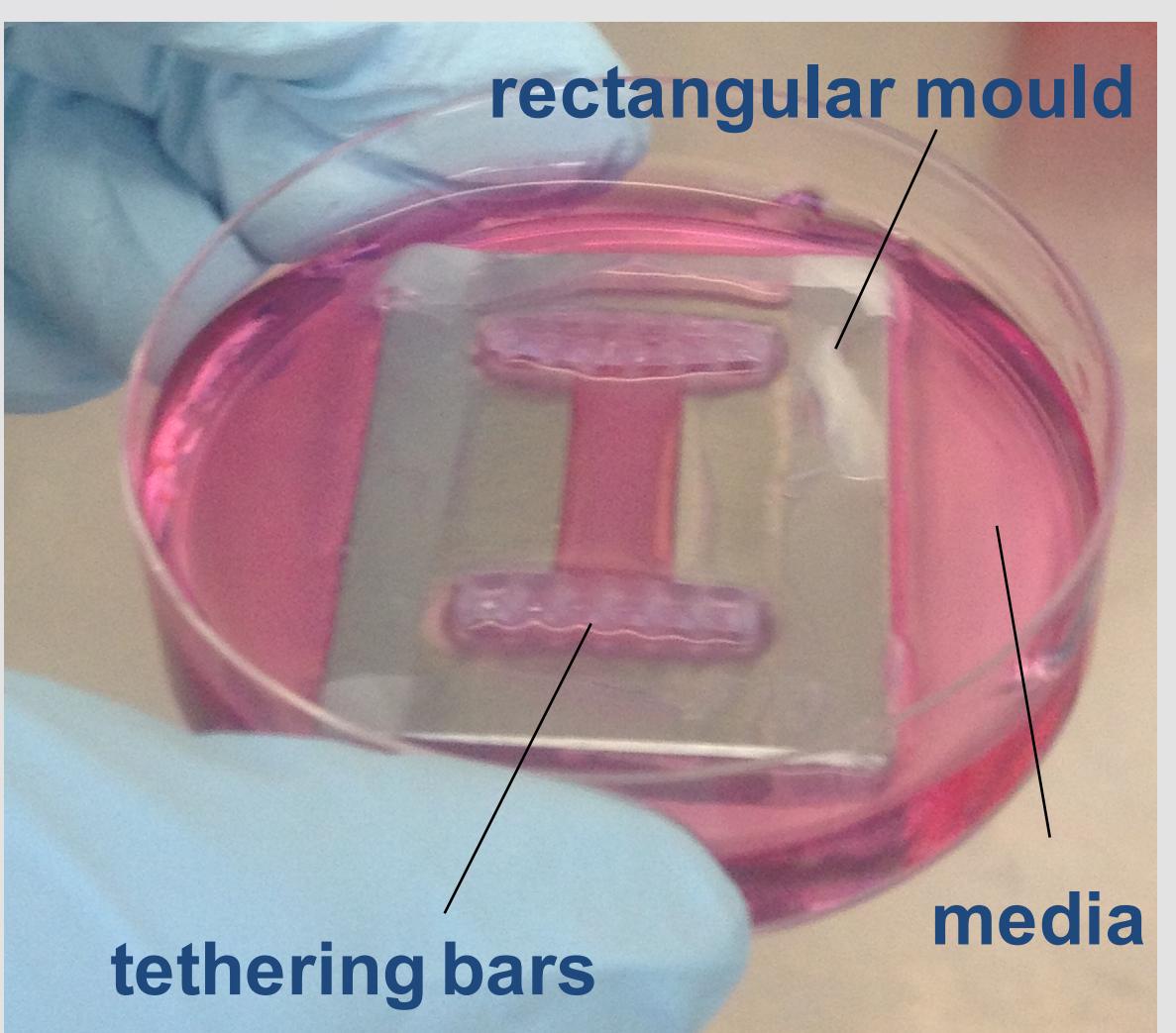


Figure 2. A 3D tethered collagen gel.

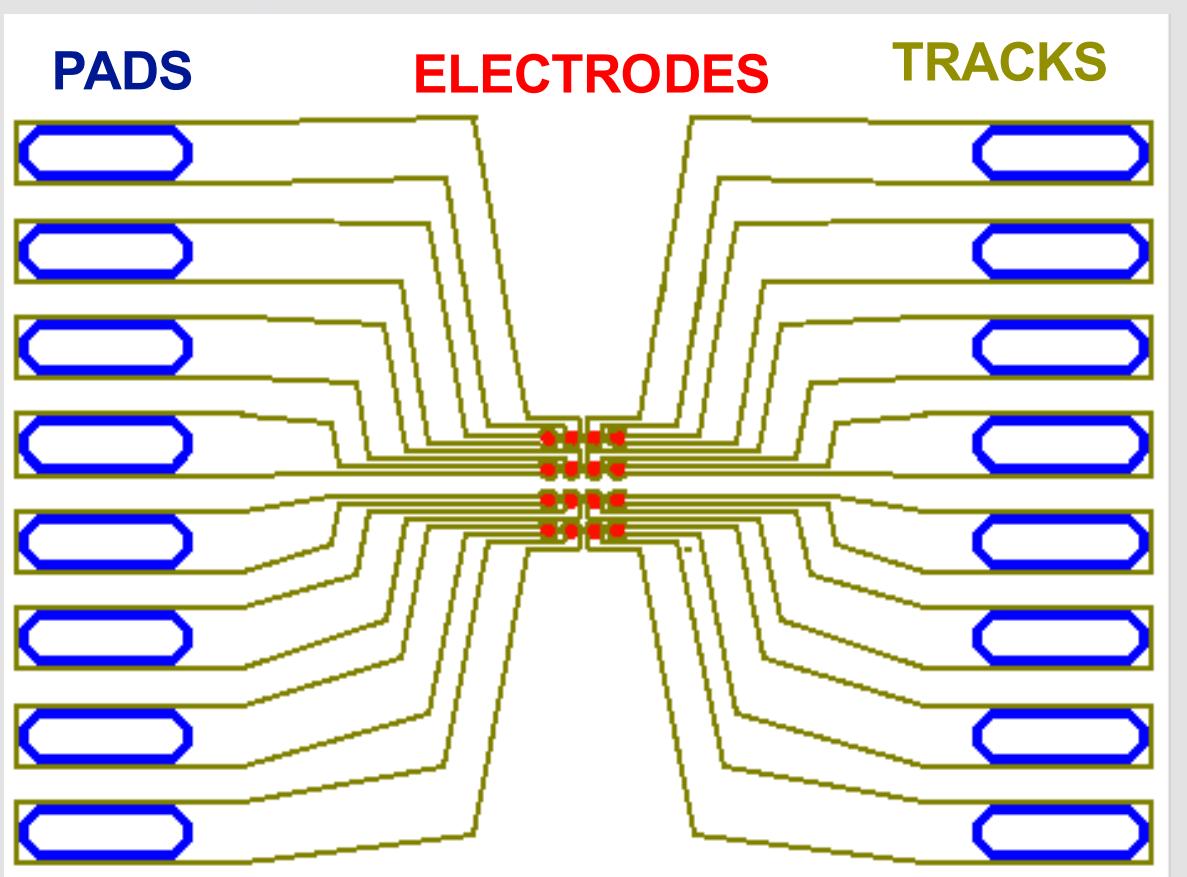


Figure 3. The microelectrode design.

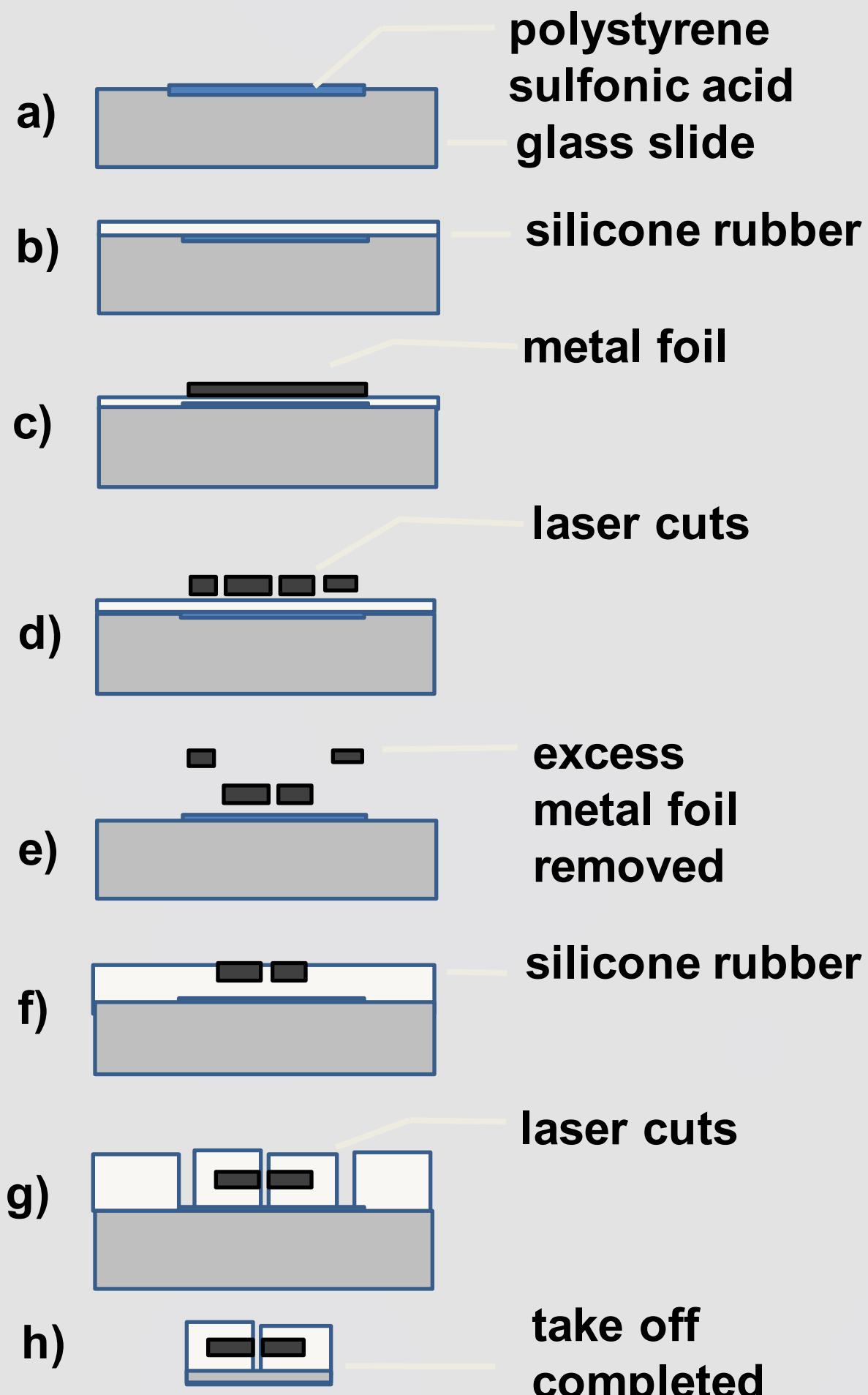


Figure 4. The manufacturing steps for the microelectrode array. Reproduced from [4].

Results

- The 4x4 microelectrode array was manufactured successfully (shown in figure 5).

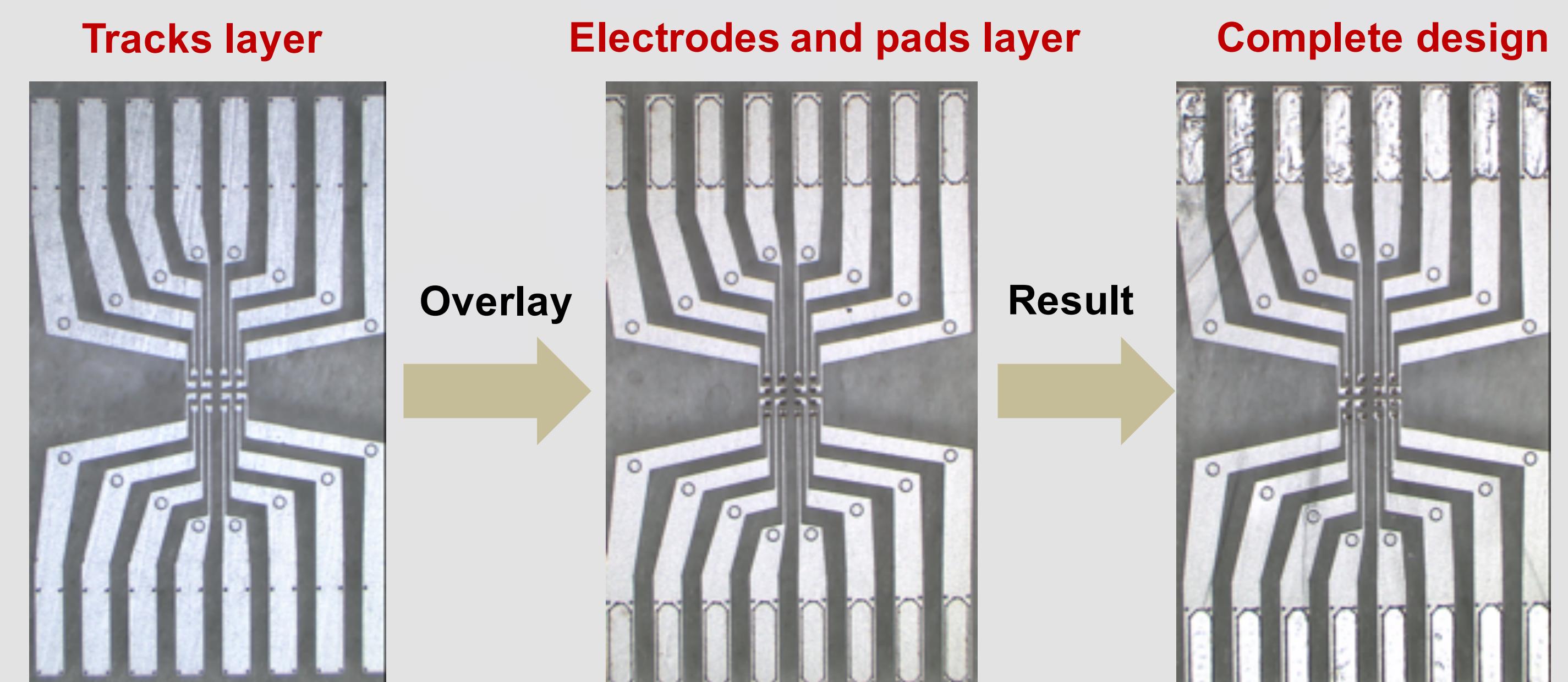


Figure 5. The microelectrode array construct.

- Engineered nerve tissue was produced using NG108-15 cells. Their neurite outgrowth is illustrated in figure 6.

Discussion

- NG108-15 cells grow motor neurons in artificial tissue. However, the length recorded is not within the range required ($\sim 200\mu\text{m}$) to create a biological interface, thus other motor neuron candidates such as primary cells and stem cells need to be considered as an alternative.
- Though the 4x4 microelectrode array was developed successfully, additional research will be required to fully understand the development required to construct a biological interface between the array, the muscles and the artificial nerves (concept is illustrated in figure 7).

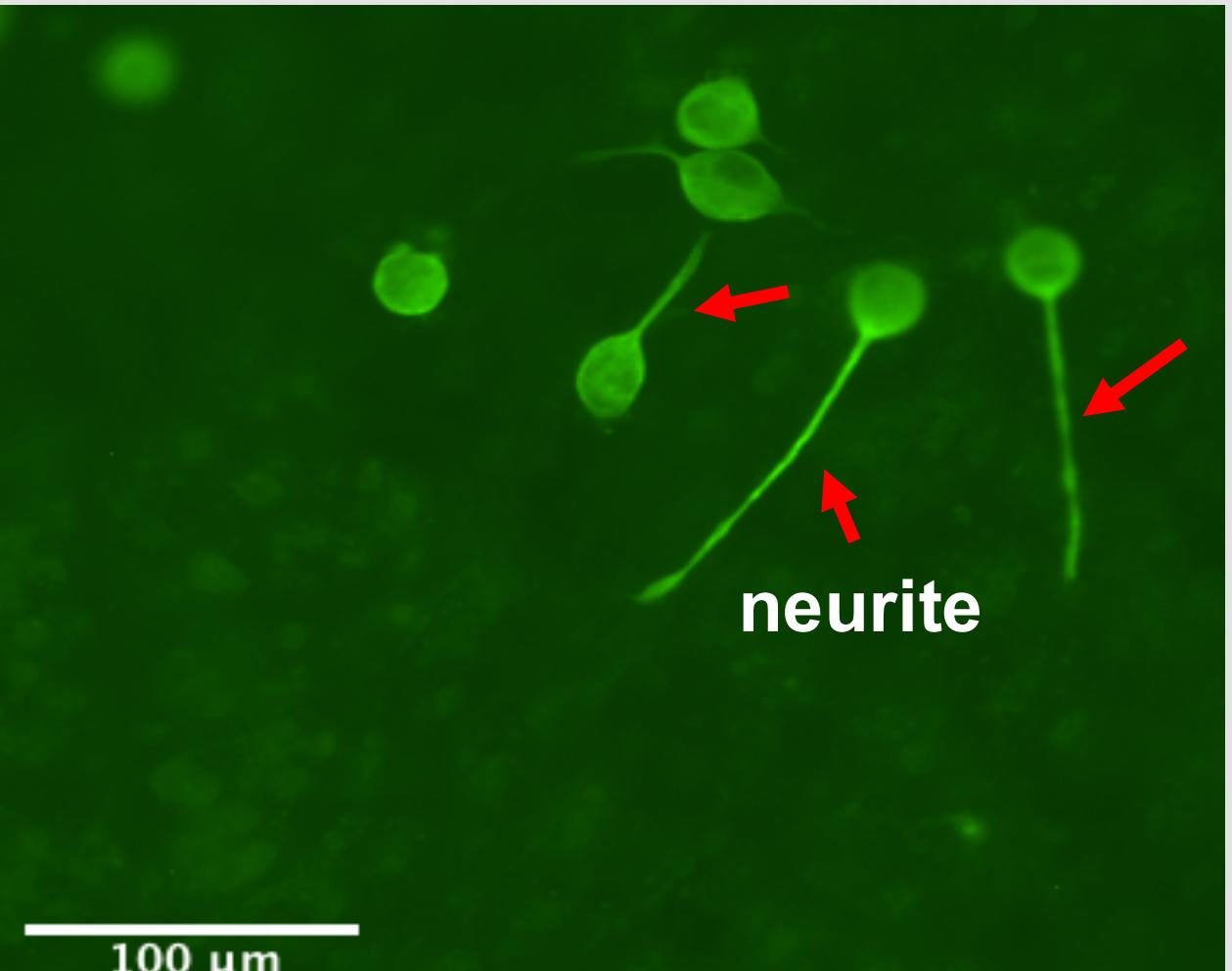


Figure 6. NG108-15 motor neuron outgrowth. The cells are positively stained for β III-tubulin. The red arrows indicate neurite outgrowth.

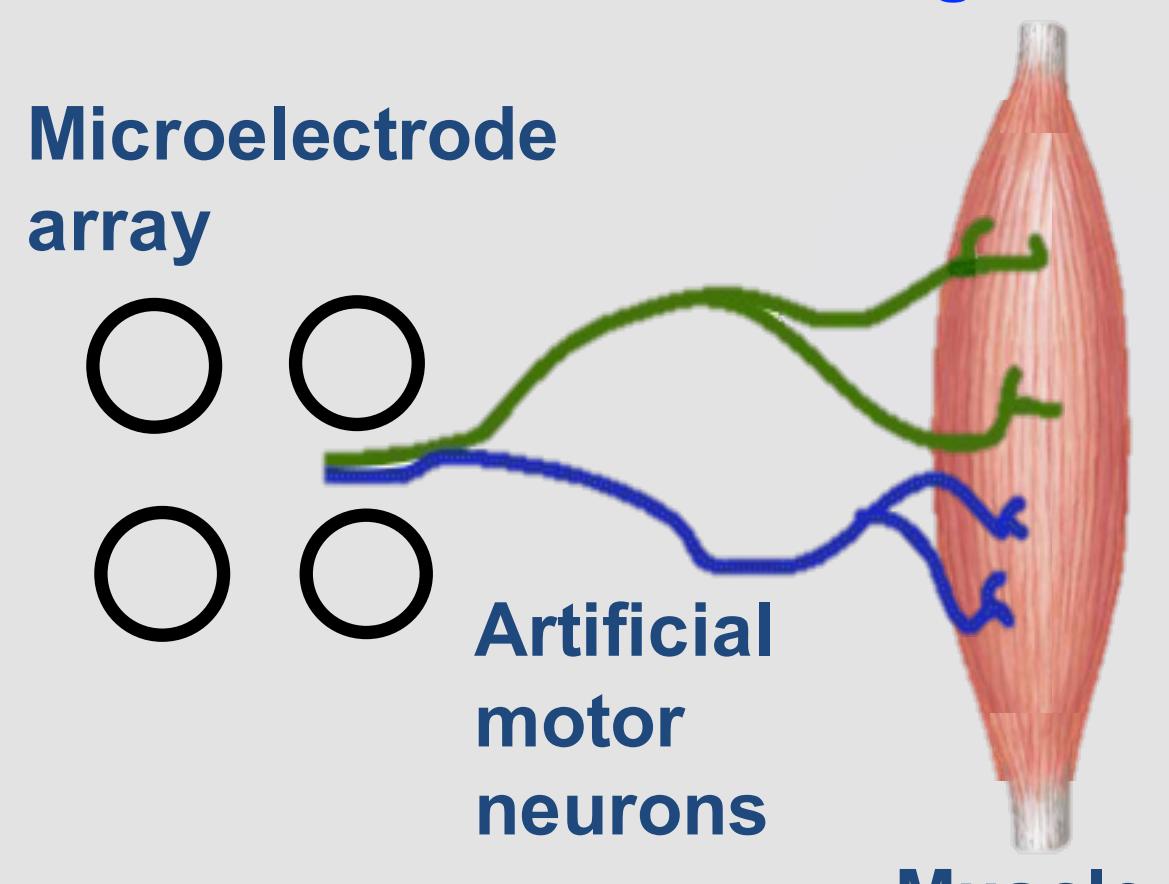


Figure 7. The biological interface that would be formed between the array, the artificial nerves and the denervated muscle.

References

- [1] Grahn P.J. et al., 2014. *Front. Neurosci.* 296(8).
- [2] Kern H. et al., 2002. *Artificial Organs*, 26(3), pp.216–218. [3] Georgiou M. et al., 2013. *Biomaterials*, 34(30), pp.7335-7343. [4] Schuettler M. et al., 2005. *Journal of Neural Engineering*, 2(1), pp.121–128.