

# BIOLOGICAL ENGINEERING SOCIETY

---

Newsletter: Volume 2

---

# Contents

Letter from the Editor	3
Home coming ... the magic of IIT Gandhinagar – <i>Dhiraj Bhatia</i>	4
Synthetic Biology: Design at the Intersections of Biology and Engineering – <i>Anu Raghunathan</i>	6
Redundancies and their evolution in metabolic networks – <i>Karthik Raman</i>	10
Microbial Biofactory for Nutrition – <i>Sanjoy Ghosh</i>	14

# Letter from the Editor

Dear friends of the Biological Engineering Society,

**I**t is my pleasure to bring to you the second newsletter of the Society. The membership of the society has grown and in a way indicates that among the faculty and scientists of different institutes across India there is wider awareness and acceptance of Biological Engineering as discipline, and a shift in the paradigm of the classical Biochemical Engineering. A motivation perhaps has been that research being conducted at the intersection of the Biological and Engineering Sciences is more in tune with trends in research, the scope of journals with better impact factor, and it helps in meeting the numbers for self-appraisals. The younger generation of faculty and scientists may also find that deeper and more fundamental questions can be investigated and the pursuit of research in this direction is relevant to health, environment and society and overall, more satisfying.

As faculty positions in the Biomolecular, Bioengineering and related Biological Science streams begin to fill up positions across institutions in India across the tiers of ranking, classical Bioengineering is metamorphosing into the interdisciplinary field of Biological Engineering. The next generation of faculty and scientist have the right background and training to push this discipline forward. They have grand ideas and aspiration and will fuel the much needed impetus.

In this edition, I bring you the experiences of a young faculty Dhiraj Bhatia at the Department of Biological Engineering, IIT Gandhinagar. There is no doubt that the initial experiences of faculty sets his attitude towards his research, collaboration and camaraderie with his fellow colleagues. Nurturing them during their early career brings huge research and funding dividends to the parent department. The next article is commentary on Synthetic Biology and how with the growing knowledge and understanding of the biological world the edges between natural and synthetic is gradually fading. The third article by Karthik Raman is a narrative of the kind of work being carried out by his group. This is conceptual note on how evolution harbours redundancies in metabolic networks and how these serve as essential components for an organism's survival. The last article has been contributed by Sanjoy Ghosh who has many years of experience in the area of alternative feedstock and biofuels. He assesses the current status of algal biofuel production suggests that economic viability of biorefineries is possible only the co-production of high-value compounds from algal biomass.

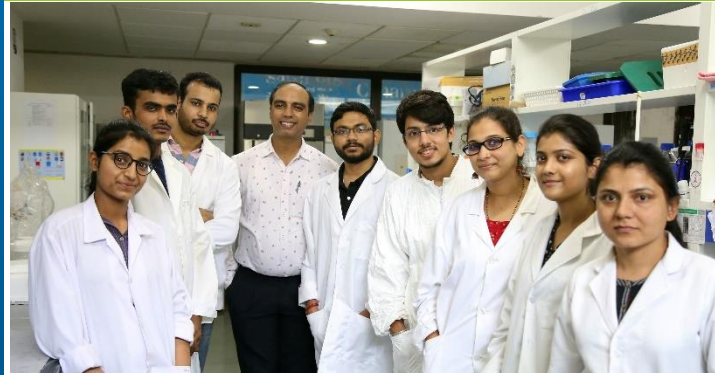
The articles give a flavour of the changing milieu in Biological Engineering discipline and trends we will be seeing in the years to come.

*James Gomes*  
Editor

Biological Engineering Society

# Home coming ... the magic of IIT Gandhinagar

“The biggest help came to me from IITGN faculty colleagues of BioE, my kind mentors”



*Like any other* postdoctoral fellow in USA or Europe, I was equally striving to return back to India to start my own research team. Having a good academic track record and more importantly the best mentoring from both in PhD and Postdoc provided a huge help in getting multiple job offers from India, and IIT Gandhinagar provided the best solution to our two-body problem. Having a job offer from a new IIT bought its own perks in terms of getting full freedom and monetary support to start my own lab. The excitement of starting an academic career brings along a huge nervousness as well as - challenges to setting up the research laboratory and arranging grants and materials. This problem pervades institutes all throughout the country and is limited not just to one or two specific institutes. Especially in the Indian scenario, this nervousness is palpable due to road blocks at multiple levels –delays in getting things done, receiving grants, recruiting personal and creating infrastructure – things can go wrong with any of these parameters.

All of us who returned to India assume that it will easily take a year or two to get our lab started and to get first bunch of good students. I was no exception to this. Completing almost half a decade of postdoctoral research at Institute Curie in Paris, I moved back to India to start my own lab in Biological Engineering Discipline at Indian Institute of Technology Gandhinagar (IITGN) with a excitement of having an academic career but along with a big aliquot of nervousness that there will be a temporal vacuum of year or two before my lab starts rolling.

However, life always has a bag full of surprises for each one of us. IIT-GN already knew the challenges and nervousness which young faculty face after returning to India and they already had a full idea of what it takes to have a fully functional laboratory. My senior colleagues at IITGN were already well prepared to welcome me in a very optimistic manner in their open laboratory system at BioE laboratory. It was like I was a new born baby

in the family of BioE discipline where the open-lab of BioE was our home. The open laboratory model has been very well established in multiple well established universities in India in terms of multiple faculties sharing their lab space, reagents, equipment and the students as well. In the very first week of joining IITGN, I had my own space and enough storage space to host a team of 5 students with complete access to all equipment and facilities. The week after my joining, I received the first round of funds to start my research. The common reagents and biochemicals needed to start experiments arrived within a week. I was grateful to have my first PhD student join my lab on my very first day at IITGN and in no time, we started working in the lab tweaking our hands with DNA Nanotechnology. I was extremely nervous in terms of the high expectations of PhD student from me but her enthusiasm and the help from colleagues and IITGN kept my nervousness at the bay. The biggest help came to me from IITGN faculty colleagues of BioE, my kind mentors. Each of my senior colleagues opened up their hearts, lab drawers and cupboards for me to share their chemicals, reagents, lab equipment to get the ball rolling for my research right from day-one of my arrival in IITGN. A few of my colleagues also gave me access to their ongoing grants to order the things I needed for my research. The first six months in IITGN will forever remain as golden memories in my career.

Setting up a lab in any institute in India these days is one of the biggest challenges any scientist can face. Given the limited funding from institutes, delays in grant arrivals from government agencies can be extremely frustrating. The bigger challenge is arranging huge sums of money to purchase the equipment required for research. In this aspect, the open lab policy of BioE at IITGN was big advantage since I did not have to write separate grants to procure the costly high-end equipment needed for research. This I had the freedom to utilize most of my grants for reagents and consumables.

BioE labs at IITGN also gives freedom to students from different groups to discuss among themselves and get their problems solved at the earliest. Most of the times, we the faculty members, are involved in teaching, administrations and conferences and are not accessible to our own students for scientific and personal discussions. The concept of open labs at BioE not only gives students the opportunity to discuss their research with other students and trouble-shooting problems but also helps them to come up with new ideas that could foster collaborative projects between different groups.

For me, open labs at BioE IITGN has transformed into a daily science hub where not only my students, but students from other groups as well come and discuss their ideas, papers and discoveries, and ways to further improve the existing system for carrying out research. Being a part of the open lab system at IITGN has been one of the best experiences of my homecoming to India and I look forward to more positive surprises in the times to come.



### **Assistant Professor**

Indian Institute of Technology Gandhinagar  
<https://dhirajbhatia1.wixsite.com/bhatialab>

The Bhatia lab seeks answers to fundamental questions in cell biology using DNA nanotechnology and chemical biology based approaches. We ask how nanometer-sized biomolecules transmit and integrate information across much larger length scales of the orders of cells and tissues. We seek to explore how collections of macromolecules work together to establish a common functional system like cellular pathways, organelles, living cells and further into tissues, organs and entire organisms.

Biological Engineering Society

# Synthetic Biology: Design at the Intersections of Biology and Engineering

“The purpose of design is not just aesthetic, nor is it only analytical or just functional. It requires holistic or systemic thinking ...”



**Synthetic biology** is the design and construction of new biological parts, devices, and systems resulting in the re-design of existing, natural biological systems for useful purposes [1, 2]. Thus, it is a new science on the block that has enormous potential to create cellular machines and transform life [3] (Figure 1). Building on the work of more traditional biologists, synthetic biologists harness what we know about modularity and hierarchy of biological systems to engineer new functions into living things. These include but are not limited to chemical compounds (like drugs, pharmaceutical intermediates) and generating biofuels [4–7]. Future applications would include cellular robots that can fight cancer [8], provide energy for our automobiles [2], and produce cheap and affordable drugs. Thus, synthetic biology is indeed a discipline of the 21<sup>st</sup> century with many implications.

STUDY OF BUILT AND MANUFACTURED MACHINES

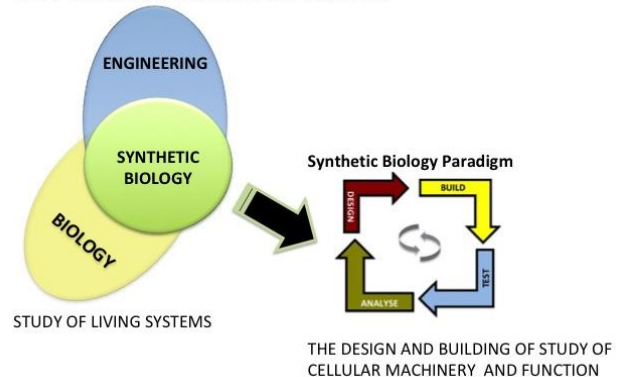


Figure 1: Synthetic Biology: The cross roads of biology, engineering & design

## Implications of Synthetic Biology and the Concept of Design

Erwin Schrodinger in his book “What is Life?” focused on one important question: “*how can the events in space and time which take place within the spatial boundary of a living organism be accounted for by physics and chemistry?*”[9]. This question underscores the importance of multidisciplinary

science and highlights the need to delineate the blue print of a living cell and study emergent properties of living systems. A synthetic biologist using cross-disciplinary expertise [10], brings the concept of design to a new space. A space of living matter separated based on the disparity of function and capable of growth with time (Figure 2). A space that can control cell function and fabricate life.

of form in terms of the fundamental unit of life, i.e., the cell. The purpose of design is not just aesthetic, nor is it only analytical or just functional. It requires holistic or systemic thinking about the relationships between the component blueprint or parts list and their interactions (Figure 3). The field of synthetic biology thus spans not only cells, organisms and their interacting environment but also engineering and industry. Nature, a grand materials engineer can organize matter and optimally edit constraints for multi-cellularity based on function. What we can make of form is that which is inspired, informed, engineered and designed by nature resultant in a new biology. Synthetic biology may allow us to create a Darwin-inspired evolutionary design of biology taking into account how each form affects the environment in which they come into.

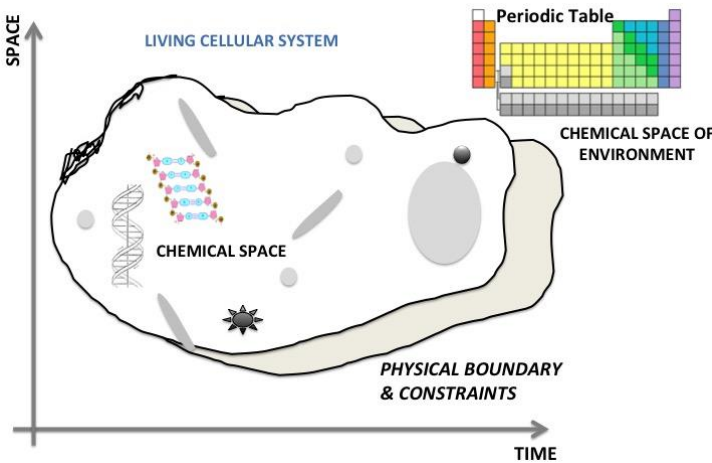


Figure 2: Design with living matter in space and time

Design can be thought of as essentially what differentiates the “natural” from the “artificial”. Then can we define the origin of natural form and move on to invent form? Generating form inspired by nature can be perceived as a preconceived notion of the existing narrative. Coupled to the impact of technology, optimization it can shape new function. The biological system allows one to think

### The Promise Of Synthetic Biology

Until recently, design was concerned only with technology and the consumer industry having a cultural impact. Microbes, insects, cell constituents have now slowly become objects of design over the last several decades. Oxitec [11] has geo-engineered RIDL, a male mosquito progeny to die by genetic design. Conception can now be precision-timed by cellulose encapsulated bull sperm activated only by hormonal changes. The pharmaceutical industry has used microbes like *Escherichia coli* to produce insulin commercially since the 1970s and saved many lives. Synthetic biologists can see themselves as revolutionizing the biotechnology industry and manufacturing (Figure 4) as DNA designers; their goal being to convert DNA sequences into biological parts, circuits and systems. Molecular blueprints engineered at the scale of genetic circuits can be manufactured inside micro-organisms like *E. coli* on a reasonable time scale. An *E.coli* that secretes drugs or bioplastics, an *E.coli* that spits cosmetics and another designer microbe for rubber to make tyres or fuel for cars may be the promise of the future.

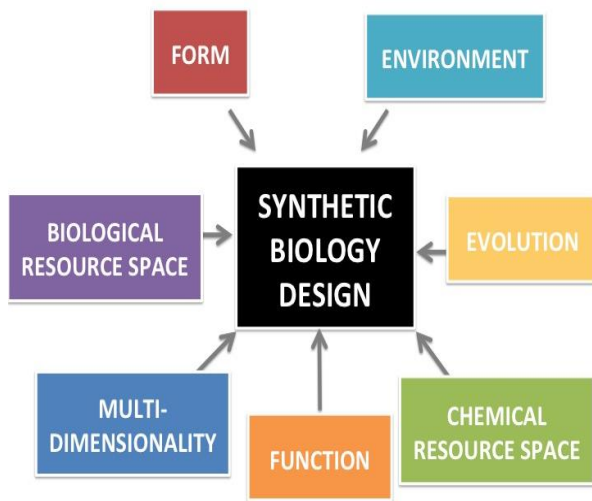


Figure 3: Towards Life 2.0 -The basis for the design concept of synthetic biology

Synthetic biology can thus literally fast forward evolution and bring us a whole new world. But as evolution responds to context, these designs may change with time. This caveat of synthetic

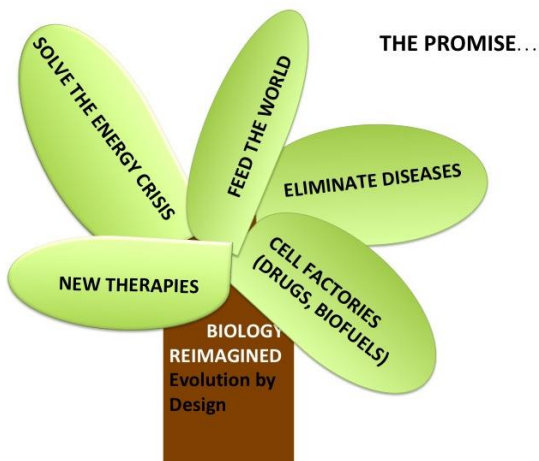


Figure 4: Growing the Promise of Synthetic biology

design may force us to push the boundary of our design far away from the natural, giving rise to the proverbial double edged sword. This could result in a major ethical dilemma for prototypes of this revolutionary “nature inspired 21<sup>st</sup> century design”. We should be wary of it.

### Pushing The Boundaries Of Synthetic Biology

The ability to tinker with nature’s optimal design allows us to push the boundaries of the known and move into the unknown. This journey has already begun by moving from applications in the chemical manufacturing sector to the medical industry. DNA sequence editing or gene editing has become a reality and there is a possibility to develop genetic editing solutions for curing disease or fix mutations in DNA of patients suffering from related diseases. CRISPR, which stands for Clustered, Regularly Interspaced, Short Palindromic Repeat, is a naturally-occurring defence mechanism used by bacteria. Scientists have harnessed this mechanism bacteria use to recognize viruses, to develop ‘molecular scissors’ that can remove mutated areas of DNA. This technology can help to cure diseases like cancer [12]; but is hugely controversial because it changes the fundamental genetic code that would be inherited by an offspring.

Several companies that have been set up to work with this cutting edge technology. Examples include **Autolus** [13] for Cancer Therapies (synthesizing novel T-cells recognizing cancer cells to destroy them), **Precision Biosciences** [14] (working on genome editing affected individuals to cure genetic diseases). **CRISPR Therapeutics** [15], to utilize the potential of CRISPR to treat some severe diseases. While companies like **Gevo** [16] are focused on advanced renewable chemicals and next-generation biofuels some others like **Impossible Foods** [17] are working on revolutionizing our ideas of **food and nutrition**.

### Perils Of Synthetic Biology

Synthetic biology has huge potential but also has serious risks and dangers (Figure 5) including the potential escape of synthetic organisms into the environment and bio-terrorism. Although highly premature, the unintended consequences for synthetic biology and CRISPR are worrisome in the context of engineering designer babies. The ethical concerns regarding the misuse of Synthetic Biology are very high.

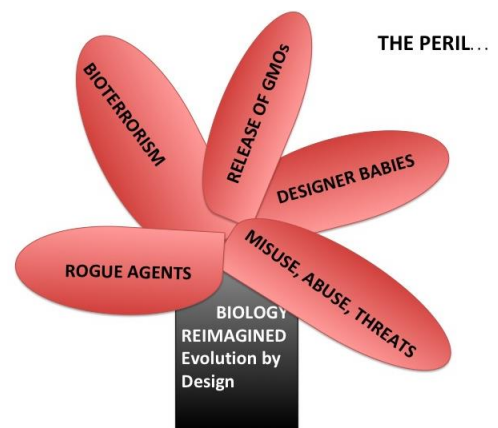


Figure 5: The Perils of Synthetic biology



## Conclusions

The ability to design life has opened up many difficult questions. Some of these include not knowing what the future holds, the unknown and the ownership of life. What new invention can we design and produce? How will synthetic biology shape the future of nature and nations? The impact of Synthetic biology on life and lifestyle can be foreseen as critical to the arrival of this brave new world.

## References

- Jia H, Schwille P., 2019, Bottom-up synthetic biology: reconstitution in space and time., *Curr Opin Biotechnol.* Jun 6;60:179-187.
- Garcia S, Trinh CT., 2019, Modular design: Implementing proven engineering principles in biotechnology., *Biotechnol Adv.*, pii: S0734-9750(19)30092-8
- Tarnopol RL, Bowden S, Hinkle K, Balakrishnan K, Nishii A, Kaczmarek CJ, Pawloski T, Vecchiarelli AG., 2019, Lessons from a Minimal Genome: What Are the Essential Organizing Principles of a Cell Built from Scratch?, *Chembiochem.* 2019, in press
- Paddon CJ, Westfall PJ, Pitera DJ, Benjamin K, Fisher K, McPhee D, Leavell MD, Tai A, Main A, Eng D, Polichuk DR, Teoh KH, Reed DW, Treynor T, Lenihan J, Fleck M, Bajad S, Dang G, Dengrove D, Diola D, Dorin G, Ellens KW, Fickes S, Galazzo J, Gaucher SP, Geistlinger T, Henry R, Hepp M, Horning T, Iqbal T, Jiang H, Kizer L, Lieu B, Melis D, Moss N, Regentin R, Secrest S, Tsuruta H, Vazquez R, Westblade LF, Xu L, Yu M, Zhang Y, Zhao L, Lievens J, Cavello PS, Keasling JD, Reiling KK, Renninger NS, Newman JD., High-level semi-synthetic production of the potent antimalarial artemisinin., *Nature.* 2013 Apr 25;496(7446):528-32.
- Ajikumar PK, Xiao WH, Tyo KE, Wang Y, Simeon F, Leonard E, Mucha O, Phon TH, Pfeifer B, Stephanopoulos G., Isoprenoid pathway optimization for Taxol precursor overproduction in *Escherichia coli.*, *Science.* 2010 Oct 1;330(6000):70-4.
- Li Y, Li S, Thodey K, Trenchard I, Cravens A, Smolke CD., Complete biosynthesis of noscapine and halogenated alkaloids in yeast., *Proc Natl Acad Sci U S A.* 2018 Apr 24;115(17):E3922-E3931
- Casini A, Chang FY, Eluere R, King AM, Young EM, Dudley QM, Karim A, Pratt K, Bristol C, Forget A, Ghodasara A, Warden-Rothman R, Gan R, Cristofaro A, Borujeni AE, Ryu MH, Li J, Kwon YC, Wang H, Tatsis E, Rodriguez-Lopez C, O'Connor S, Medema MH, Fischbach MA, Jewett MC, Voigt C, Gordon DB., A Pressure Test to Make 10 Molecules in 90 Days: External Evaluation of Methods to Engineer Biology., *J Am Chem Soc.* 2018 Mar 28;140(12):4302-4316
- Sedlmayer F, Aubel D, Fussenegger M., 2018, Synthetic gene circuits for the detection, elimination and prevention of disease., *Nat Biomed Eng.*;2(6):399-415
- Erwin Schrodinger, 1944, *What Is Life?* Cambridge University Press
- Hays SG, Patrick WG, Ziesack M, Oxman N, Silver PA., 2015, Better together: engineering and application of microbial symbioses., *Curr Opin Biotechnol.* Dec;36:40-9
- <https://www.oxitec.com/friendly-mosquitoes/>
- Therapeutic potential of CRISPR/Cas9 gene editing in engineered T-cell therapy. Gao Q, Dong X, Xu Q, Zhu L, Wang F, Hou Y, Chao CC. *Cancer Med.* 2019
- <https://www.autolus.com>
- <https://precisionbiosciences.com>
- <http://www.crisprtx.com>
- <https://gevo.com>
- <https://impossiblefoods.com>



### Dr. Anu Raghunathan

Principal Scientist  
Chemical Engineering Division  
National Chemical Laboratory, Pune  
Email: anu.raghunathan {at} ncl.res.in  
<https://sites.google.com/micelabatncl>

Our group, the Metabolic Inquiry and Cellular Engineering (MICE) group, uses systems approaches (both experimental and computational) to understand biological cell behaviour and function. We build computer models of the cell through genome-scale metabolic network reconstruction and compute cell phenotype using constraints-based flux balance analysis. Experimental approaches in prokaryotes involve genome-engineering of *Escherichia coli* for value added chemicals using recombinant and synthetic biology techniques.

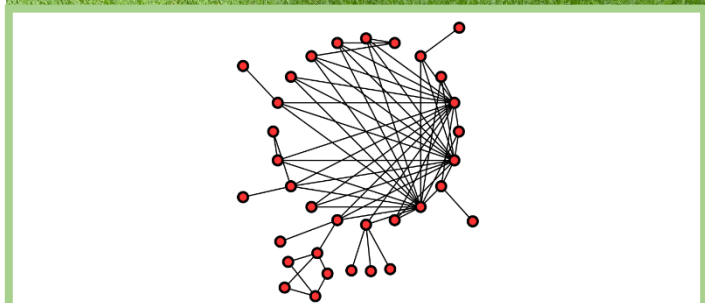
Our goals include understanding drug resistance both in antibiotic resistant pathogens and also in chemo-resistant cancer cells. We foresee clinical application in tailoring micro-environments to overcome the problem of drug resistance.

We strive to practice model-driven science by validation of *in-silico* discoveries experimentally at different levels of molecular organization in both prokaryotic and eukaryotic systems.

For more details visit our Metabolic Inquiry and Cellular Engineering (MICE) Lab web page.  
<https://sites.google.com/micelabatncl>

# Redundancies and their evolution in metabolic networks

“Given the redundancies that exist in metabolic networks, how do new redundancies add up in the system?”



The largest component of the double lethal network of *E. coli*. The nodes represent reactions and edges connect reactions that form a double lethal



## Introduction

**Biological systems** are highly complex network structures (Wagner, 2005). Robustness is an inherent nature of all biological systems in every level of abstraction. Such robustness is conferred via a number of mechanisms, one of which is redundancy (Hartman et al., 2001). Redundancy occurs when the same biochemical function is performed by two or more entities. Redundancy can influence various levels in a biological system namely, genetic, metabolic, signalling and proteins. Metabolism is central to all biological processes; they build up components necessary for the growth and survival of the organism. Metabolic network is composed of numerous enzyme-catalysed reactions that catalyse the conversion of various biomolecules. There exist redundant reactions in these metabolic networks that compensate for one another in case of any perturbations in the system (Sambamoorthy et al., 2019). Synthetic lethals are a pair of reactions that exhibit

redundancy, thus upon deletion of both the reactions the organism will not survive (Hartman et al., 2001). However, even if one of the reactions is present, the organism is still able to sustain life with the reactions compensating for one another.

### Synthetic lethals

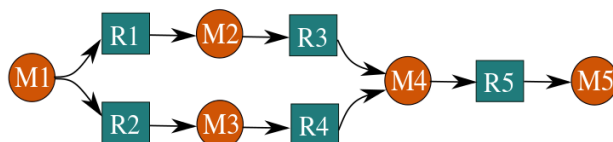


Figure 1. Synthetic lethals in metabolic networks.

The figure 1 shows a toy metabolic network, where metabolite M5 is essential for the growth of the organism. The reactions R1 and R2 are synthetic lethals, on deletion of both the reactions, the metabolite M5 cannot be produced. The presence of either one of the reactions R1 or R2, the metabolite M5 can still be produced via the two different pathways {R1-M2-R3-M4-R5-M5} or {R2-M3-R4-M4-R5-M5}

Albeit the multitudinous studies conducted to understand synthetic lethals in metabolic networks, interesting questions still remain unanswered. Given the redundancies that exist in metabolic networks, how do new redundancies add up in the system? Does evolution play a role in the addition of reactions that can form new synthetic lethal pairs? As and when an organism evolves in a habitat, are there redundancies pertaining only to that growth condition or can the metabolic networks specialise to eventually exhibit redundancies in other growth conditions as well?

Thus, we aim to understand the evolution of such redundancies in metabolic networks (workflow as described in Figure 2) and how they serve as essential design principle for survival and growth in a multitude of growth conditions (Sambamoorthy and Raman, 2018).

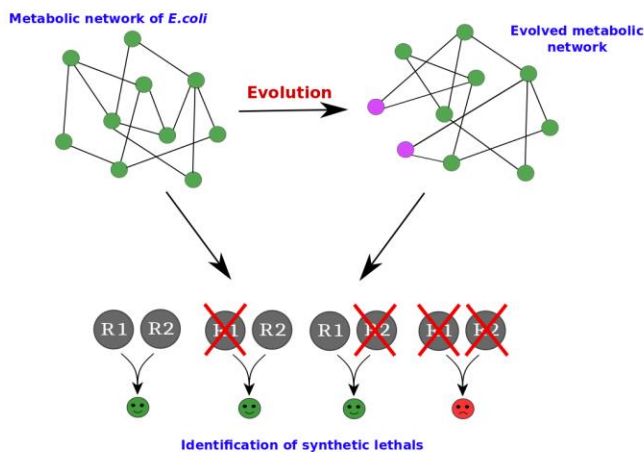


Figure 2. Workflow for understanding the evolution of functional redundancy in metabolic networks.

### Evolution of metabolic networks and evaluation of growth phenotypes for identifying synthetic lethals

With the advent of numerous computational studies and techniques, it is possible to analyse the metabolic networks in silico. Flux balance analysis (FBA) (Varma and Palsson, 1994; Kauffman et al., 2003) is a constraint-based approach to evaluate a metabolic phenotype given a metabolic network of an organism. FBA is conducive to analyse the metabolic capabilities of an organism in a variety of growth conditions. Using FBA and a variation of an

already existing MCMC approach (Barve and Wagner, 2013) to evolve metabolic networks, we generated 2000 evolved metabolic networks. The metabolic network of *E. coli* was evolved using multiple reaction swaps with those present in the universe of reactions. This universe of reactions consists of the entire set of reactions known to occur in all organisms (from ModelSEED). After each reaction swap, the metabolic networks are constrained to grow on a minimal glucose medium. Further, the reaction redundancies in these metabolic networks were identified by finding the synthetic lethals using Fast-SL (Pratapa et al., 2015) by evaluating 39 billion phenotypes. Fast-SL is an efficient algorithm that minimizes the search space and to evaluate a large number of phenotypes to identify synthetic lethals. The metabolic phenotypes and the synthetic lethals in the evolved metabolic networks were assessed in ten different growth conditions. These growth conditions are minimal nutrient environments that differ only in the sole carbon source.

### Organisms exhibit higher level of redundancy

The number of synthetic lethals in various growth conditions varied depending on the evolved metabolic networks. On comparison with the synthetic lethals found in the starting organism, *E. coli*, we could observe that the synthetic lethals in *E. coli* were significantly higher than the evolved metabolic networks. This observation was found to be true in all ten growth conditions under study. This explains that real networks that exist in nature (*E. coli* here) are robust with a large number of redundancies. These redundancies thus enable the organism combat single mutations that occur in the organism.

### Redundancies are dependent on the growth medium

The analysis of the synthetic lethals identified in all the ten different growth conditions revealed that there are certain lethals that are common across these growth conditions. However, they constitute a very less proportion when compared to the synthetic lethals specific to environments. We identified that 163 synthetic lethals are common

across all ten environments under study whereas 8043 synthetic lethals were unique to environments. Of the environmentally dependent lethals, inosine had the maximum fraction of lethals specific to the environment. The maximum fraction of synthetic lethals specific to inosine signifies that the reactions that can assimilate inosine are very different from those that metabolise other carbon sources. The common lethals in all growth conditions belong to pathways that are involved in the assimilation of all the carbon sources under study. Further inclusion of more such growth medium would eventually reduce the number of synthetic lethals common across all growth conditions.

### **Evolution enables the addition of new redundancies**

The evolved metabolic networks cover a wide range of redundancies as a result of subsequent reactions added. These new reactions further play compensatory roles for numerous reactions that occur in the metabolic network. Reaction compensation index (RCI) of a reaction is defined as the number of lethal pairs that can be formed with other reactions across all evolved networks. There were 82 reactions that had a RCI of  $\geq 100$ , 12 of which had an RCI greater than 200. The reaction with the maximum RCI was found to be ATP synthase reaction, that involves in the catalysis of ADP to ATP. ATP is the key energy molecule of the cell, thus evolution adds reactions to compensate the reaction catalysing the formation of ATP. Thus, compensation can occur in a multitude of ways and networks evolve such that they add reactions that can compensate for the reactions necessary for growth.

### **Redundancies acquired during evolution are diverse**

The redundancies acquired as a result of the evolution on glucose are very diverse with respect to their functional roles. Looking closely at some of the reaction lethals that occurred in the evolved networks, we could fathom the variety of functions they catalyse. For example, the reaction for the conversion of chorismate to pyruvate and 4-Hydroxybenzoate, which forms a part of the

ubiquinone biosynthesis forms a synthetic lethal pair with the production of 4-Hydroxymandelate from p-hydroxyphenylpyruvate, which is involved in the biosynthesis of antibiotics. The two reactions however are catalysed by very different enzymes, where the former is catalysed by a lyase (EC 4.1.3.40) and the latter by oxidoreductase (EC 1.13.11.46). Thus, we could identify reaction lethals that were not a part of the native *E. coli* metabolic network, yet play different functional roles and present in diverse pathways.

### **Conclusion**

Redundancies benefit organisms to compensate for the functional roles performed by one another. Nature preserves redundancies enabling the organism to withstand single point mutations. As an organism evolves, new redundancies appear, thus enabling more number of compensation mechanisms. The redundancies facilitate compensation of key reactions in the network, further increasing the network's ability to combat single mutations. Redundancies need not comply to specific pathways, there can be reactions in diverse pathways, yet deletion of both reactions can be lethal to the organism. Therefore, our study throws light on one of the key design principles that exists in metabolic networks eventually making the organism more robust.

### **References**

- Barve,A. and Wagner,A. (2013) A latent capacity for evolutionary innovation through exaptation in metabolic systems. *Nature*, 500, 203–206.
- Hartman,J.L. et al. (2001) Principles for the Buffering of Genetic Variation.) *Science*, 291, 1001–1004.
- Kauffman,K.J. et al. (2003) Advances in flux balance analysis. *Curr. Opin. Biotechnol.*, 14, 491–496.
- Pratapa,A. et al. (2015) Fast-SL: An efficient algorithm to identify synthetic lethal sets in metabolic networks. *Bioinformatics*, 31, 3299–3305.
- Sambamoorthy,G. et al. (2019) Evolutionary design principles in metabolism. *Proc. R. Soc. B Biol. Sci.*, 286.

Sambamoorthy, G. and Raman, K. (2018) Understanding the evolution of functional redundancy in metabolic networks. In, *Bioinformatics.*, pp. i981–i987.

Varma, A. and Palsson, B. O. (1994) Metabolic flux balancing: Basic concepts, scientific and practical use. *Bio/Technology*, 12, 994–998.

Wagner, A. (2005) Robustness, evolvability, and neutrality. *FEBS Lett.*, 579, 1772–1778.



**Karthik Raman**

Associate Professor

**Gayathri Sambamoorthy**

PhD Scholar

Department of Biotechnology  
 Bhupat Jyoti Mehta School of Biosciences  
 Initiative for Biological Systems Engineering (IBSE),  
 Robert Bosch Centre for Data Sciences and Artificial  
 Intelligence (RBC-DSAI)  
 Indian Institute of Technology Madras  
 Chennai 600036, India

**Dr. Karthik Raman** is an *Associate Professor* at the *Department of Biotechnology, Bhupat and Jyoti Mehta School of Biosciences, Indian Institute of Technology Madras*. Karthik's research group at IIT Madras works on the development of scalable algorithms and computational tools to understand, predict and manipulate complex biological networks. The key areas of research in his group encompass *in silico* metabolic engineering, network biology and biological data analysis. Karthik also co-ordinates the Initiative for Biological Systems Engineering at IIT Madras and is a core member of the Robert Bosch Centre for Data Science and Artificial Intelligence (RBC-DSAI). For more information, see <https://home.iitm.ac.in/kraman/lab>

# MICROBIAL BIOFACTORY FOR NUTRITION

“Strategies for the co-extraction of multiple components involve consecutive fractionation steps ...”



**The world population** is expected to reach nearly 10 billion by 2050, and as the demand for food increases, the arable land is rapidly shrinking because of urbanization, climate change, and land degradation. As a result, there is a need for easy-to-produce and cost-effective food sources that can provide proper nourishment.

Microalgae are fast-growing microorganisms capable of utilizing carbon-dioxide and light to produce biomass and energy. For a very long time, microalgae have been considered a promising feedstock for biofuel production due to their ability to grow in non-arable land using waste resources and produce large amounts of lipids (up to 50-60% of biomass). They also produce metabolites that can be beneficial to human health. Large scale cultivation of microalgae in closed photo-bioreactors can be seen as a commercially feasible option as it can achieve very high biomass productivity in a controlled environment and also avoid contamination, compared to raceway ponds.

## Algae As Nutrient Source

Microalgae are an excellent source of nutritional compounds including proteins, pigments (carotenoids and phycobiliproteins) and polyunsaturated fatty acids (PUFAs). Astaxanthin (produced by *Haematococcus pluvialis*) and Phycocyanin (from *Arthrospira platensis*) are pigments used as food colorants and are known for their strong antioxidant properties. Eicosapentaenoic acid, a PUFA with applications in preventing and reversing heart disease, asthma, and other ailments, has been produced using the microalgae *Chlorella minutissima*. Sulfated algal polysaccharides, such as carrageenan, fucoidan and ulvan, have diverse biological functions. Their possible therapeutic properties include antitumor, immunomodulatory, anti-inflammatory, anti-thrombotic, and anti-coagulant effects. Many microalgae are also rich in vitamins like alpha-tocopherol and ascorbic acid that can be used as dietary supplements.

## Need for an Integrated Biorefinery

According to the International Energy Agency (IEA), a biorefinery is defined as “the sustainable processing of biomass into a spectrum of marketable products (food, feed, materials, and chemicals) and energy (fuels, power, heat)”. With the current status of the technology in algal biofuel production, their economic viability is possible only with the commercialization of high-value co-products from algal biomass.

In 2013, Nobre et al. used *Nannochloropsis* sp. Microalga to extract oils and pigments by supercritical fluid extraction (SFE), using the left over biomass to produce biohydrogen. *Chlorella protothecoides* was used by Campenni et al. (2013) as a source of both lipids and carotenoids. The microalgal biomass of *Spirogyra* sp. has also been used for pigment extraction and hydrogen production (Pacheco et al., 2014). In 2018, Zhang et al. extracted fucoxanthin, EPA and chrysolaminarin from *Phaeodactylum tricornutum* biomass. Various studies have described the cultivation of *Chlorella vulgaris* for the production of bioethanol, pigments and proteins.

## Challenges and Opportunities

The current approach to microalgal biorefineries is unprofitable mainly due to expensive downstream processes that are designed for a single main product. Moreover, all the exploitable products are not accumulated in the same growth phases and conditions. There are phases, such as the late exponential phase, where the production of non-growth-associated molecules (like carotenoids and lipids) is still balanced with a relatively high amount of growth-associated molecules (proteins and chlorophyll). Strategies for the co-extraction of multiple components involve consecutive fractionation steps like two-phase extraction, filtration and chromatography.

Another factor that limits microalgal biomass productivity is the low penetration of light into the culture. To reduce the optical path length and increase biomass concentration, cascade raceways can be used instead of open ponds and tubular PBRs can be replaced by thin flat plate PBRs.

Finally, it is necessary to investigate all the microalgal components for their potential commercial value to create an optimal microalgal biorefinery.

## References

- Buono, S., Langellotti, A. L., Martello, A., Rinna, F., & Fogliano, V. (2014). Functional ingredients from microalgae. *Food & function*, 5(8), 1669-1685.
- Campenni, L., Nobre, B. P., Santos, C. A., Oliveira, A. C., Aires-Barros, M. R., Palavra, A. M. F., & Gouveia, L. (2013). Carotenoid and lipid production by the autotrophic microalga *Chlorella protothecoides* under nutritional, salinity, and luminosity stress conditions. *Applied microbiology and biotechnology*, 97(3), 1383-1393.
- de Jesus Raposo, M., de Morais, A., & de Morais, R. (2015). Marine polysaccharides from algae with potential biomedical applications. *Marine drugs*, 13(5), 2967-3028.
- Gong, M., & Bassi, A. (2016). Carotenoids from microalgae: a review of recent developments. *Biotechnology Advances*, 34(8), 1396-1412.
- Kumar, B. R., Deviram, G., Mathimani, T., Duc, P. A., & Pugazhendhi, A. (2019). Microalgae as rich source of polyunsaturated fatty acids. *Biocatalysis and agricultural biotechnology*.
- Nobre, B. P., Villalobos, F., Barragan, B. E., Oliveira, A. C., Batista, A. P., Marques, P. A. S. S., ... & Gouveia, L. (2013). A biorefinery from *Nannochloropsis* sp. microalga—extraction of oils and pigments. Production of biohydrogen from the leftover biomass. *Bioresource technology*, 135, 128-136.
- Pacheco, R., Ferreira, A. F., Pinto, T., Nobre, B. P., Loureiro, D., Moura, P., ... & Silva, C. M. (2015). The production of pigments & hydrogen through a *Spirogyra* sp. biorefinery. *Energy conversion and management*, 89, 789-797.
- Zhang, W., Wang, F., Gao, B., Huang, L., & Zhang, C. (2018). An integrated biorefinery process: Stepwise extraction of fucoxanthin, eicosapentaenoic acid and chrysolaminarin from the same *Phaeodactylum tricornutum* biomass. *Algal research*, 32, 193-200.



**Sharika Sachin**

PhD Scholar

Sarika is currently working in Biochemical Engineering Laboratory, Department of Biotechnology, Indian Institute of Technology Roorkee. She completed B.Tech in Biotechnology from GGSIPU, New Delhi and M.Tech in Biotechnology from Anna University, Chennai.



**S. Rohith**

PhD Scholar

Rohit is currently working in Biochemical Engineering Laboratory, Department of Biotechnology, IIT Roorkee. He completed B.Tech in Biotechnology from NIT Durgapur and M.Tech in Biotechnology from Anna University, Chennai.



**Sanjoy Ghosh**

Professor

Biochemical Engineering Laboratory  
Department of Biotechnology  
Indian Institute of Technology Roorkee



# BESCON 2019

## ICSR Auditorium, IIT Madras, Chennai

### TENTATIVE PROGRAM

(as on 1.07.2019)

### Friday, October 18, 2019

08:00 - 17:00	Registration
09:00 – 09:30	Inauguration
09:30 – 10:15	Plenary Talk
10:15 – 10:30	High Tea
10:30 – 13:00	Technical Session 1
13:00 – 14:00	Lunch
14:00 – 16:30	Technical Session 2
16:30 – 16:45	High Tea
16:45 – 18:45	Poster Session

#### In parallel Start-up Conclave

17:30 – 19:30	Invited talks by Start-ups
17:00 – 17:30	Keynote address
18:00 – 19:30	BES annual GB meeting
15:00 – 17:00	Participation certificate distribution & Registration receipt distribution
19:30 – 21:00	Dinner

### Saturday, October 19, 2019

08:00 – 12:00	Registration
09:30 - 11:45	Technical Session 3
11:45 – 12:00	Tea break
11:45 – 14:00	Poster Session
13:00 – 14:00	Lunch
14:00 – 16:30	Technical Session 4
16:30 – 17:00	Concluding remarks & Prize distribution
14:00 – 17:00	Participation certificate distribution & Registration receipt distribution
17:00 – 17:30	High Tea