Indian Institute of Technology Delhi

Department of Biochemical Engineering and Biotechnology

PhD projects offered in Sem I, 2021-2022

(Updated on 22nd May 2021)

Faculty	No. of open slots	Project number and Title
A. Narang	2	Project no. 1. Development of systematic methods for overcoming catabolite repression in *Escherichia coli.*
		Project no. 2. Enhancing the ethanol productivity of glucose-limited cultures of *Scheffersomyces (Pichia) stipitis*.
P. Mishra	2	Project no. 3. Fabrication of bioactive peptide loaded multifunctional mesoporous silica nanoparticles for cancer treatment
		Project no. 4. Biomarker based noninvasive method for detection of oral cancer using nanosensor.
		Project no. 5. Nanostructured stimuli-responsive molecularly imprinted polymers for the targeted delivery of produg and detection of breast cancer.
R. Kulshreshtha	1	Project no. 6. Investigating the role of long non-coding RNAs in meningioma pathogenesis
R. Elangovan	2	Project no. 7. Molecular source tracking of AMR pathogens based on Whole Genome Sequencing
		Project no. 8. Optimization of light sheet microscopy for large clinical specimen analysis
R. Jain	1	Project no. 9. Recovery of furfural, acetic acid and 5 HMF from torrefaction condensate using solvent extraction, adsorption, distillation and other technologies
M. Sumit	1	Project no. 10. Novel supplementation strategies in mammalian fedbatch processes using mathematical modeling and at line metabolite monitoring
K.J. Mukherjee	1	Project no. 11. Modulating the stress response in Escherichia coli as a strategy for design of improved host cell platforms

Indian Institute of Technology Delhi

Project no. 1

Department of Biochemical Engineering and Biotechnology

PhD project

Project details	
Project title	Development of systematic methods for overcoming catabolite repression in *Escherichia coli.*
Project description	**Background:** In the presence of "good" carbon sources such as glucose, "poor" carbon sources, such as lactose or galactose, are not consumed because synthesis of the enzymes required for metabolizing the "poor" carbon sources is abolished. This phenomenon, referred to as catabolite repression, is a major limitation in many biotechnological processes. It is of considerable interest to find ways of overcoming catabolite repression, but there are currently no systematic methods for achieving this goal. **Objectives and Methodology:** Our preliminary work suggests that catabolite repression of the *lac* and *mel* operons of *E. coli* can be overcome by small changes in the expression of the structural genes. The goal of this work is to construct a comprehensive genotype-to-phenotype map that specifies which mutations lead to substantial decrease of catabolite repression.

PhD supervisors			
Role	**Faculty**	**Academic unit at IITD**	**E-mail**
Supervisor	Prof. Atul Narang	DBEB	anarang@dbeb.iitd.ac.in

Skills required	
Qualification	B. Tech. or M. Tech. (Life Sciences or Biotechnology)
Skills	Interest in basic scientific questions. Hands-on experience with cloning and strain construction techniques of molecular biology.

References

1. Aggarwal RK, Narang A. Deconstructing glucose-mediated catabolite repression of the *lac* operon of *Escherichia coli*: II. Positive feedback exists and drives the repression. bioRxiv. 2020 Jan 1: 99348. Under review in Biophysical Journal. https://doi.org/10.1101/2020.06.23.166959
2. Aggarwal R, Narang A. Deconstructing glucose-mediated catabolite repression of the *lac* operon of *Escherichia coli*: I. Inducer exclusion, by itself, cannot account for the repression. bioRxiv. 2020 June:739458. Under review in Biophysical Journal. https://doi.org/10.1101/739458

Project no. 2

Indian Institute of Technology Delhi

Department of Biochemical Engineering and Biotechnology

PhD project

Project details	
Project title	Enhancing the ethanol productivity of glucose-limited cultures of *Scheffersomyces (Pichia) stipitis*.
Project description	**Background:** The yeast *S. cerevisiae*, which is typically used for ethanol production, ferments (ie., produces ethanol) only in the presence of a few sugars such as glucose. In contrast, the yeast *S. stipitis* ferments almost all sugars — a considerable advantage for fermentation of the sugar mixtures that occur in lignocellulosic hydrolysates. However, *S. stipitis* is completely outperformed by *S. cerevisiae* in the presence of glucose, the most common sugar in lignocellulosic hydrolysates. Specifically, *S. cerevisiae* ferments glucose 3 times faster than *S. stipitis*. Moreover, *S. cerevisiae* ferments glucose under oxygen-excess, oxygen-limited, and oxygen-free conditions, whereas *S. stipitis* does so only under oxgyen-limited conditions. If these two limitations of *S. stipitis* could be overcome, it would be superior to *S. cerevisiae* in every way. **Objectives and Methodology:** The literature suggests that the abovementioned deficiencies of *S. stipitis* in the presence of glucose are due to a limitation at the level of transport. The goal of this work is test this hypothesis by studying ethanol production in cells over-expressing the glucose transporter(s). To this end, we have constructed a plasmid specifically for engineering *S. stipitis*, and identified potential glucose transporters for overexpression. The efficacy of strains overexpressing glucose transporter(s) will be tested in shake flasks, and their genetic stability will be determined in bioreactors.

PhD supervisors			
Role	**Faculty**	**Academic unit at IITD**	**E-mail**
Supervisor	Prof. Atul Narang	DBEB	anarang@dbeb.iitd.ac.in

Skills required	
Qualification	B. Tech. or M. Tech. (Biotechnology or Biochemical Engineering)
Skills	The project involves cloning and strain construction techniques of molecular biology as well as operation of bioreactors.

References
1. Maitra, Shraddha, and Atul Narang. "Quantifying the parametric sensitivity of ethanol production by *Scheffersomyces (Pichia) stipitis*: development and verification of a method based on the principles of growth on mixtures of complementary substrates." *Microbiology (Reading, England)* 164, no. 11 (2018): 1348-1360. Available at https://doi.org/10.1099/mic.0.000719 2. Maitra, Shraddha, and Atul Narang. "Existence of a scaling relation in continuous cultures of Scheffersomyces stipitis: the steady states are completely determined by the ratio of carbon and oxygen uptake rates." *Biotechnology for biofuels* 12, no. 1 (2019): 19. Available at https://link.springer.com/article/10.1186/s13068-019-1357-3

Project no. 3

Indian Institute of Technology Delhi

Department of Biochemical Engineering and Biotechnology

PhD project

Project details	
Project title	**Fabrication of bioactive peptide loaded multifunctional mesoporous silica nanoparticles for cancer treatment**
Project description	**Objectives:** 1. To synthesis mesoporous silica nanoparticles (MSNs) 2. To fabricate gate/ homing for silica nanoparticles for delivery peptide drugs 3. Testing these nanoparticles for their in vitro efficacy 4. To have dual drug loading and delivery strategies for MSNs **Background:** The current global crisis of people suffering from cancer and long term treatment burden is rising and hence sustainable nanoparticle based drug delivery systems are being developed. In this proposal, a novel strategy to design a mesoporous silica nanoparticle (MSNs) based nano-carrier (NC) system with iron as the core is planned. The MS have well-ordered internal mesopores, larger pore volume and surface area, tunable size and shape, robustness make them an ideal platform to design multifunctional nanosystems. Their high drug loading capacity can deliver the effective concentration of drug to the target cell and released smartly via external stimuli such as change in pH, wherein tumors (pH~6.5) and endosomes and lysosomes (pH~5–6). It is anticipated that precisely engineered nanoparticles will emerge as the next-generation platform for cancer therapy. The gated NPs will provide additional tool for sustainable delivery. **Methodology** Well established protocols developed in lab will be used
Instruments required	All equipment required are available with me at Nano Research Facility as Principal Investigator.
Any other comments	**For detailed publication see:** http://scholar.google.co.in/citations?user=pCOEvOIAAAAJ http://web.iitd.ac.in/~pmishra/

PhD supervisors			
Role	**Faculty**	**Academic unit at IITD**	**E-mail**
Supervisor	Prashant Mishra	DBEB	pmishra@dbeb.iitd.ac.in

Skills required	
Qualification	B.Tech /MSc/M.Tech Biotechnology/Biochemistry/Microbiology/Life sciences
Skills	Background in Life Sciences/Biotechnology

References

Thymoquinone loaded mesoporous silica nanoparticles retard cell invasion and enhance in vitro cytotoxicity due to ROS mediated apoptosis in HeLa and MCF-7 cell lines
Goel S, **Mishra P**
Materials Science & Engineering C (2019) 109881 **IF 4.959**

Surface Molecularly-Imprinted Biomimetic Magnetic Nanoparticles for Enantioseparation
Goyal G, Bhakta S, **Mishra P**
ACS Applied Nano Materials 2 (2019) 6747-6756.

Asparaginase conjugated magnetic nanoparticles used for reducing acrylamide formation in food model system
Alam S, Ahmad R, Kumar P, **Mishra P** and Khare SK
Bioresource Technology 269, 121-126 (2018) **IF 6.669**

Co-delivery of curcumin and serratiopeptidase in HeLa and MCF cells through nanoparticles show improved cancer activity
Jaiswal S and **Mishra P**
Material Science and Engineering C 92, 673-684 (2018) **IF 4.959**

Thymoquinone inhibits biofilm formation and has selective antibacterial activity due to ROS generation
Goel S and **Mishra P**
Applied Microbiology and Biotechnology 102, 1955–1967 (2018) **IF 3.67**

Antimicrobial and antibiofilm activity of curcumin-silver nanoparticles with improved stability and selective toxicity to bacteria over mammalian cells
Jaiswal S and **Mishra P**
Med Microbiol Immunol 207, 39-53 (2018) **IF 2.96**

Permeation behavior of lysozyme-loaded poly(lactic-co-glycolic acid) nanoparticle through procine oesophageal mucosa and its microscopic studies.
Shankarayan R and **Mishra P**
J Nanopharmaceutics Drug Delivery 3: 85-96 (2016)

Modulation of toxic assembly of human gelsolin amyloids by emetine and curcumin-conjugated PLGA-nanoparticles.
Srivastava A, Arya P**,** Goel S, Kundu B, **Mishra P** and Ashish FNU
PLoS One 10 (5)e0127011 **(**2015**) IF 2.766**

Differential permeation of piroxicam- loaded PLGA micro/nanoparticles and their in vitro enhancement
Shankarayan R, Kumar S and **Mishra P**
J Nanopart Res 15 1496-1502 (2013) **IF 2.009**

Indian Institute of Technology Delhi

Department of Biochemical Engineering and Biotechnology

PhD project

Project no. 4

Project details	
Project title	**Biomarker based noninvasive method for detection of oral cancer using nanosensor.**
Project description	Oral cancers are part of a group of cancers commonly referred to as head and neck cancers. One of the most common oral cancer, oral squamous cell carcinoma (OSCC) is a threat to the public health across the globe due to increasing rate of mortality. Recently, occurrence of oral cancer has also been attributed due to HPV16 in non-tobacco consuming young population. In early stage oral cancer is not noticed by patients, grows without pain and is asymptomatic. Hence, often, it is discovered when cancer is at a late stage of metastasis to another location such as lymph node of the neck. Thus early diagnosis is key to reduce the rate of mortality. Diagnosis of oral squamous cell carcinoma (OSCC) is mainly based on clinical examination, histopathology of biopsy and various microscopic methods. Since these methods are invasive, requires time, labour and expertise, an alternative diagnostic tool is needed. In this regards, biosensors offer a reliable, patient friendly and quick method of diagnosis. A number of biomarkers are known to be elevated in oral cancer in serum, tissue samples and saliva. Due to localization of oral cancer in oral cavity, saliva becomes obvious choice of biological fluid. In addition, collection of saliva is noninvasive, efficient and cost effective. A number of biomarkers are known to be elevated in saliva during oral cancer. Most common biomarkers of oral cancer are specific cytokines such as IL-8, IL-6, tumor necrosis factor (TNF-a), vascular endothelial growth factor (VEGF), epidermal growth factor receptor (EGFR). In addition, CYFRA-21-1 is a water-soluble proteinaceous biomarker representing 40 kDa cytokeratin and found in elevated concentration in saliva in oral cancer patients.In the present proposal, it is planned to design and develop novel biosensing element for detection of biomarkers using either impedance based or FET based point of care nanosensor.
Instruments required	All the facilities are available in my lab.
Any other comments	No comments

PhD supervisors			
Role	**Faculty**	**Academic unit at IITD**	**E-mail**
Supervisor	Prashant Mishra	DBEB	pmishra@dbeb.iitd.ac.in

Skills required	
Qualification	M.Sc. / B.Tech/ M.Tech (other than chemical engineering graduates)
Skills	Biochemistry/Microbiology/Biotechnology/Molecular Biology

References

Gahlaut SK, Savargaonkar D, Sharan C, Yadav S, **Mishra P,** Singh JP. SERS platform for dengue diagnosis from clinical samples employing hand held Raman spectrometer. **Analytical Chemistry 92, 2527-2534** (2020) IF 6.35

Singh S, Moudgil A, Mishra N, Das S, **Mishra P.** Vancomycin functionalized WO3 thin film-based impedance sensor for efficient capture and highly selective detection of Gram-positive bacteria. **Biosensors and Bioelectronics** 136, 23-30 (2019) IF 9.518.

Gahlaut SK, Kalyan N, Sharan C, **Mishra P**, Singh JP. Smartphone based dual mode in situ detection of viability of bacteria using Ag nanorods array. **Biosensors and Bioelectronics** 126, 478-484 (2019) IF 9.518

Moudgil A, Kalyani N, **Mishra P**, Das S. Azurin-TiO 2 hybrid nanostructure field effect transistor for efficient ultraviolet detection. **Nanotechnology** 30 (2019) 495205 IF 3.399

Moudgil A, Singh S, Mishra N, **Mishra P**, Das S. MoS2/TiO2 Hybrid Nanostructure-Based Field- Effect Transistor for Highly Sensitive, Selective, and Rapid Detection of Gram-Positive Bacteria. **Advanced Materials Technologies**(2019) 1900615 IF:5.395

Moudgil A, Kalyani N, Sinsinbar G, Das S and **Mishra P**. S-Layer Protein for Resistive Switching and Flexible Nonvolatile Memory Device. **ACS Applied Materials and Interfaces** 10 (5), 4866– 4873 (2018) IF 8.456

Kalyani N, Moudgil A, Das S and **Mishra P.** Metalloprotein based scalable field effect transistor with enhanced switching behaviour. **Sensors and Actuators B** 246: 363–369 (2017). IF 6.393

Indian Institute of Technology Delhi

Department of Biochemical Engineering and Biotechnology

PhD project

Project no. 5

Project details	
Project title	Nanostructured stimuli-responsive molecularly imprinted polymers for the targeted delivery of produg and detection of breast cancer.
Type of project	PhD project
Project description	Chemotherapy alone or in combination with radiotherapy is well known for the treatment of cancers. However, due to the side effects caused by non-selective nature of drugs it has been challenging to treat cancer effectively without harming normal cells. Strategies employed to tackle this challenge may be addressed by using targeted delivery by attaching a homing moleclule and prodrug based delivery. In this case produg is delivered to targeted tissues and becomes active once delivered in side the cancer cells. Advancement in molecular imprinting technology for synthesizing smart tailor-made binding sites on polymers complementary to template molecule in shape, size and functional groups have allowed them to be used as vehicle for drug delivery. The careful selection of monomers also allows the MIPs to become stimuli responsive and help in release of drugs in reponse to environmental trigger such as pH, temperature or excited light. In this project it is planned to synthesize stimuli-responsive nanoMIPs for delivery of prodrugs like 5-amino-levulinic acid or deoxy 5-fluorocytidine and ligand such as folate for studying their effect on breast cancer cell lines. Microenvironment like pH, temperature and photodynamic trigger based release of drug and their effectiveness will be studied. Incorporation of fluorecent dye or quantam dots will allow simultaneous detection of these cancer cells.
Instruments required	All the facilities are available in the lab

PhD/MSR supervisors			
Role	**Faculty**	**Academic unit at IITD**	**E-mail**
Supervisor	Prashant Mishra	DBEB	pmishra@dbeb.iitd.ac.in

Skills required	
Qualification	B.Tech./M.Tech in Biotechnology/Biochemical Engineering Or M.Sc. in any branch of Life Sciences/Biochemistry/ Chemistry

Skills	Interest in synthesis of MIPs and mammalian cell culture

References

1. Biomarker imprinted magnetic core–shell nanoparticles for rapid, culture free detection of pathogenic bacteria.
S Rajpal, S Bhakta, **P Mishra**
Journal of Material Chemistry B 9, 2436-2446 (2021) **IF: 5.344**

2. Surface Molecularly-Imprinted Biomimetic Magnetic Nanoparticles for Enantioseparation
Goyal G, Bhakta S, **Mishra P**
ACS Applied Nano Materials 2 (2019) 6747-6756.

3. Thymoquinone loaded mesoporous silica nanoparticles retard cell invasion and enhance in vitro cytotoxicity due to ROS mediated apoptosis in HeLa and MCF-7 cell lines
Goel S, **Mishra P**
Materials Science & Engineering C (2019) 109881 **IF 5.88**

4. Co-delivery of curcumin and serratiopeptidase in HeLa and MCF cells through nanoparticles show improved cancer activity
Jaiswal S and **Mishra P**
Material Science and Engineering C 92, 673-684 (2018) **IF 5.88**

Indian Institute of Technology Delhi

Department of Biochemical Engineering and Biotechnology

PhD project

Project no. 6

Project details	
Project title	Investigating the role of non-coding RNAs in meningioma pathogenesis
Type of project	PhD project
Project description	Meningiomas are the most common benign intracranial tumor with ~ 20% of patients showing aggressive phenotype with significant patient morbidity and mortality. However, there are no molecular markers for meningioma grading which currently relies solely on histology. Surgery and radiation are the mainstays of meningioma treatment but are insufficient to control 40%–75% of high-grade tumours. There are no curative therapies or effective molecular treatments for aggressive meningiomas. The recent development in the field of RNA biology shows the importance of Circular RNAs (circRNAs) in carcinogenesis. However, there are no studies on role of circRNA in meningiomas. Therefore, transcriptomic profiling of meningiomas would be an efficient route to improved understanding of meningioma tumorigenesis, and will lead to development of newer prognostic biomarkers and rational therapeutic agents. The proposed study involves 1) miRNA and circRNA expression profiling 2) Analysis of circRNA-miRNA regulatory network and 3) Functional studies to identify the role of top deregulated circRNA in meningioma pathogenesis.
Instruments required	Mammalian Cell Culture Facility (Biosafety Hood, Co2 incubator etc), PCR, Molecular biology related equipments (Gel Running Apparatus, PCR, Real-time PCR etc.)
Any other comments	None

PhD/MSR supervisors			
Role	**Faculty**	**Academic unit at IITD**	**E-mail**
Supervisor	Dr. Ritu Kulshreshtha	DBEB	ritu@dbeb.iitd.ac.in

Skills required	
Qualification	MSc/MTech in any field of Life Science
Skills	Experience in Basic Mammalian Cell Culture and Molecular Biology Experiments

References

1. Suppiah S, Nassiri F, Bi WL, Dunn IF, Hanemann CO, Horbinski CM, Hashizume R, James CD, Mawrin C, Noushmehr H, Perry A, Sahm F, Sloan A, Von Deimling A, Wen PY, Aldape K, Zadeh G; International Consortium on Meningiomas . Molecular and translational advances in meningiomas. Neuro Oncol. 2019 Jan 14;21: i4-i17.

2. Watson MA, Gutmann DH, Peterson K, Chicoine MR, Kleinschmidt-DeMasters BK, Brown HG, Perry A. Molecular characterization of human meningiomas by gene expression profiling using high-density oligonucleotide microarrays. Am J Pathol. 2002 Aug;161(2):665-72.

3. Vo JN, Cieslik M, Zhang Y, Shukla S, Xiao L, Zhang Y, Wu YM, Dhanasekaran SM, Engelke CG, Cao X, Robinson DR, Nesvizhskii AI, Chinnaiyan AM. The Landscape of Circular RNA in Cancer. Cell. 2019 Feb 7, 176(4):869-881.

Project details	
Project title	Molecular source tracking of AMR pathogens based on Whole Genome Sequencing
Type of project	PhD project
Project description	Background: Antibiotic resistance has been reported as one of the greatest threats to global health and food security today by World Health Organization (WHO). It has been indicated that new resistance mechanisms are emerging and spreading globally, threatening the ability to treat common infectious diseases. Use of antibiotics has become a major cause of water pollution in aquaculture as this is changing the structure of the environmental microbiota due to the accumulation of antibiotics in water environments. Project plan: With the rapid development of the global aquaculture industry, the presence of antibiotics and ARGs in aquaculture environment is of increasing concern. Therefore, in recent years, much attention has been paid to ARGs in farming processes, which are regarded as one of the main human activities that contributes to the selection and dissemination of ARGs (Durso LM et al., 2014). To our knowledge, few studies have evaluated the diversity and abundance of ARGs in aquaculture environment. Moreover, the mechanisms by which ARGs are transferred among fish, shrimp guts, the sediment and pond water of their aquatic environment remain unknown. Therefore, understanding the molecular mechanisms of antimicrobial resistance prevalent in aquaculture environment is important to design effective disease treatment strategies, to prioritize the use and registration of antimicrobials for aquaculture use, and to assess and minimize potential risks to public health. Due to the large-scale, high-density use of antibiotics in Indian aquaculture, we deemed it necessary to conduct an extensive investigation of the main aquaculture areas in India in order to understand the levels of antibiotics being used in Indian aquaculture. Objectives: 1) To investigate the comprehensive profiles of ART populations associated with different types of samples acquired from the aquaculture farm 2) Identification of a new resistant variant from domestic aquaculture products. Methodology: DNA extraction and library preparation: Samples will be concentrated by filtering through a 0.22 μm membrane, and then the bacteria will be

	suspended in 10 ml of 0.1% peptone water using a vortex mixer. All samples will be subjected to total DNA extraction (Ref.). Extracted DNA of samples from different sources/ponds will be subjected to NGS assessment. Illumina shotgun DNA library construction will be prepared. High-throughput metagenomic sequencing and data analysis High-throughput sequencing on a Miseq 2000 sequencer (Illumina, San Diego, CA, USA) will be done. The generated quality-filtered reads will be aligned using the basic local alignment search tool (BLASTx) with databases downloaded for ARGs (from the Antibiotic Resistance Genes Database (ARDB), http://ardb.cbcb.umd.edu/index.html), MGEs and integrons (from INTEGRALL, http://integrall.bio.ua.pt/), insertion sequences (ISs) (from IS Finder, https://www-is.biotoul.fr/) and plasmids (from the NCBI RefSeq database; 2408 plasmid genome sequences).
Instruments required	High-throughput sequencing on a Miseq 2000 sequencer (Illumina, San Diego, CA, USA
Any other comments	None

PhD/MSR supervisors			
Role	**Faculty**	**Academic unit at IITD**	**E-mail**
Supervisor	R. Elangovan	DBEB	elangovan@dbeb.iitd.ac.in

Skills required	
Qualification	
Skills	

Project no. 8

Indian Institute of Technology Delhi

Department of Biochemical Engineering and Biotechnology

PhD project

Project details	
Project title	Optimization of light sheet microscopy for large clinical specimen analysis
Type of project	PhD project
Project description	Background: Histopathological examination of tissues remains as current gold standard in Cancer diagnostics. Current histopathological techniques are based on paraffin embedded thinly cut tissues sections for microscopy evaluations. This is due to limitation in the current microscopy methods to visualize thick samples. Current thin section based histopathology has many limitations, i.e., tumor heterogeneity across the volume of tissue sample can not be identified; sample is lost due to thin section processing; with limited volume imaging there is high error rate in the results. Project plan: Light sheet microscopy is recent technique that illuminate samples at an orthogonal angle. Sample is immersed with refractive index matching liquid to clear the sample for deep penetration. In this project, we propose to develop and optimize sample preparation methods for large clinical specimen clearing and imaging with light sheet microscopy. Objectives: 1. Develop tissue clearing protocol for large clinical samples 2. Develop sample labeling protocol for large clinical samples 3. Develop 3D rendering of images of large volume samples Methodology: 1. Development of tissue clearing protocol: Small tissue samples from poultry chicken will be used to optimize tissue clearing protocol optimization. Samples will be immersed in PBS with triton X for 6 hours, following with treatment with eoysin Y and DRAQ5. Finally appropriate amount of 2,2'-thiodiethanol will be added to match the refractive index. 2. Samples will be labelled for nucleic acid stains and additional immune-labelling will be decided on the type of clinical sample processed. 3. Large 3D data set needs to be rendered to visualize and extract feature information.

PhD/MSR supervisors			
Role	**Faculty**	**Academic unit at IITD**	**E-mail**
Supervisor	R. Elangovan	DBEB	elangovan@dbeb.iitd.ac.in

Project no. 9

Indian Institute of Technology Delhi

Department of Biochemical Engineering and Biotechnology

PhD project

Project details	
Project title	Recovery of furfural, acetic acid and 5 HMF from torrefaction condensate using solvent extraction, adsorption, distillation and other technologies
Type of project	PhD project
Project description	Lignocellulosic agricultural waste are produced at 500 million tonnes in India per year. There is no suitable industrially relevant technology present for dealing with such wastes. Torrefaction process is process that can convert such wastes to biocoal with similar calorific values as coal. Essentially, the waste in the torrefaction reactor is heated between 200 and 300 degree celsius and hemicelluolosic fractions are volatilized. So, far these volatile fractions are simply burnt. However, these fraction contain valuable base chemicals like furfural, acetic acid and 5 HMF. The aim of this project is to recovery these chemicals through variety of downstream processes like distillation, adsorption and solvent extraction. The diference in the properties of furfural and acetic acid like hydrophobicity, charges will be exploited to separate them using adsorption process. Further, distillation and solvent extraction will be used to not only improve the quality of the furfural but also recovery other valuable compounds like 5-HMF from torrefaction condensate. Finally, the aim is to carry out a process integration and run a pilot scale torrefaction plant at a capacity of 1000 kg per day scale. The successful integration and demonstrated cost-effectiveness of the technology will lead to commercialization of the technology.
Instruments required	GC-MS, adsorption column, distillation system, solvent extraction systems

PhD/MSR supervisors			
Role	**Faculty**	**Academic unit at IITD**	**E-mail**
Supervisor	Rohan Jain	DBEB	rjain@iitd.ac.in

Skills required	
Qualification	BTech or MTech in chemical engineering
Skills	Studied the subjects like mass transfer, heat transfer and unit operations.

References
1. T.R.K.C. Doddapaneni*, **R. Jain**, P. K. Ramasamy, J. Rintala, H. Romar, J. Konttinen, Adsorption of furfural from torrefaction condensate using torrefied biomass, Chem. Eng. J. 334 (2017) 558–568

Project details	
Project title	Novel supplementation strategies in mammalian fedbatch processes using mathematical modeling and at line metabolite monitoring
Type of project	PhD project
Project description	In upstream mammalian cell culture for therapeutic protein and vaccine production, a key challenge is to mitigate accumulation of byproducts as well as to ensure minimal availability of other essential nutrients. Existing media design strategies focus on empirical methods of controlling nutrient availability, and thus pose limitations to the optimization of key components that are involved in multiple pathways across cellular metabolism. This project aims to construct a minimalistic metabolic model for mammalian cells incorporating key media nutrients to undertand their interconnectedness and the consequent non-linearity in their uptake rates. Focus of the study will be to understand the effects of lipid supplementation on uptake rates of amino acids and on glucose, lactate and ammonia metabolism and how it overall impacts growth and productivity in fedbatch processes.
Instruments required	Computational softwares (MATLAB and R) Fed-shakes and mammalian bioreactor system UPLC/HPLC and other cell culture analytical techniques (leverage existing facility to establish lab protocols)
Any other comments	N/A

PhD/MSR supervisors			
Role	**Faculty**	**Academic unit at IITD**	**E-mail**
Supervisor	M. Sumit	DBEB	msumit@dbeb.iitd.ac.in
Co-supervisor	As required by the department		

Skills Required	
Qualification	As per departmental requirement of qualification (no special requirements)
Skills	Basic cell culture/aseptic techniques Analytical techniques (HPLC/UPLC) Basic acquaintance of working in any of the programming languages or MATLAB/R

References

M. Sumit et al, (2019) Dissecting N-Glycosylation Dynamics in Chinese Hamster Ovary Cells Fed-batch Cultures using Time Course Omics Analyses, iScience (Cell Press), 12, 102-120

H. Hefzi et al, (2016) A Consensus Genome-scale Reconstruction of Chinese Hamster Ovary (CHO) Cell Metabolism, 3, 5, 434-443

Y. Chen et al, (2019) An unconventional uptake rate objective function approach enhances applicability of genome-scale models for mammalian cells, Nature Systems Biology and Applications, 5-25

T. Abbate et al, (2019) Inference of dynamic macroscopic models of cell metabolism based on elementary flux modes analysis. Biochemical Engineering Journal, 151, 107325

Project no. 11

Project details	
Project title	Modulating the stress response in *Escherichia coli* as a strategy for design of improved host cell platforms
Type of project	PhD project
Project description	A stress response is triggerred due to the diversion of fluxes for recombinant protein synthesis which feedback regulates both growth and product formation. We have previously identified critical gene knock outs which can block this stress response and help enhance recombinant protein yields. The actual role of these knock outs is still not clear because most of them have no assigned function and also are not known to regulate any downstream genes.We plan to conduct CHIP based equencing the elucidate the role of these genes and hence determine the signalling pathway that triggers the onset of the cellular stress response. Additionally we plan to generate knock out combinations which enhance recombinant protein yields and then study the post induction transcriptomic profiles to locate the exact signalling pathways that are effected by the knock outs. Finally we wish to cultivate the modified strains in bioreactors and use on-line monitoring to determine the dynamic physiological response of the culture. The online tmonitoring tools will involve use of GC-MS, NIR, Fluoroscence and LC-MS to quantify intracellular metabolites and follow the time course to create dynamic models of cell response. The genome engineering studies and the bioprocess modeling will be synergistically combined to have a better undertanding of cellular behaviour leading in turn to the rational design of improved cell platforms for both protein and metabolite overexpression
Instruments required	Basic molecular biology equipment like Electrophoresis, centrifuge, shakers,PCR, gel Doc. Bioreactors and online tools like GC-MS, LC-MS, NIR fluoroscence, Gas analyser
Any other comments	

PhD/MSR supervisors			
Role	**Faculty**	**Academic unit at IITD**	**E-mail**
Supervisor	KJ Mukherjee	DBEB	KJmukherjee@dbeb.iitd.ac.in

Skills required	
Qualification	B.Tech/ M.Sc/ M.Tech in Biotechnology

Skills	Molecular biology, genetic engineering, Bioreactor operation, Handling analytical equipment like GC-MS etc, Mathematical ability to do dynamic modeling

References
1. Designing next generation recombinant protein expression platforms by modulating the cellular stress response in Escherichia coli Richa Guleria, Priyanka Jain, Madhulika Verma & Krishna J. Mukherjee Microbial Cell Factories volume 19, Article number: 227 (2020) 2. A novel knock out strategy to enhance recombinant protein expression in *E. coli.* Ashish Sharma, Esha Shukla, Deepak Janhoti, K.J. Mukherjee and Joseph Shiloach Microbial Cell Factories 19 **148** (2020)