

NICHED BIOREACTORS FOR STEM CELL APPLICATIONS

Monash University supervisors: Prof Kerry Hourigan, Dr George Thouas, Prof Tam Sridhar

Monash University contact: Prof Kerry Hourigan (kerry.hourigan@eng.monash.edu.au), or Dr George Thouas, George.Thouas@eng.monash.edu.au

IIT(Bombay) supervisors: Prof Jayesh Bellare, Dr Sarika Mehre, Dr Sameer Jadhav

IIT(Bombay) contact, Prof Jayesh Bellare jb@che.iitb.ac.in

The Problem

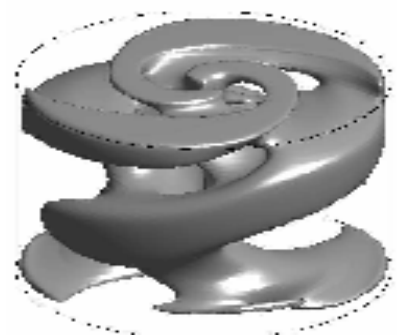
Stem cell research efforts are growing exponentially at present, and in parallel with this trend is a major need for convergence of more efficient and appropriate laboratory biotechnologies. One such technology is the bioreactor, an industrial form of contained reaction vessel with emerging applications to the controlled, large-scale production of human cells and tissues, in the fields of tissue engineering, regenerative medicine and stem cell science. Bioreactors have advantages over standard systems for laboratory production of stem cells, mainly due to features such as controlled fluid flow for controlled mechanical stimulation of tissues and homogenous nutrient dispersal. These stimuli are absent from standard cultures but occur naturally in living tissues, particularly in highly specialized, discrete domains where stem cells reside (also called “niches”). The “niche” concept is pivotal to understanding the underlying biology and improving the efficiency of stem cell production in a laboratory environment, from a bio-mimetic approach. The proposed project is therefore focussed on the development of niched bioreactors for stem cell applications at Monash University and IITB, as a multidisciplinary approach between interdisciplinary engineering and biomedical science research.

The Project

The project will be divided equally between two main components:

1. Experimental bioreactor process engineering (fluid mechanics simulation and experimental modelling, chemical engineering simulation and modelling and involve the design, computational simulation)
2. Direct application of optimized prototypes for production of stem cell types that rely on niche environments (including human embryonic (universal tissue forming) stem cells, haemopoietic (blood forming) stem cells, and osteogenic (bone forming) stem cells).

Monash University houses a range of state-of-the-art facilities and technology that will be used in this project. The faculty of engineering has recently established an advanced computational simulation and experimental modelling laboratory dedicated to understanding complex fluid mechanics problems, such as microfluidic flows. These facilities have already been used to simulate perfusion dynamics in simplified niche environments and stirred bioreactors (**Fig 1**). The same facility houses a high-speed computer grid for unprecedented speed of simulation and image processing. The local mechanical engineering workshop facilities are operated by trained technical staff that also design and manufacture experimental bioreactors rigs and prototype models for direct application to laboratory use. Also located at the Faculty of Engineering is a newly established Stem cell bioreactor development laboratory (SBDL), used for preliminary testing of prototypes before application to stem cell production. The recently developed rotating disc stirred bioreactor is an example of a preliminary prototype tested using mammalian cell lines (**Fig 2(a) and (b)**). The SBDL also has access to biochemical engineering



environment (upper). Three dimensional flow in a stirred bioreactor (lower)

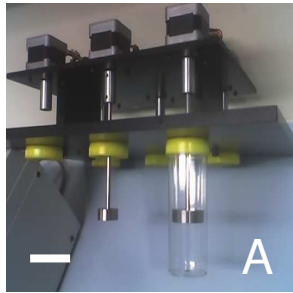


Figure 2 (a). Rotating disc bioreactor rig for mammalian cell culture. (b) Bioreactor set up to contain cell culture fluid under tissue culture conditions inside an incubator .

equipment and bioinformatics. Clayton campus is home to the Australian Stem Cell Centre and MISCL, which contain suites of biotechnology and tissue culture laboratories dedicated to all aspects of stem cell science, including optimized stem cell production and ongoing projects involving different tissue and organ systems (eg., nerve, blood, kidney, prostate, skin and lung regeneration). The same facility also houses advanced microscopy, molecular biology and cell based analysis equipment.

HDR STUDENT INVOLVEMENT

The project will provide an opportunity for students to work directly with researchers in solving problems related to the design, simulation, fluid mechanics modelling, biochemical engineering, mechanical construction and computer-based control of bioreactors for stem cells production. Students will work initially with internationally recognised engineering researchers, and at later stages with stem cell scientists toward the directed application of the biotechnology and bioprocess for specific stem cell protocols. These protocols will also involve cell based assays such as immunophenotyping (**Fig 3**) and FACS sorting. Ideally, students should have interests in developing a research orientated career in biotechnology and bioprocess development. Attributes that would be of advantageous would be backgrounds in chemical and biochemical engineering, mechanical engineering (materials or fluids) and computer programming.

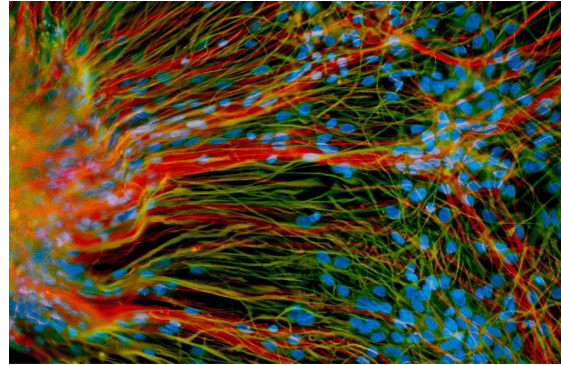


Figure 3. Fluorescence microscope image of neural cell outgrowth from embryonic stem cells. Red lines represent nerve fibres. (mag X200)