

Micro and Nano Fabrication for Cell Engineering

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INTRODUCTION: Adam Curtis has been interested in the response of cell to surfaces throughout his career. This talk will discuss the construction of exercise grounds for cells and the techniques used beginning with the first structures made for Adam by lithographic techniques in 1982 and going on to the present.

The fabrication facilities in the Department of Electrical Engineering were established in the late 70's to make nano-electronic and opto-electronic devices. Devices for biological purposes brought new challenges. The use of clean air and control over contaminants is similar. But the nature of the contaminants is different and the conditions of final use are very different – as cells like to live in corrosive liquids. However at a deeper level, the disciplines of semiconductor device engineering and cell biology have a great similarity – they are both concerned with surface phenomena (and that surface is usually an oxide).

METHODS: Interestingly the requirements of structures for studies in Cell Biology have always pushed the state of the art in microfabrication. In the 80's the masks for defining a pattern in resist using photolithography were made using photographic reduction. Typical final pattern sizes were a few millimeters square, but to get good statistics on cell behaviour, one needs a square centimeter at least. So we had to improve the narrowness of our initial lines, even inspecting the edge of the cutting tool under a scanning electron microscope. We wanted to make grooves in a bio-degradable polymer so that a sheet of polymer patterned with guiding grooves could be used to make a prosthesis for tendon repair. Such polymers often dissolve the solvents used in lithography and while a route could be found for a particular polymer, the idea of embossing was much more attractive. The die required to stamp into the heated polymer was made using conventional lithography. This an important step forward for it enables the possibility of the use of

micro and nano patterning in prosthesis at a reasonable cost.

RESULTS: It was found that some cells respond to very shallow grooves – the obvious question was do they response to very small features. In the early 90's the Department acquired a large area electron beam lithography tool, so small features could be written. In the initial work 100 nm diameter pillars, 100 nm high spaced in a regular array 300 nm apart inhibited the adhesion of fibroblasts. To make this structure over a 1 cm square area requires the formation of 10^9 dots, and each dot could require requires 100 bytes of information to define it. An electron beam machine writes pattern information in a small field ($1/4 \text{ mm}^2$) and then the fields are stitched together by moving the stage under interferometric control. Considerable development was required to develop strategies to reduce the time taken by the writing to about 1 hour/ cm^2 and to ensure that the alignment of the fields was good enough that cells do not see any un-patterned area (a gap of 150 nm would suffice to cause adhesion). In the specification of a new electron beam machine, we reviewed the needs of the various groups that would use the new machine, and for alignment, the biological needs were the most demanding.

DISCUSSION & CONCLUSIONS: Lithographic techniques produce flat structures. Scaffolds for cells to be implanted in prostheses require 3-dimensional structures. The next challenge is to use the patterning techniques to give cues to the cells to align to each other as *in vivo*, to create a 3-D structure and to provide channels through this scaffold to assist in vascularisation and enervation.