Journey so far

School of International Biodesign

- 11 batches trained at Stanford University in biodesign program from 2008 onwards;
- More than 100 Medical Technology innovators (Doctors, engineers, Designers, entrepreneurs) have been trained so far in biodesign program;
- More than 50 prototype have been developed so far which have been further refined validated internationally and tested (both preclinical and clinical trials).
- This has led to the development of over 30 medical devices which has been possible by the innovators i.e.33 Fellow and over 70 Interns who have been meticulously trained in the efforts of young Biodesign innovation process by the faculty of AIIMS and IITD with international partners.
- 21 technologies have been transferred and twelve start-ups companies i.e. “Consure Medical Pvt. Ltd”, Wind Mill Pvt. Ltd, Sohum Innovation Labs Pvt. Ltd , Indo Labs Pvt. Ltd , Observe Design Pvt. Ltd., New Delhi, Brun Health Pvt. Ltd., Telangana, JC Orthoheal Pvt. Ltd., Gujarat, M/s Crimson Health, Inochicare Pvt Ltd., Unino Healthcare Pvt. Ltd, Mumbai , Silicic Innova Technologies Pvt. Ltd and RCupe Lifesciences Pvt. Ltd, Bangalore have been established by the fellows of this programme.
- Twelve Annual Med-Tech Summits organised with national and international experts to provide platform for close interaction among industry and innovators.
- In 2014, the scope was expanded and more international (university) partners in addition to USA and Singapore were added (Australia and Japan). The Programme has been renamed as School of International Biodesign.
- As an outcome, iFellowship (Indigenous Innovation Fellowship) has been successfully launched in 2014 for end to end process i.e. from ideation to commercialization. This fellowship includes several teams and each team has 3 Indian Fellows and one International Fellow.
- This school of International Biodesign (SIB) in collaboration with The British Medical Journal (BMJ) has launched the first international journal on Medtech innovations (BMJ innovations: BMJi) to serve as a platform for publishing novel innovations in medical devices, diagnostics, assistive devices and system and processes innovation. This has led to further growth of the medtech ecosystem nationally as well as internationally
- SIB has been successful in enriching and creating an ecosystem of innovators from academia, Industry and start-ups to overcome clinical challenges by

devising low cost, yet high quality medical devices and technologies over the last nine years.

During Financial year 2018-19 two technologies under SIB programme have been licensed to Start-up companies. Technology for “Intraosseous Device” was transferred to M/s. RCupe Lifesciences Pvt. Ltd., Bangalore and “pleuraGoh-“ technology to M/s UNINO Healthcare Pvt. Ltd, Mumbai on June 4th, 2018.

<table>
<tr><td>  </td><td>  </td></tr>
<tr><td>Licensing of technology for “Intraosseous Device” to M/s. RCupe Lifesciences Pvt. Ltd., Bangalore</td><td>Licensing of technology for “pleuraGoh- A Chest Tube Fixator and Sealing Device” to M/s UNINO Healthcare Pvt. Ltd, Mumbai</td></tr>
<tr><td colspan="2">About the technology</td></tr>
<tr><td>Intraosseous Device: The innovative, Intraosseous Device has been designed to assist healthcare professionals to address the need of intravascular access in resource constrained environment. IO Device is a manually-operated, fully disposable, ready-to-insert sterile to provide emergency vascular access. This device is expected to benefit about 365 million patients globally.</td><td>pleuraGoh: pleuraGoh is an elegant non-messy solution that addresses all major issues pertaining to chest-tube fixation and sealing. pleuraGoh has been designed to improve outcome from effective chest tube fixation and sealing. This device is expected to benefit an estimated 20 billion chest tube market globally.</td></tr>
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Healthcare Technology Innovation Centre, HTIC

- Healthcare Technology Innovation Centre (HTIC), a multi-disciplinary R&D centre, is a joint initiative of Department of Biotechnology (DBT), Government of India and Indian Institute of Technology Madras (IITM) with the vision to develop technologies that create impact and drive innovation for healthcare area. The HTIC aims to bring together technologists, engineers, doctors and healthcare professionals, industry and government to develop healthcare technologies for the country. The Centre is located in IITM Research Park which

has a vibrant technology ecosystem.

HTIC collaborates with leading medical institutions and wide range of industry players in various areas such as ophthalmology, ultrasonography, orthopaedics, neonatal care and patient monitoring, to develop and deploy healthcare technologies.

In addition to technology research and development, HTIC works closely with industry in developing R&D solutions, joint development of technology products, technology assessment and evaluation.

- HTIC also works to develop human resources in healthcare technology in the country through various channels including Innovation fellowships, IITM students and interns.
- Currently, about 30 medical institutions and industry are collaborating to develop technologies and about Six technologies translated to field and/Industry such as Mobile Eye Surgical Unit (MESU),Eye-PAC®: Comprehensive eye image processing, computing and analysis platform, ARTSENS®: Image free ultrasound for vascular stiffness evaluation, Wearable health monitor for COPD, Neonatal Ambulance, iQuant™ Analyser
- Several technologies in areas of ophthalmology, cardiovascular, ultrasound, neonatal, oncology, intensive care, are under development in collaboration with leading organisations. HTIC has successfully developed seven technologies in collaboration with industries and clinical collaborators such as Design innovations on transport incubator, Alternate blood collection systems, Smart phone based pulse oximeter, Pre-operative plate contouring technology, Cervical cancer screening in India using liquid based cytology, Remote Intensive care units and Practical feasible thermal care system
- The research output of R&D work is published in reputed journals. It is the one of the most prominent Indian groups in leading biomedical engineering conferences worldwide having about more than 140 publications till date
- Attracted 24 Industry Projects worth Rs. 12.62 Crore and 4 Extramural Projects (DBT/DST) worth Rs. 6.24 Crore
- Collaboration with BIRAC for setting up med-tech incubator and core facility at HTIC.
- Within a short period of operationalizing the med-tech incubator, about 14 companies have been incubated by leading doctors, experienced entrepreneurs, faculty and students.

During the FY 2018-19, phase II of the program has been sanctioned. Following achievements have been made during the year:

1. Development of advanced medical technologies on:
    - Cuffless blood pressure measurement
    - Non-contact neonatal vitals monitoring

- Automated immunodiagnostics
- Minimally invasive image guided surgery
- Deep learning and AI based medical image computing

2. Commercialization of technologies into products through industry partnerships and startups
   - Immunodiagnostic analysers with minimal sample preparation (ongoing product development in partnership with J Mitra)
   - Image guided minimally invasive spine surgery system (ongoing product development in partnership with Perfint)
   - Fever monitor (ongoing product development in partnership with Helyxon)
   - Endoscopy video processor (ongoing product development in partnership with Mitra Medical)

iQuant Analyser : HTIC, in partnership with J Mitra has developed the iQuant Analyser - the country's first indigenous immunoanalyser instrument that can be used for rapid testing of multiple key blood markers for diabetes (HbA1C), vitamin deficiencies (Vitamin D), hormones (TSH, T3,T4, TSH), inflammations (cRP) , infectious diseases (Dengue , Influneza) etc., at an affordable cost. The instrument is meant for tier-II and tier-III labs in rural and semi-urban areas and has been successfully commercialized with more than 400 installations at laboratories across the country till date.

Bioengineering and Biodesign Initiative at IISc, Bangalore

- The Biodesign-Bioengineering programme at IISc Bangalore was implemented in collaboration with St. John’s Medical College and Majumdarshaw centre for translational research, Bangalore. The focus of the programme is to established strong linkages between biologists, engineers, clinicians for translational clinically oriented research focusing areas of Biomaterials, biomechanics, computational bioengineering & neural engineering.
- Currently, more than 40 faculty members from about 20 science and engineering departments in IISc are collaborating on bioengineering projects. Hospitals like St. John’s Research Foundation and Hospital, Fortis Hospital, and Narayana

Hridayala and Mazumdar Shaw Centre for Translational Research have worked with IISc faculty members.

- Developed five biomedical assistive devices under this project (Patient transfer device; Cerebral palsy exercise gaming chair; ICU simulator; a modest, fast and sensitive device for detection and quantification of viral nucleic acids and the EndoMimyk, an endoscopy simulator).
- A formal entity with a rising PhD programme in bioengineering with the name BioSystems Science and Engineering (BSSE) has been established at IISc which has taken the initiative to conduct annual BioEngineering summer training programme (BEST) for engineering and MBBS undergraduates in BSSE.
- BSSE currently has 26 PhD students, two primary faculty, 14 associate faculty, more than 30 academic programme faculty, and eight technical staff
- A MoUs is signed with CMC jointly-supervised MD-PhD programme with the arrangement that CMC gives the MD degree and IISc the PhD degree.

During FY 2018-19, phase II of the project has been sanctioned and an MoUs was signed with CMC jointly-supervised MD-PhD programme with the arrangement that CMC gives the MD degree and IISc the PhD degree. Further, two product technologies viz. a modest, fast and sensitive device for detection and quantification of viral nucleic acid and EndoMimyk, an endoscopy simulator has been developed in IISc and the system is under commercialization by Mimyk Pvt. Ltd.

Centre for Biodesign and In-vitro Diagnostics, THSTI

- The Center for Biodesign and in-vitro Diagnostics (CBD) has been established as one of the Centers of THSTI with the mission to undertake innovation in medical technologies for affordable health care in India.
- This center has been successful in establishing a foundation for multi-disciplinary translational science and technology, tightly integrating biotechnology with engineering and clinical medicine.
- The program broadly employs biodesign process with emphasis on clinical-needs driven innovation. Center has evolved around 4 strategic translational foci i.e., 1) Diagnostics Products 2) Platform Technologies 3) Drug Delivery Systems and 4) Medical Devices & Implants.
- The Centre has developed several product leads. Center has earned notable success in developing numerous international and national collaborations, securing extramural funding, developing translational support infrastructure and significantly expanding capacity building for healthcare innovation in India.
- The technology developed on clone of recombinant human tissue transglutaminase has been successfully transferred to J. Mitra Pvt. Ltd. this year for development of tests for celiac disease.
- An MoU was signed between THSTI and University of Turku for creation of an Indo Finnish Diagnostic Research Center.

- CBD has created a broad platform to facilitate clinical needs-inspired biomedical innovation to lead THSTI's efforts in translational research.

Biomedical Engineering- Journey so far (may be provided in Link)

The Department has supported several projects during last 10 years in key areas of bioengineering. Some of the significant achievements are as follows:

Devices and Implants

Implantable device for multifunction prosthesis hand control has been fabricated successfully. The implantable device pickup and transmit electromyographic signals transcutaneously. An auxiliary device placed over the skin receives the transmitted signal and also supply electrical power by electromagnetic induction. The signal transmission uses a digital packet radio network to provide high reliability of the EMG signal. The final design and fabrication of the circuits for implantation completed and miniature electronics with power and data transmitter accomplished. The prototype testing in animal models are under process.

Mannequin-based training simulator specifically for detection of different types of heart attacks or AMI (Acute Myocardial Infarction) has been developed to train the cardiologists (trainer). The researchers have developed an interactable (hardware) mannequin, with software simulated Cardiovascular System incorporating parameters like radial artery pulse measurement, ECG determination, BP measurement, heart sound, injection of life-saving drugs etc that can be programmed by the trainer.

Bio-artificial liver– Designing and optimization of a support for the temporary treatment of patients with acute and acute on chronic liver failure is being developed under this project. The idea behind is to help in bridging the gap for patients awaiting for an appropriate liver donor, as well as aid in spontaneous native hepatic regeneration.

Fiberoptic Laser Raman spectrometer has been standardized to develop and evaluate fiberoptic probes designs for the diagnosis of oral precancers (erythtoplakia, leukoplakia and OSMF) and cancers in the clinical setting.

Non-invasive, hand-held, compact and wireless technology based **easy-to-use device for display of ECG signals** for monitoring chest pains devised successfully. The technology has been combined with mobile phone technology using GPRS.

Nanosurface Engineering of Bare Metallic Coronary Stents for Combating In-stent Restenosis: By adopting a nanotexturing approach, investigators have been able to demonstrate that bare metal stents which are polymer-free and drug-free, but with a uniform surface nanotopography, possesses excellent mechanical stability and offers good corrosion resistance. A biocompatible, anti-thrombogenic metallic stent surface that promotes rapid endothelialization *in vitro* was developed which concurrently inhibits smooth muscle cell proliferation. The nanotextured surface thereby addresses the problem of in-stent restenosis and thereby presents a superior treatment modality without the use of costly drug eluting stents that demand continual use of anti-platelet therapy for prolonged durations and have long term toxicity effects.

Biosensors and Bio-instruments

A **low cost biosensor** for rapid detection of Salmonella typhi has been developed by surface modification of nylon membrane & polyacrylonitrile fibre (PAN) with an aim to use them as solid matrices for ELISA/FIA.

Calibration-free pulse oximeter has been successfully developed for non-invasive measurement of oxygen saturation in arterial blood. A couple of novel algorithms has been designed for computation of oxygen saturation and method is independent of source intensity, detector sensitivity, coloration of skin of patient or volume of intervening tissue. Three prototypes have been developed and field testing is underway.

Development of novel peptide imaging biomarker/s for early detection of cisplatin-resistant ovarian cancer: Several phage clones were tested and a novel WIGTFQH peptide was identified that can bind to early resistant cells with higher specificity as proven by fluorescence microscopy and FACS. Following that, the peptide with DyLight800 dye was labelled and tumor homing was monitored using Non-invasive Fluorescent Imaging in nude mice. A 100 fold higher uptake of the peptide in tumors developed from early resistant (9th Cis) cells compared to tumors of sensitive cells indicated the specificity of the novel peptide. The peptide could be used as a diagnostic marker of cancer cells developing resistance towards cisplatin. This peptide could also be used for delivering drugs using targeted nanoparticles.

A duplex PCR targeting the *opa* and *porA* pseudogene for detection of *Neisseria gonorrhoeae* has been standardized and Initial prototype for biosensor against *opa* gene has been developed. A multiplexed DNA biosensor for *N. gonorrhoeae* is currently under fabrication.

A lab-on-a-chip device for the detection of cholesterol, creatinine and glucose was fabricated and tested with the meter.

Several cell based assays for screening cancer drugs inducing caspase mediated apoptotic cell death employing FRET based genetically encoded probes were developed. New cell based assay employing Ametrine DEVD Td tomato and Td Tomato DEVD m plum with excellent performance for in vitro screening and in Vivo imaging. A robust live cell method to discriminate apoptosis from necrosis using FRET based probes that is easy to utilize for high throughput screening is also developed.

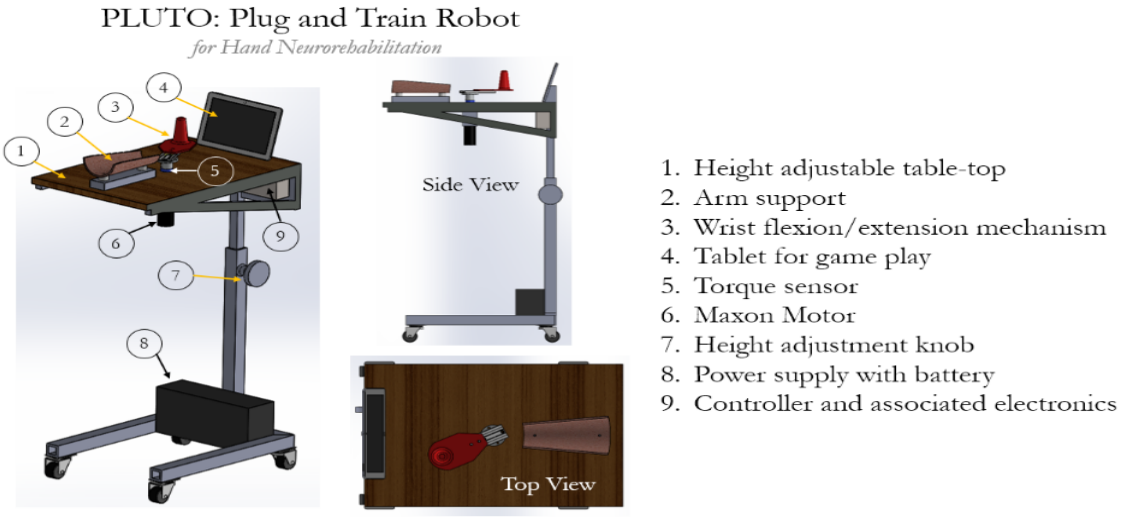
A system as a point-of-care sensor is developed which can be used to rapidly detect cell proliferation for applications such as sensing food or water contamination much faster than conventional cell culture based methods.

A dual mode paper analytical device (PAD) is developed through simple photolithography with an easy way to incorporate the three electrode system without employing sophisticated screen-printing machine. The fabricated dual PAD could be used to develop a point-of-care testing platform coupled with a palm device for community based screening and diagnosis.

Photoacoustic Imaging Technique (PAT) for Non-Invasive Imaging is developed which is capable of imaging tissue mimicking phantoms with desired resolution.

Robotic wheelchair to provide comfort or to give independence of mobility to physically challenged persons has been designed successfully. Prototypes of two models have been developed: a low cost one and an advanced one. The most important feature of the advanced version is its autonomous navigational capability in user's residence and office.

A plug-and-train robotic kit for hand neurorehabilitation- The scientists at CMC vellore and IIT Madras completed the design and fabrication of basic structure of the system including the robot actuator and the WFE, WURD, and FPS mechanisms under a DBT supported project. A preliminary implementation of three types of robot controllers, along with two computer games to train wrist flexion/extension movements has also been completed. The project is still in its developmental phase, and several technical issues needs to be addressed before the robot can be evaluated in the patient population. However, we strongly believe that a simply and versatile system proposed in this project will have strong potential for commercialization and result in a more economical system for hand neurorehabilitation. This can potentially result in better infiltration of this technology into the market



Robot Design for 3D Bio Printing of Tissue Embedded Cellular Vascular Constructs-

A 3D bioprinter with movement in 4-axes such as x,y,z and a-axis (rotary) was custom built and validated for bioprinting application. Photo- and ionic cross-linked bioink κ-Carrageenan /Gelatin Methacrylate (κ-CRG/GelMA) was developed which demonstrated biocompatibility with multiple cell types such as fibroblasts, smooth muscle cells and endothelial cells and could be bioprinted as vascular construct with multiple layers.

Researchers established Breast tumor growth in Athymic nude mice using MCF-7 cells and tumor progression was evaluated on different time points post MCF-7 cells inoculation by photoacoustic spectroscopy. A particular frequency at 93.6 KHz is found to be increased with the progression of tumor growth, may be considered as marker frequency of tumor progression. Further, discrimination analysis of malignant clinical breast samples from controls using supervised logical regression analysis demonstrated classification sensitivity, specificity and accuracy of 100%, 93.75% and 96.2% respectively. This technology has the capability to capture molecular alterations before the advancement of the disease adding to its prognostic potential. Hence, early breast cancer detection can be possible with this technique and accordingly treatment modalities can be planned to reduce the sufferings associated with the currently followed treatment of chemo and radiation therapy and thus life expectancy can be improved.

Breast tumor growth/development post-*MCF-7* cells injection

Biomaterial for biomedical applications

Microparticle-based dual drug delivery system for the treatment of lung cancer has been extrapolated as a therapeutic option for solid tumors. A model drug, ampicillin along with an anti-cancer drug has been incorporated within the delivery vehicle for the study of release kinetics and bioactivity on various lung cancer cell lines.

Nanostructured Surface/Tip enhanced Raman Substrates (TERS) have been developed for recording unique Raman signatures of normal and malignant oral cancer tissues. TERS substrates were used for tissue imaging from ~ 20 cancer

patients. Unique differential signature pattern were identified for normal and cancer tissue sections.

Process optimized for developing **suitable machinable green ceramics and dental crown** of custom specific products fabricated through direct machining of green ceramic compacts using computer numerical control (CNC) machine.

Novel intelligent peptides for targeting PNA (Peptide-nucleic acids) into cells are synthesized for its use as antiviral therapeutics.

Flexible and microporous biopolymeric hyrdrogel bandages based on alginate, chitin and chitosan with non-toxic ZnO/Herb *Hemigraphis ulternata* nanoformulations developed for wound dressing applications.

Tissue Engineering

An animal model of **physical injuries** in the goat successfully demonstrated utilizing the autologous chondrocyte culture.

Tissue engineered osteochondral grafts developed and tested successfully *in vitro* in terms of gene expression, biochemistry and biomechanics. Significant efforts also undertaken modifying tissue engineered cartilage system to develop *in vitro* disease models of Osteoarthritis.

Silk protein scaffold for tissue engineering/biotechnological applications: The silk fibroin proteins isolated from domesticated mulberry, *Bombyx mori* and wild *non-mulberry*; Antheraea mylitta silkworms have been exploited to develop multilayer 2D films for controlled drug release. The study envisages the versatile and tunable properties of silk making them exciting candidates for the tissue engineering and biotechnological applications.

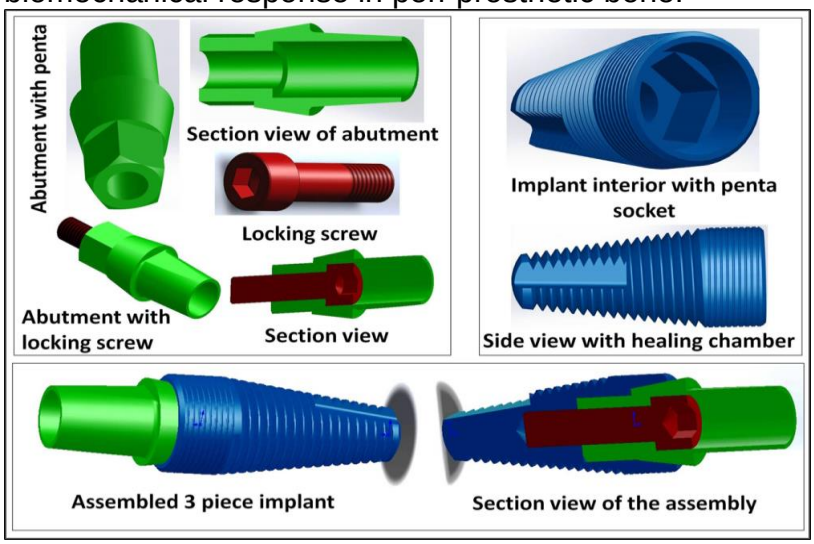
Silk-based Direct-write scaffolds to create osteogenic microenvironment: Culture conditions of the silk-gelatin-hydroxyapatite 3D printed construct were successfully optimized. The study provides an experimental insight towards the establishment of a 3D printed *in vitro* model system for studying osteoblast to osteocytic differentiation with respect to varied geometry and matrix mechanics. An interesting observation was the increase in stiffness of the scaffolds (from SF-G to HAP) directed the differentiation of cultured osteoblasts and mesenchymal progenitors towards osteocytic phenotype; which is the ultimate target of any tissue engineering bone model.

Translational Centre of Excellence on Biomaterials:

A Translational Centre of Excellence on Biomaterials for Orthopedic and Dental Applications at Indian Institute of Science was supported at IISc., Bangalore. During FY 2018-19, a new generation of polymer-ceramic hybrid acetabular socket of different sizes (40,44,46 mm) is fabricated using compression molding approach
The scientists developed a unique manufacturing technology to develop ceramic femoral heads for total hip joint replacement surgery and patented. Optimization of the process conditions and material parameters to obtain an excellent combination of

strength, toughness and wear resistance of the zirconia-toughened alumina-based femoral head is accomplished.

CAD based 3D models of a complete 3 piece-dental implant system comprising of implant screw, straight and angulated abutments, locking screw, healing abutment and cover screw are designed. This implant system is designed with pentagonal anti-rotation feature and single healing chamber. Also, a novel acrylic ink was formulated for 3D inkjet printing of Titanium and ceramics. The surface topographical features of the implant have been benchmarked against that of the Straumann implant by conventional machining, followed by sand blasting and acid etching. Using ANSYS-based finite element analysis, the implant design was optimized for clinically desired biomechanical response in peri-prosthetic bone.



3D models of a complete 3 piece-dental implant system