INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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Thesis Title:
BIOMIMETIC SILK-BIOCERAMIC BASED COMPOSITES FOR BONE TISSUE ENGINEERING APPLICATIONS

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Bone, a structurally and functionally important organ is hierarchically built through bottom-up approach using organic - collagen biopolymer and inorganic - apatite bioceramic. Composited into a biomineralized tissue, bone is considered to be nature's most robust, nano-assembled biological structures contributing to its strength and fracture toughness. Though the bone possesses innate healing abilities, clinical interventions are necessitated for bone defect repair during pathological or degenerative conditions. In this thesis, few of the major long bone defects which arise due to degeneration, infection or trauma were identified. Biomaterials-based regenerative strategies were explored in addressing these issues through five objectives which are progressively presented in this thesis. Inspired by bone's nano-architecture, different fabrication strategies were investigated towards recreating biomimetic, cell instructive composites using resorbable and bioactive biomaterials. Silk fibroin was chosen as the bioactive biopolymer, sourced from mulberry (*Bombyx mori*) or non-mulberry (*Antheraea assama*) silk types, for development of composites along with sol-gel derived bioactive glass or wet chemical synthesized apatites (as the ceramic constituents).

In the first objective, electrospun silk-bioactive glass mats were investigated as prospective bilayered grafts for osteochondral lesion management. The hierarchically structured composite electrospun mats helped in preserving the chondrogenic and osteogenic phenotype of seeded chondrocytes and osteoblasts preferentially due to the innate physicochemical cues presented by the biomimetic mats. In the second objective, functionalised silk microfiber-reinforced freeze-dried composite silk sponges were investigated as resorbable bone grafts for volumetric bone defect management. The copper doped bioactive glass used for functionalising the microfibers, helped attribute proangiogenic traits to the scaffold, which aided in restoration of volumetric defects in rabbit femur with total resorption of implants noticed after 3 months. In the third objective, advanced additive manufacturing technique was investigated to develop 3D bioprinted cellularized osteochondral grafts, thereby circumventing drawbacks associated with conventional acellular grafts. Similarly, in the fourth objective, diaphyseal cross-sectional unit was biofabricated with an outer mechanically robust bioprinted cortical bone shell, encompassing an engineered bone marrow towards serving as orthobiologic substitute for atrophic non-union repairs. In the fifth objective, to improve implant patency of metal implants used as fixtures or prosthesis in orthopaedic reconstruction, silk-bioactive glass nanocomposites were used to create multifunctional interface on these metal surfaces. Conformal coatings of these mesoporous nanocomposites enabled in releasing antibiotics or glucocorticoids towards preventing implant associated infection and improving osseointegration of these metal implants.

Thus, the conventional and additive manufacturing strategies demonstrated in this thesis helped develop pro-regenerative, cell instructive matrices in different length scales, to suit the clinical need of the investigated bone pathology. These matrices were functionally validated under both *in vitro* and preclinical *in vivo* conditions. Thus, the positive findings from this work hold promise for the viable clinical translation of these interventions for bone tissue engineering applications.