CHAPTER I
INTRODUCTION

Tissue engineering is an interdisciplinary technology that applies materials engineering, cellular biology and genetic engineering towards the development of biological substitutes for tissues regeneration process (Langer *et al.*, 1993). The primary objectives of these substitutes are to restore, maintain and/or improve tissue functions. A functional scaffold for tissue engineering must support and define the three-dimensional (3D) organization of the tissue-engineered space and maintain the normal differentiated state of cells within the cellular compartment. Ideally, a functional scaffold should mimic the structure and biological function of native extracellular matrix (ECM) proteins (Teo *et al.*, 2006), so as to provide mechanical support and regulate cellular activities (Rho *et al.*, 2006). Therefore, the selection of polymer, the manufacturing process and the modification of substitute materials play an important role in scaffold fabrication.

A wide variety of fabrication techniques have been used to generate 3D polymeric scaffolds for potential use in tissue regeneration. Electrospinning is a technique capable of producing ultra-fine fibers with diameters in sub-micrometer down to nanometer range through the action of a high electric field (Reneker *et al.*, 2008). The 3D structure and topography of the electrospun polymeric fiber mats resemble those of the collagen bundles in the natural ECM (Teo *et al.*, 2006). In addition, fibrous scaffolds with different topographical feature can be readily obtained by adjusting fiber diameter, alignment and surface chemistry (He *et al.*, 2010). Many researchers have shown that fiber direction and surface topography may be influence the cell orientation and promoted the cell differentiation during *in vitro* culturing (Wang *et al.*, 2011; Lee *et al.*, 2005; Zong *et al.*, 2005; Schnell *et al.*, 2007).

Over the past decade, development of scaffolds for cell/tissue culture based on biodegradable and biocompatible synthetic or natural polymers has been investigated (Chen *et al.*, 2002; Coombes *et al.*, 2002; Masuko *et al.*, 2005; Boccafoschi *et al.*, 2005; Neamnark *et al.*, 2007). Synthetic polymers provide many advantages over natural polymers because they can be tailored to give a wider range

of properties with predictable lot-to-lot uniformity and reliable source of raw materials. However, naturally occurring polymers normally exhibit better biocompatibility and low immunogenicity. A wide variety of biocompatible and biodegradable synthetic polymers have been studied for their potential use in tissue engineering application, because of their suitable mechanical strength, processability and their controllable degradation rates in biological environment (Supaphol *et al.*, 2012). Despite its inherent biocompatibility and biodegradability, actual utilization of synthetic polymers as artificial scaffolding material is limited by theirs hydrophobicity which diminishes the initial response of cells to materials. A variety of surface modification techniques have been used for improving cell affinity of scaffolding materials. Most of those methods need to combine the immobilization of some bioactive molecules to achieve cell affinity on polymer surface for enhancing the discrete biological information which is transmitted to the cell through cell surface receptors (Mattanavee *et al.*, 2009; Koh *et al.*, 2008; Zhu *et al.*, 2004; Ho *et al.*, 2005; Bhang *et al.*, 2009).

It is well known that, the initial response of cells to the biomaterial mostly depends on surface properties (Lim *et al.*, 2009). Despite the numerous reports on the *in vitro* responses of various cell lineages on the various types of substrates, a similar report that examined the influence of surface topography is still lacking. In the present contribution, we report the *in vitro* responses and cellular behavior on the various types of electrospun fibrous substrates in comparison with the corresponding solvent-cast films and divide the studies into 4 parts.

Part I: *In vitro* biocompatibility of electrospun and solvent-cast chitosan substrata towards Schwann, Osteoblast, Keratinocyte and Fibroblast cells.

Part II: Effect of surface topography and chemistry of poly(3-hydroxybutyrate) substrates on the cellular behavior towards Murine Neuroblastoma Neuro 2a cell lineage.

Part III: Enhancement of biocompatibility on aligned electrospun poly(3-hydroxybutyrate) scaffolds immobilized with laminin towards Murine Neuroblastoma Neuro 2a cell lineage and rat brain-derived neural stem cells.

Part IV: Poly(3-hydroxybutyrate)/magnetite composite nanofibers via combining electrospinning technique with the ammonia gas-enhancing *in situ* co-precipitation.