Registration Deadline 1 August 2016

Discussion meeting on
Conflict and Cooperation in Cellular Populations

NCBS – InSTEM, Bangalore , India
16–19 October 2016

Speakers

Alessandro Esposito, *University of Cambridge, UK*
Catherine Wakeman, *Texas Tech University, USA*
David Queller, *Washington University, St. Louis, USA*
Dipankar Chatterji, *IISc, Bangalore, India*
Duncan Greig, *Max Plank Institute for Evolutionary Biology, Plön, Germany*
E. Peter Greenberg, *University of Washington, Seattle, USA*
Gerard Wong, *University of California Los Angeles, USA*
Joan Strassmann, *Washington University, St. Louis, USA*
Maithreyi Narasimhan, *TIFR Mumbai, India*
Marvin Whiteley, *University of Texas, Austin, USA*
Randal Halfmann, *Stowers Institute for Medical Research, Kansas City, USA*
Rupinder Kaur, *CDFD, Hyderabad, India*
Sine Svenningsen, *University of Copenhagen, Copenhagen, Denmark*
Subhadeep Chatterjee, *CDFD, Hyderabad, India*
Supreet Saini, *IIT Bombay, Mumbai, India*
Szabolcs Semsey, *University of Copenhagen, Copenhagen, Denmark*
Varsha Singh, *IISc, Bangalore, India*
Vidyanand Nanjundiah, *Centre for Human Genetics, Bangalore, India*
Wenying Shou, *Fred Hutchinson Cancer Research Center, Seattle, USA*
William Harcombe, *University of Minnesota, St. Paul, USA*

Organizers
Sandeep Krishna & Sunil Laxman

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(for the above dial only the last four digits from phones in guest house or NCBS/InStem offices)

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Reception team for coordinating transport arrangements


North
Centre for Cellular and Molecular Platforms
Champaka guest house
Mallige guest house
Dasheri auditorium (ground floor)
Main reception Open 24/7
Colonnade (1st floor) Tea/Coffee/Posters
Parijata Hostel
National Centre for Biological Sciences
NCBS dining hall 1st floor (conference breakfast)
Simons Centre
Pool/Gym
InStem dining hall ground floor (conference lunch/dinner)
NCBS Canteens (1st floor) espresso/capuccino/tea/snacks
Canara bank layout guest house

Schedule at a glance

Talks: Dasheri auditorium; Tea/Coffee/Posters: Colonnade; Breakfast: 1st floor of NCBS dining hall; Lunch/Dinner: InStem dining hall

	Oct 16, Sun	**Oct 17, Mon**	**Oct 18, Tue**	**Oct 19, Wed**
8:15-9:15	**Breakfast**	**Breakfast**	**Breakfast**	**Breakfast**
9:30-10:00		Gerard Wong	Rupinder Kaur	Marvin Whiteley
10:00-10:30		Alessandro Esposito	Vidyanand Nanjundiah	Subhadeep Chatterjee
10:30-11:30		**Tea/Coffee/Posters**	**Tea/Coffee/Posters**	**Tea/Coffee/Posters**
11:30-12:00		Szabolcs Semsey	Mukund Thattai	Randal Halfmann
12:00-12:30	Registration (outside Dasheri)	Wenying Shou	Duncan Greig	William Harcombe
12:30-1:00	**Lunch**	Flash talks: Aarthi Ravikrishnan, Sandeep Kumar	Flash talks: C. S. Srinandan, Samay Pande	Poster prizes and closing remarks
1:00-2:00	**Lunch**	**Lunch**	**Lunch**	**Lunch**
2:00-2:30	Registration continues **Opening remarks at 2:15pm**	Poster Session	Poster Session	
2:30-3:00	Sine Svenningsen			
3:00-3:30	Catherine Wakeman	Dasaradhi Palakodeti	Varsha Singh	
3:30-4:00	Flash talks: Glen D'Souza, Yuma Fujimoto	Tina Mukherjee	Dipankar Chatterji	
4:00-4:30	**Tea/Coffee/Posters**	Maithreyi Narasimha	Flash talks: Ramya Purkanti, Sriram Varahan	
4:30-5:30		**Tea/Coffee/Posters**	**Tea/Coffee/Posters**	
5:30-6:00	**Keynote:** E. Peter Greenberg	**Keynote:** Joan Strassman and David Queller		
6:00-6:30				
6:30-7:00	Discussion/Free time	Discussion/Free time		
7:00-8:30	**Beverages & Dinner**	**Beverages & Dinner**	**Beverages & Dinner**	

Detailed Schedule

October 16, Sunday

12:00 - 12:30pm: Registration (outside Dasheri auditorium)

12:30 - 2:00pm: **Lunch**

2:00 - 2:15pm: Registration continues

2:15 - 2:30pm: Opening remarks

Chair: Sandeep Krishna

- 2:30pm: Sine Svenningsen, Quorum sensing control of phage-bacterial interactions – lessons learned from Escherichia coli and Vibrio anguillarum
- 3:00pm: Catherine Wakeman, Factors driving cooperativity versus competition in cystic fibrosis pathogens
- 3:30pm: Flash talk by Glen D'Souza, Experimental evolution of metabolic dependency in bacteria
- 3:40pm: Flash talk by Yuma Fujimoto, Hierarchical Prisoner's Dilemma in Hierarchical Public-Goods Game

3:50 - 5:30pm: **Tea/Coffee/Posters**

Chair: Sine Svenningsen

- 5:30pm: **Keynote talk** by E. Peter Greenberg, Communication, cooperation and conflict among cells of the pathogenic bacterium Pseudomonas aeruginosa

6:30 - 7:00pm: Discussion/Free time

7:00 - 8:30pm: **Beverages & Dinner**

October 17, Monday

Chair: Shashi Thutupalli
- 9:30am: Gerard Wong, Memory, surface sensing, and behavior adaptation during the first 20 generations of bacterial life on a surface
- 10:00am: Alessandro Esposito, A 'systems biology' of cell fate: insights into the biochemical determinants of cellular decisions and cell-to-cell variability

10:30 - 11:30am: **Tea/Coffee/Posters**

Chair: S. Mahadevan
- 11:30am: Szabolcs Semsey, Birth and life of (p)ppGpp induced persisters
- 12:00pm: Wenying Shou, Rapid evolution of metabolic dependence
- 12:30pm: Flash talk by Aarthi Ravikrishnan, Rational development of microbial consortia for metabolic engineering
- 12:40pm: Flash talk by Sandeep Kumar, Microenvironmental regulation of intra-tumor heterogeneity

12:50 - 2:00pm: **Lunch**

2:00 - 3:00pm: Poster Session

Chair: S. Ramaswamy
- 3:00pm: Dasaradhi Palakodeti, Planarian Schmitdea meditteranea: a regenerative model system to study polarity and tissue organization critical for multicellularity
- 3:30pm: Tina Mukherjee, Maintaining Myeloid Cell Fate and Function During Drosophila Hematopoiesis Through Stress-Sensing Pathways
- 4:00pm: Maithreyi Narasimha, Multicellular sensing and the spatial patterning of tissues: competition and cooperation in a Drosophila epithelium.

4:30 - 5:30pm: **Tea/Coffee/Posters**

Chair: Deepa Agashe
- 5:30pm: **Keynote talk** by Joan Strassman and David Queller, Social behavior and mutualism in the social amoeba Dictyostelium discoideum and its bacterial symbionts

6:30 - 7:00pm: Discussion/Free time

7:00 - 8:30pm: **Beverages & Dinner**

October 18, Tuesday

Chair: Mukund Thattai
- 9:30am: Rupinder Kaur, Analysis of Candida glabrata-macrophage interaction
- 10:00am: Vidyanand Nanjundiah, Cooperation via competition in groups of free-living amoebae

10:30 - 11:30am: **Tea/Coffee/Posters**

Chair: Arjun Guha
- 11:30am: Mukund Thattai, Turbocharged evolution in a bacterial arms race
- 12:00pm: Duncan Greig, Sexual signalling in yeast
- 12:30pm: Flash talk by C. S. Srinandan, Emergence of heterogeneity in a bacterial population
- 12:40pm: Flash talk by Samay Pande, Positive effects of natural within-group diversity on spore productivity of social bacteria

12:50 - 2:00pm: **Lunch**

2:00 - 3:00pm: Poster Session

Chair: Akash Gulyani

- 3:00pm: Varsha Singh, Swarming in Pseudomonas aeruginosa: Why and how?
- 3:30pm: Dipankar Chatterji, Second Messengers (p)ppGpp and Cyclic di-GMP mediated regulation of Cell Shape, Cell Division and Antibiotic Sensitivity in Mycobacterium smegmatis
- 4:00pm: Flash talk by Ramya Purkanti, Novel intracellular compartments in hybrid yeast
- 4:10pm: Flash talk by Sriram Varahan, Metabolic Regulation of Fungal Morphogenesis

4:20 - 7:00pm: **Tea/Coffee/Posters**

7:00 - 8:30pm: **Beverages & Dinner**

October 19, Wednesday

Chair: Arati Ramesh

- 9:30am: Marvin Whiteley, Biogeography of in vivo microbial biofilms
- 10:00am: Subhadeep Chatterjee, Phenotypic heterogeneity in bacterial quorum sensing: cooperation and individuality in social structure of bacteria

10:30 - 11:30am: **Tea/Coffee/Posters**

Chair: Sunil Laxman

- 11:30am: Randal Halfmann, Reciprocal cheating drives epigenetic switching of facultative multicellularity
- 12:00pm: William Harcombe, Systems biology and eco-evolutionary feedbacks in microbial communities
- 12:30pm: Poster prizes and Closing

12:45 - 2:00pm: **Lunch**

Speaker Abstracts

- Subhadeep Chatterjee, Centre for DNA Fingerprinting and Diagnostics, Hyderabad, India.
  Phenotypic heterogeneity in bacterial quorum sensing: cooperation and individuality in social structure of bacteria. Bacteria coordinate their social behavior in a density dependent manner by production of diffusible signal molecules by a process known as quorum sensing (QS). It is generally assumed that in homogenous environments and at high cell density, QS synchronizes cells in the population to perform collective social tasks in unison which maximize the benefit at the inclusive fitness of individuals. However, evolutionary theory predicts that maintaining phenotypic heterogeneity in performing social tasks is advantageous as it can serve as a bet-hedging survival strategy. Using Pseudomonas syringae and Xanthomonas campestris as model organisms, which use two diverse classes of QS signals, we have shown that two distinct subpopulations of QS-responsive and non-responsive cells exist in the QS-activated population. Our work has also elucidated how fine tuning of QS regulatory circuits in closely related members of the Xanthomonas group of phytopathogens contribute to their lifestyle change inside the host. Overall, these results support the model that bacteria maintain QS-responsive and non-responsive subpopulations at high cell densities in a bet-hedging strategy to simultaneously perform functions that are both positively and negatively regulated by QS to improve their fitness in fluctuating environments. We are also trying to understand how the QS-mediated social structure and individuality in the bacteria coexists to improve their fitness in fluctuating environments.

- Dipankar Chatterji, Indian Institute of Science, Bangalore, India.
  Second Messengers (p)ppGpp and Cyclic di-GMP mediated regulation of Cell Shape, Cell Division and Antibiotic Sensitivity in Mycobacterium smegmatis. Quorum Sensing, a cell to cell communication phenomenon, is involved in modulating the social behavior of bacteria. Nucleotide based second messengers like (p)ppGpp and c-di-GMP are known to regulate such communication in mycobacteria. (p)ppGpp is synthesized by bacteria to face any kind of stress; while the signalling nucleotide c-di-GMP is synthesized principally to switch from motile (planktonic) to sessile (biofilm) life style. We investigated the effect of disrupting (p)ppGpp and c-di-GMP signalling on the antibiotic sensitivity in M. smegmatis. Using Phenotype Microarray (PM) technology, the growth of rel and dcpA knock out strains was compared to those of the wild-type and respective complemented strains in 240 different antimicrobials. It was found that the knockout mutants displayed enhanced

survival in the presence of multiple antibiotics. The PM data was corroborated by the independent determination of minimum inhibitory concentrations of seven different antibiotics. Microscopy analyses revealed that the rel and dcpA strains are elongated, multinucleate and multiseptate in M. smegmatis. The higher levels of (p)ppGpp and c-di-GMP caused M. Smegmatis assume coccoid morphology. The overproduction of (p)ppGpp and c-di-GMP, achieved through overexpression of Rel and DcpA proteins, encased the overexpression strains relOE and dcpAOE in a biofilm like matrix. Literature cited: (1) Gupta et al., Appl.and Environ.Microbiol (2015)81,2571; (2) Gupta et.al., J. Bacteriol. (2016)198,1414; (3) Krishnan et.al., Mol. Microbiol.(2016)102,168

- Alessandro Esposito, University of Cambridge, UK.
  A 'systems biology' of cell fate: insights into the biochemical determinants of cellular decisions and cell-to-cell variability. Cellular decisions exhibit significant cell-to-cell variability caused by non-genetic determinants that often obstacle our capabilities to model biological systems accurately. For instance, in the face of an identical stimulus, non-genetic heterogeneity can manifest itself as broad distributions in the timing at which individual cells respond to the stimulus or as distinct choices of cell fates (e.g., self-renewal versus differentiation or survival versus cell death). These differences are rooted in the distinct responses that biochemical networks underlying cellular decisions exhibit. Therefore, I will argue for the necessity to complement ensemble measurements (e.g., genomic and proteomics) with single cell non-invasive techniques thatby preserving the identity and integrity of cellsenable to establish causal relationships between biochemical determinants, cellular choices, their heterogeneities and context-dependencies. I will illustrate the most recent work on single cell systems biology of cellular decisions, including novel methodologies and applications dedicated to the imaging of biochemical network activities and their control by Optogenetics means. More specifically, I will illustrate the role of biochemical networks in the maintenance of cellular checkpoints during DNA damage with a perspective on how we may be able, in the future, to follow complex cellular and biochemical processes in living three-dimensional tissue. Our aim is to determine how oncogenes rewire signalling networks (e.g. RAS and RAS-dependent signal transduction networks) to alteroften in subtle wayscell fate decisions therefore contributing to tumorigenesis. Cell signalling, cell fate choices and the process of transformation exhibit significant variability within identical clones. Therefore, we envisage that a single-cell systems biology approach to study signalling networks underlying cellular transformation will enable us to explore cell-to-cell variability in the process of oncogene-induced transformation and to investigate the role of non-genetic heterogeneity during early oncogenesis.

- Glen D'Souza, EAWAG, Zurich, Switzerland.
  Experimental evolution of metabolic dependency in bacteria. Bacteria frequently lose biosynthetic genes and functions, thus making them dependent on an environmental uptake of the corresponding metabolite. Despite the ubiquity of this genome streamlining, it is generally unclear whether the concomitant loss of biosynthetic functions is favored by natural selection or rather caused by random genetic drift. Here we demonstrate experimentally that a loss of metabolic functions is strongly selected for when the corresponding metabolites can be derived from the environment. Serially propagating replicate populations of the bacterium Escherichia coli in amino acid-containing environments revealed that auxotrophic genotypes rapidly evolved in less than 2,000 generations in almost all replicate populations. Moreover, auxotrophs also evolved in environments lacking amino acids yet to a much lesser extent. Loss of these biosynthetic functions was due to mutations in both structural and regulatory genes. In competition experiments performed in the presence of amino acids, auxotrophic mutants gained a significant fitness advantage over the evolutionary ancestor, suggesting their emergence was selectively favored. Interestingly, auxotrophic mutants derived amino acids not only via an environmental uptake, but also by cross-feeding from coexisting strains. Our results show that adaptive fitness benefits can favor biosynthetic loss-of-function mutants and drive the establishment of intricate metabolic interactions within microbial communities.

- Yuma Fujimoto, University of Tokyo, Japan.
  Hierarchical Prisoner's Dilemma in Hierarchical Public-Goods Game. Dilemma in cooperation is one of the major concerns in game theory. In public-goods game, each individual pays a cost for cooperation or not for defection, while receives reward from the collected cost in a group. Thus, defection is beneficial for each individual, while cooperation is beneficial for the group. Now, groups (say, countries) consisting of individual players also play games. To study such a multi-level game, we introduce a hierarchical public-goods (HPG) game in which two groups compete for nite resources, by utilizing costs collected from individuals in each group. From analysis of this HPG game, we found the hierarchical Prisoners Dilemma, in which groups choose defective policy (say armament) as Nash strategy to optimize each groups benefit while cooperation optimizes the total benefit. On the other hand, for each individual within a group, to refuse cost (say tax) is Nash strategy, which, turns to be cooperation policy for group, thus leading to hierarchical dilemma. Here, the reward of one group receives increases with the population, as the collected cost does. In spite of it, we find existence of an optimal group size that maximizes its payoff. Furthermore, when the population

asymmetry between the two groups is large, a smaller group will choose cooperation policy (say disarmament), to avoid excessive response from the larger group, which leads to the resolution of the Prisoners Dilemma between the groups. HPG model can be applied to, not only animal society, but conflict-cooperation problem in the multicellularity, that is also discussed.

- E. Peter Greenberg, University of Washington, Seattle, USA.
  Communication, cooperation and conflict among cells of the pathogenic bacterium Pseudomonas aeruginosa. Acyl-homoserine lactone quorum sensing circuits allow cell-cell communication in many species of Proteobacteria. There are two acyl-homoserine lactone quorum-sensing (QS) circuits in Pseudomonas aeruginosa, LasR-I and RhlR-I. LasR activates RhlR-I and thus serves as a master QS regulator. Together, these circuits activate hundreds of genes, many of which code for production of secreted or excreted factors. These factors are considered public goods and can be shared among individuals in the group. P. aeruginosa requires QS-activated secreted proteases for growth on casein as the sole carbon and energy source, and over time LasR mutants emerge and invade populations of LasR-intact cooperators. These mutants are social cheaters that reap the benefit of the cooperator-produced proteases without being burdened by the metabolic costs of public goods production. We, and others, have observed that under certain conditions these social cheaters come to an equilibrium with cooperators and do not cause the population to collapse, as would occur if the number of cooperators fell below the quorum threshold. We have probed the molecular basis of the equilibrium. We hypothesized that cooperators can police cheaters by intoxicating them. RhlR activates genes coding for production of several reactive toxic compounds, including peroxides and hydrogen cyanide. We believe RhlR also induces immunity to these factors. We reasoned that RhlR-activated genes allow P. aeruginosa cooperators to police cheaters, and that LasR+, RhlR- cooperators are policing mutants. Policing mutants will not have a capacity to limit invasion by LasR-, RhlR- cheaters and we expect population crashes for failure to achieve a quorum. This prediction was borne out by experiments where LasR-, RhlR- social cheaters rapidly arose to high frequencies and caused a population crash. We then showed that policing involves cyanide production by wildtype P. aeruginosa by following social evolution in an HcnC- cooperator, which cannot synthesize hydrogen cyanide. Like the RhlR- cooperators, populations of HcnC- cooperators were overrun by LasR mutants. To test the hypothesis that wildtype P. aeruginosa and LasR- cheaters coexist by virtue of RhlR-activated toxin secretion, and not a direct cell-cell interaction, we used dialysis membranes to separate LasR+, RhlR- cooperator populations from either LasR+,, RhlR+,or HcnC- cooperators. Over 48 hours, the cell yields of LasR+, RhlR- cooperators with the wildtype were two logs lower than when they were when grown

with the HcnC-cooperators. Our studies support the notion that groups of cooperating P. aeruginosa can police social cheaters and we provide a plausible mechanism for this phenomenon.

- Duncan Greig, Max Planck Institute for Evolutoinary Biology, Plön, Germany.
  Sexual signalling in yeast. Mating is a well-studied form of cooperation. Prior to mating, yeast cells court each other by sending and receiving signals in the form of short peptide pheromones. Cells that do not produce pheromone fail to mate. Information about potential mates is conveyed by both the quantity of a pheromone and its amino acid sequence. Ill talk about experiments that manipulate both these factors, showing what yeast look for in a mate. Ill talk about theory that explains the physiological constraints that limit just how sexy a yeast cell can be.

- Randal Halfmann, Stowers Institute for Medical Research, Kansas City, USA.
  Reciprocal cheating drives epigenetic switching of facultative multicellularity. Cooperation between genetically identical cells is the basis of multicellularity. Despite an extensive theoretical framework, the molecular mechanisms that engender the evolution of cooperation remain enigmatic. We demonstrate that prions and other switch-like mechanisms that regulate yeast cell surfaces suffice to create stable divisions of labor within genetically homogeneous populations. These switches produce phenotypic granularity, with discrete subpopulations differing according to whether or not they express the adhesin, Flo11. Cells that express Flo11 exhibit a wasteful metabolic strategy in which tremendous resources are expended on the production of a secreted lubricant that enables them to slide into uncolonized territory. Doing so allows them to secure more than their fair share of common resources, albeit at the expense of the more-efficient, non-Flo11 expressing cells and therefore to the detriment of the population as a whole. Counter to theoretical expectations, we observe that non-Flo11-expressing cells nevertheless persevere, in part because they too are mobilized by the surfactant produced by Flo11-expressing cells. Moreover, they exhibit a conservative metabolic strategy that takes advantage of the nutritional niche created in the wake of Flo11-driven colonization. Thus, "cheating" by one cell type entails the production of a new public good, which is in turn exploited by the second cell type. Epigenetic switching between the two cell types enables an individual genome and each of the individual genes that promotes switching to benefit from both the original and reciprocal forms of cheating, resulting in a population that is relatively resistant to invasion by unrelated individuals.

- William Harcombe, University of Minnesota, St. Paul, USA.
  Systems biology and eco-evolutionary feedbacks in microbial communities. Conflict and cooperation between bacterial species drive the composition and function of microbial communities. Stability of these emergent properties will be influenced by the degree to which species interactions are robust to genetic perturbations. We use genome-scale metabolic modeling to computationally analyze the impact of genetic changes when Escherichia coli and Salmonella enterica compete, or cooperate. We systematically knocked out in silico each reaction in the metabolic network of E. coli to construct all 2,583 mutant stoichiometric models. Then, using a recently developed multi-scale computational framework, we simulated the growth of each mutant E. coli in monoculture and in the presence of S. enterica. The type of interaction between the species was set by modulating the initial metabolites present in the environment. We found that both the species ratios and community productivity are most robust to genetic perturbation when the two species cooperate. Additionally, the number of mutations that have a substantial effect is lower when the species cooperate than when they are competing. These results highlight the utility of connecting metabolic mechanisms and studies of ecological stability. Cooperation and conflict alter the connection between genetic changes and properties that emerge at higher levels of biological organization.

- Rupinder Kaur, Centre for DNA Fingerprinting and Diagnostics, Hyderabad, India.
  Analysis of Candida glabrata-macrophage interaction. Invasive mycoses pose a serious therapeutic challenge and resistance of fungal pathogens to current antifungal targets is a major clinical issue. Candida species are the most common cause of invasive fungal infections with Candida glabrata accounting for up to 30% of total Candida blood stream infections. C. glabrata is also the second to fourth most frequently isolated Candida species from Intensive Care Unit patients depending upon the geographical location. Treatment of C. glabrata infections is particularly challenging as C. glabrata inherently is less susceptible to widely used azole antifungals. Our current research is focused on delineating the strategies that C. glabrata employs to acquire resistance to antifungals and survive antimicrobial environment of the mammalian host. Towards our goal, we have screened a mutant library, representing 50% of the C. glabrata genome, for altered fitness in macrophages, and identified a set of 56 genes that is required for survival and/or proliferation of C. glabrata cells in human THP-1 macrophages. These genes are implicated in diverse biological processes including chromatin and cell wall organization, signal transduction and Golgi vesicle transport. Molecular and biochemical characterization of identified factors has revealed that the communication between C. glabrata and macrophages is multifactorial in

nature. These findings along with an essential role for the C. glabrata class III phosphoinositide 3-kinase (PI3K) in interaction with host cells will be presented.

- Sandeep Kumar, Indian Institute of Technology Bombay, Mumbai, India.
  Microenvironmental regulation of intra-tumor heterogeneity. Heterogeneity within single tumor population referred as intra-tumor heterogeneity has been observed in many experimental studies and has been implicated in development of multi-drug resistance, increased cancer aggressiveness, and metastasis organotropism. Understanding the mechanism(s) that induces this heterogeneity can significantly improve our understanding of cancer progression and that knowledge can be used to identify novel cancer drugs and therapies. However, due to involvement of multiple length/time scale processes and complex cell-cell and cell-surrounding interactions, it is very difficult to study the emergence of intra-population heterogeneity within tumor population in purely experimental framework. To address this, we are using multi-scale computational modeling approach augmented with experimental studies to understand the emergence of phenotypical heterogeneity like heterogeneity in cell size/shape, migration, and, its implication in cancer metastasis. Specifically, we are using cellular Potts model (CPM) and cellular automata (CA)-based in silico study to understand how remodeling of extracellular matrix (ECM) – as observed during cancer progression can alter the tumor population composition. During this meeting, I would like to discuss about some of our recent findings where we are studying how the confinement geometry, cell-cell adhesion and cell migration can cause the emergence of intra-tumor heterogeneity. I will also discuss about some of the relevant experimental observations pertaining to populations of HT-1080, MCF7 and MDA-MB-231 cells.

- Tina Mukherjee, Institute for Stem Cell Biology and Regenerative Medicine, Bangalore, India.
  Maintaining Myeloid Cell Fate and Function During Drosophila Hematopoiesis Through Stress-Sensing Pathways. Drosophila hematopoiesis gives rise to stem-like myeloid progenitor cells that differentiate into macrophages or platelet like blood cells. The development of the myeloid system relies on utilizing both systemic and locally derived signaling cues for maintenance of myeloid precursor cells and their subsequent differentiation into mature cells. As we learn more about this system, it is apparent that blood cells rely on utilizing stress-sensing molecules such as ROS, NO, adenosine and other small metabolites for development, maintenance and differentiation into mature cell types. The cues are generated by progenitor/differentiating cells themselves, or are neuronally derived upon sensory or nutritional stimulation. What is fascinating is that these stress molecules

perform developmental roles and are also coopted by the myeloid system to combat stress scenarios such oxidative stress, hypoxia, starvation or infection. The dual regulation by such metabolites in myeloid development and stress response provides an interesting paradigm to explore the importance of stress sensing in myeloid development and function. In line with this idea, our latest findings elucidate how GABA, a well characterized neurotransmitter functions as a signaling ligand to control myeloid progenitor development and the same molecule is co-opted by blood cells as a metabolite to overcome immune challenges by parasitic wasps. The talk will dwell into some of these recent findings and finally elucidate the importance of odor perception in regulating hematopoiesis via GABA.

- Vidyanand Nanjundiah, Centre for Human Genetics, Bangalore, India.
  Co-authors: Santosh Sathe(1), Bandhana Katoch(1), Chhavi Chawla(1), Viraj Torsekar(1), Lee Altenberg(2)
  (1) Centre for Ecological Sciences, Indian Institute of Science; (2) University of Hawaii, USA
  Cooperation via competition in groups of free-living amoebae. Cellular slime mould amoebae switch from solitary to cooperative social behaviour when starved. As part of the process, a substantial number of cells die (as stalk), apparently in order to enhance the reproductive fitness of the rest (as spores). The relative proportions of stalk and spore are approximately the same in clonal and genetically heterogeneous groups. As a first step towards understanding the principles that underlie the allocation of cells to the spore and stalk pathways, we have studied two-way and three-way mixes between genetically distinct wild-type strains of various Dictyostelium species. In heterogeneous pairwise mixes, there is often a bias in the relative contribution of the two strains to the spore population, and the bias can vary depending on the proportions in which cells were mixed as amoebae. The extent of bias decreases markedly when a third strain is present, which adds to the evidence that highly nonlinear interactions lie behind differentiation into a spore or stalk cell. We suggest that pre-aggregation cellular quality, and post-aggregation competition for the ability to complete a life cycle via the spore route, are the main factors responsible for multicellular cooperation.

- Maithreyi Narasimha, Tata Institute of Fundamental Research, Mumbai, India.
  Multicellular sensing and the spatial patterning of tissues: competition and cooperation in a Drosophila epithelium. Tissue sculpting during development and upon wounding relies on dynamic and heterogeneous cell behaviors that need to be coordinated in space and time. The origin of these heterogeneities and mechanisms that underlie their

coordination remain poorly understood. We have investigated both using Drosophila dorsal closure, a model for wound healing and epithelial fusion. In my talk I will describe our attempts to understand the molecular and physical bases of stochastic and collective cell behaviors in the amnioserosa and the mechanisms that underlie their coordination to ensure stereotypical and robust tissue dynamics. I will present evidence that competitive interactions at the molecular and cellular scale underlie stochastic cell behaviours and cooperative interactions underlie collective behaviours. I will describe the nature of these interactions and suggest mechanisms that enable the coordination of these behaviours.

- Dasaradhi Palakodeti, Institute for Stem Cell Biology and Regenerative Medicine, Bangalore, India.
  Planarian Schmitdea meditteranea: a regenerative model system to study polarity and tissue organization critical for multicellularity. Planarians are bilateral symmetrical, fresh water platyhelminths, which emerged as a tractable model system to study regeneration. Regeneration is a complex process, which involves formation of new cells facilitated by stem cells in communication with its niche followed by remodeling of old and new tissue to form functional organ. Planaria in particular is an interesting model because of its capacity to regenerate whole body from tiny piece of tissue. The prerequisite for the formation of new tissue at a right place and right size is determined by the ability of the animal to establish body axis. In the lab, we study the brain regeneration because of the availability of the markers, easy of conducting functional assay, distinct spatial organization and presence of various cell types (Neural subtypes). Here, I will present the work, which show the critical role of microRNAs in regulating neural specificity, brain organization and neural wiring during planarian brain regeneration. I will also present the preliminary data, which demonstrates the gradient-based regulation of tissue formation and the role of post-transcriptional regulators in establishing the gradients during planarian regeneration.

- Samay Pande, Institute for Integrative Biology, ETH Zurich, Switzerland.
  Positive effects of natural within-group diversity on spore productivity of social bacteria. Myxococcus xanthus is a predatory soil bacterium that exhibits vegetative growth and multicellular fruiting body development as two distinct life history stages. It was previously demonstrated that genetically heritable social variation within fruiting bodies is common. However, factors that affect the maintenance of such natural within-group variation remain unknown. We tested the effects of within-group diversity on both total-group and individual-strain spore productivity using eight representative isolates derived from

a single natural fruiting body. Interestingly, total productivity of chimeric populations containing all eight isolates was higher than expected from monoculture controls. Further analyses suggest that chimerism does not stimulate total productivity by affecting just one or two isolates, but rather a majority of the eight isolates respond positively to chimerism. We also tested for pair-specific interactions by performing all possible pairwise-mixes. In these experiments, positive responses to mixing were more common than negative ones. Finally, we show that positive effects of mixing several isolates on total group productivity are specific to isolate sets that derive from the same fruiting body group, whereas effects of chimerism on total productivity among isolates from different fruiting bodies were negative, and increasingly so as a function of mean distance between the soil sites from which fruiting bodies were derived. Our study shows that chimerism among distinct but closely related individuals from the same natural social-group can enhance the absolute fitness of a majority of group members. These studies also show the importance of incorporating information on spatial locations of individuals for analyses of interactions.

- Ramya Purkanti, Simons Centre for the Study of Living Machines, National Centre for Biological Sciences, Bangalore, India.

  Novel intracellular compartments in hybrid yeast. We are interested in the ancient origins of the eukaryotic compartmentalized cell plan. Eukaryotes arose from a prokaryote-like ancestor probably during the global oxygenation event 2.5 billion years ago which evolved into the common ancestor of living eukaryotes dated around 1.8 billion-years ago. The shared features of all extant eukaryotes suggest that this last eukaryotic common ancestor (LECA) was already a complex unicellular organism with quintessentially eukaryotic features: a nucleus, mitochondria, compartmentalized organelles, cytoskeletal machinery, and vesicle traffic. In the absence of any intermediate proto-eukaryotic forms, the challenge is to understand how LECA arose from a prokaryote-like ancestor. The endomembrane system of eukaryotes consists of membrane bound compartments which exchange matter amongst themselves by means of vesicles. To explain their origins, the autogenous theory of compartmentalization has been proposed (Dacks & Field, 2007). Briefly, it states that organellar diversification is caused by the duplication and divergence of compartment's "identity-encoding" genes, an idea which issupported by biophysical models of endomembrane trafficking (Ramadas & Thattai, 2013). We have asked which biological scenario would result in concurrent duplication of the entire set of identity-encoding genes while providing opportunity for loss of cross-interactions. Inter-species hybridization fit the bill. Our study of one such inter-species hybrid, Saccharomyces pastorianus, whose parents diverged apart for 20 million yrs, suggests novelty in endomembrane

trafficking of the hybrid in terms of gene regulation and ultrastructural complexity.

- Aarthi Ravikrishnan, Indian Institute of Technology Madras, Chennai, India.
  Rational development of microbial consortia for metabolic engineering. Microorganisms are ubiquitous and rarely occur in isolation. They always tend to form communities, where they exhibit different types of interactions such as mutualism, commensalism and predation. A consortium enjoys division of labour and provides a wider scope to leverage the joint metabolic capabilities of the organisms vis--vis a single organism. Although there are several naturally occurring microbial communities, their systematic exploitation through rational design and metabolic engineering has rarely been performed. Consortia have been chosen randomly in the past for carrying out fermentations, particularly in wastewater treatments and fermented food products, but a framework to design a well-defined consortium by exploiting the metabolic diversity is still lacking. Methods to characterise and define consortia for industrial applications is still in infancy. To improve our understanding of these relationships, it is imperative to focus on the development of systems-level modelling oriented towards communities. Towards this end, we have designed an algorithm based on principles from graph theory that can be used for designing industrially useful consortia. This algorithm predicts the potential metabolic interactions between a given set of microorganisms, given the source (s) and the target (s) of interest. Results from the algorithm are used to rank the combinations to determine the best consortium. We applied our algorithm to determine the set of microorganisms that can lead to enhanced bioethanol production while being together in a consortium and also predict the metabolic interactions that happen between these organisms. Currently, we are trying to experimentally verify some of the predictions of our algorithm, by understanding how the microorganisms interact while being together in a consortium. Once established, this algorithm can be used for generating a number of productive consortia for the production of a wide array of compounds from biofuels to pharmaceuticals. This would pave way for systematically analysing and harnessing the full potential of microbial consortia.

- Szabolcs Semsey, University of Copenhagen, Denmark.
  Birth and life of (p)ppGpp induced persisters. Bacterial persistence is a common phenomenon in isogenic populations of antibiotic-sensitive bacteria. Persister cells are slow-growing or non-growing cells that are transiently multidrug tolerant. The bacterial stress alarmone ppGpp plays a central role in the emergence of persister cells, by activating toxin-antitoxin systems

through a regulatory cascade. However, persistence remains a stochastic phenomenon even if this regulatory cascade is impaired or if ppGpp synthesis is enhanced. In order to address the source of stochasticity, we have designed a system where intracellular ppGpp levels and the activity of toxin-antitoxin systems can be followed in single cells using fluorescent reporters. We find that persister cells are solitary and maintain a high level of transcription of TA moduls. Our results also suggest that the source of stochasticity in persister formation originates from a process downstream of ppGpp in the regulatory cascade.

- Wenying Shou, Fred Hutchinson Cancer Research Center, Seattle, USA.
  Rapid evolution of metabolic dependence. Microbes are often found to have lost their ability to make essential metabolites (auxotrophs) and instead rely on other individuals for these metabolites. How might metabolic dependency evolve to be so common? When microbes live inside a host (endosymbionts), amply host metabolites support auxotrophic endosymbionts. If the host transmits only a small number of endosymbionts to its offspring, then auxotrophic endosymbionts can rise to high frequency simply by chance. On the other hand, auxotrophs have also been observed in abundant free-living bacteria found in ocean water where nutrient supply is low. How might auxotrophs rise to an appreciable frequency in a large population when nutrient supply is low? We found that nutrient limitation can facilitate the evolution of certain types of metabolic dependency. Metabolic interactions can in turn shape spatial organization of microbial communities. Rapid evolution of metabolic dependency can contribute to complex interactions in microbial communities, and help explain the difficulty of culturing microbes in isolation.

- Varsha Singh, Indian Institute of Science, Bangalore, India.
  Swarming in Pseudomonas aeruginosa: Why and how? Bacteria have been traditionally regarded as solitary individuals in a planktonic phase. In the past few decades it has increasingly become clear that many cells can come together to form multi cellular communities in the face of competition, predation and other unknown factors to ensure survival of the species. One such multi cellular community is called biofilm. This is a surface associated aggregate of mostly sessile cells covered in matrix of secreted exopolysaccharides. Swarming population of bacteria is a quorum dependent community but comprises motile bacteria that show rapid and coordinated movement over semisolid surfaces. Pseudomonas aeruginosa (PA) is a ubiquitous environmental organism that is also an opportunistic human pathogen in immune compromised individuals with cystic fibrosis, and in burn wounds or diabetic foot ulcers. When solitary, PA can swim, twitch or slide, but swarms or forms biofilm when in a community and has

reached quorum. The swarming patterns of PA comprise dendrites which branch at regular intervals reminding one of fractal patterns. Since no two species of swarming bacteria produce similar patterns, we are motivated to understand if motives and mechanisms of swarming are distinct in these bacteria. Using PA as a model swarming bacterium, we use both genetic and modelling approaches to understand the why and how of swarming.

- C. S. Srinandan, SASTRA University, Tanjavur, India.
  Emergence of heterogeneity in a bacterial population. Fluctuating environmental conditions or stochastic gene expression could cause emergence of heterogeneity in a bacterial population. This could also be a bet-hedging strategy of the population. In this study, we observed a pattern of extrapolymeric substance (EPS) producing, non- producing and hyper-swarming cell types of Uropathogenic E.coli (UPEC) colony on Congo red agar (CRA) plate. UPEC is the causative agent in majority of urinary tract infections (UTIs) throughout the world. During infection, persistent, biofilm forming and antibiotic resistant sub-populations emerges and these could be phenotypic or genotypic in nature. We characterized the sub-populations of the UPEC colony for their other phenotypic traits and the susceptibility towards environmental stresses like the effect of antibiotics, chlorine, heat, etc. The overall bet- hedging strategy of the UPEC population will be discussed.

- Joan Strassmann and David Queller, Washington University, St. Louis, USA.
  Social behavior and mutualism in the social amoeba Dictyostelium discoideum and its bacterial symbionts. With microbial studies we can see how well theories of social behavior derived from organisms with brains apply to organisms where cell adhesion, receptors, and secretions prevail. Furthermore, we can test specific predictions of kin selection and mutualism using experiments, experimental evolution, and genomics. Here we explore the behavioral ecology of social amoebae, introduce some of the genes behind these interactions, and delve into some of the complex interactions between amoebae and bacteria. Are the bacteria a disease, a crop, or a weapon?

- Sine Svenningsen, University of Copenhagen, Denmark.
  Quorum sensing control of phage-bacterial interactions lessons learned from Escherichia coli and Vibrio anguillarum. The goal of our research is to clarify the role of bacterial cell-cell signaling, called quorum sensing, in shaping the interactions between bacteria and the viruses that prey on them, bacteriophages. Since bacteriophages

require a bacterial host in order to multiply, it follows that the abundance of bacteriophages is tied to the abundance of host cells. Therefore, we suggest that quorum-sensing signals, which confer information about the types and numbers of bacteria present in a given environment, may also serve as a proxy for information about the potential bacteriophage predation pressure. In support of this hypothesis, we have shown that quorum sensing is involved in regulating bacterial susceptibility to bacteriophages both in the classic model system of Escherichia coli K-12 and bacteriophage , and in an environmental isolate of the fish pathogen Vibrio anguillarum. In the latter case, we demonstrated that Vibrio anguillarum employs quorum-sensing information to choose between two complementary antiphage defense strategies.

- Mukund Thattai, National Centre for Biological Sciences, Bangalore, India.
  Turbocharged evolution in a bacterial arms race. Satoshi Omura made his 2015-Nobel-Prize-winning discovery on golf course: he isolated a soil-dwelling bacterium that secreted avermectin, a drug which revolutionised the treatment of parasitic diseases. Such stories are surprisingly common: we find potent bioactive compounds in almost any niche that has a rich microbial ecology. This is because bacteria are engaged in an ongoing arms race to generate novel molecules, to be deployed as weapons against enemies or as signals among friends. Just as our immune system uses a combinatorial strategy to generate antibodies, bacteria could use combinatorial chemistry to synthesise useful molecules. I will discuss an amazing set of bacterial proteins called polyketide synthases (PKSs) that actually use such a strategy. These enzymes produce compounds like the anti-parasitic avermectin, the antibiotic erythromycin, and the immunosuppressant rapamycin. We have shown that the unusual structure of PKSs allows them to convert the random process of DNA recombination into an efficient strategy to explore chemical space. PKSs thus appear optimised not to produce a single chemical product, but rather to search for new products: they are the innovation engines that keep bacteria one step ahead of the competition.

- Sriram Varahan, Institute for Stem Cell Biology and Regenerative Medicine, Bangalore, India.
  Metabolic Regulation of Fungal Morphogenesis. Unicellular organisms employ multiple strategies to adapt to changing environments around them. Once such strategy deployed unicellular organisms is the ability to form complex multicellular communities. During this transition from a unicellular form to a multicellular community which is often reversible, cells usually undergo division of labor wherein different cells of the community perform distinct specialized functions. This process of Cellular

specialization is critical for the survival of these multicellular complex communities. Fungal morphogenesis is one such process wherein fungal cells can reversibly switch from a sessile unicellular state to numerous types of facultative multicellular forms including biofilms (liquid medium), rugose mats (solid medium) hyphal/pseudohyphae, flocculation etc. to name a few. These morphogenetic changes allows the fungi to quickly adapt to varying environmental conditions and even thrive in them. For example, Candida albicans, an opportunistic pathogen that causes a variety of human infections can reversibly switch between its yeast like form (non-pathogenic) and its hyphal form (pathogenic) when it enters into a vertebrate host. Several studies have shown that this morphogenesis is crucial for C. albicans to cause successful infections in a host. Candida glabrata has recently emerged as the second leading cause of infective candidiasis and forms robust biofilms on both biotic as well as abiotic surfaces to cause persistent infections. Pathogenic isolates of C. glabrata forms rugose mats on solid surfaces compared to the smooth colonies formed by the non-pathogenic isolates. Although many genes involved in these morphogenetic behaviors are known, we lack an understanding of the driving principles behind such behavior. We hypothesize that specific metabolic demands of these aforementioned fungal pathogens in a particular host niche are primary determinants of fungal morphogenesis, with key metabolic events determining the ability to switch to complex communities. Saccharomyces cerevisiae can serve as an excellent model for understanding these metabolic regulations of fungal morphogenesis as it can reversibly switch from a single-cell form to multiple distinct types of complex communities under specific nutrient conditions. These complex communities formed by S. cerevisiae show spatial organization, morphological differences, and can survive harsh environmental conditions. Such features in S. cerevisiae includes flocculation, biofilm formation, and invasive or pseudohyphal growth of cells. We therefore propose to address this hypothesis by using biofilms with rugose morphology (BRM) and pseudohyphal formation as outputs of fungal morphogenesis. Our initial findings show that S. cerevisiae can form robust BRMs when grown at low glucose conditions, in contrast to the uniform, smooth colonies they form when glucose is abundant. We also have discovered gluconeogenesis to be a critical process for this morphogenetic change since the deletion of the gene encoding a key gluconeogenic enzyme, PCK1 (Phosphoenol pyruvate carboxykinase) completely abrogates the BRM phenotype. We also observe that the availability of free amino acids are critical for the formation of biofilms with rugose morphology.

- Catherine Wakeman, Texas Tech University, USA.
  Factors driving cooperativity versus competition in cystic fibrosis pathogens. Microorganisms demonstrate numerous types of community behaviors that range from cooperative to competitive interactions. Cooperative behaviors

include biofilm formation in which microorganisms work together to create a barrier that is capable of protecting against various environmental insults. However, most microbes also demonstrate competitive behaviors ranging from superior nutrient acquisition capabilities to active killing of competitors. These behaviors are often influenced by environmental nutrient fluctuations. The interactions between bacterial pathogens surviving within chronic polymicrobial infections are of particular interest to many researchers in both basic and translational sciences. Pseudomonas aeruginosa and Staphylococcus aureus are well-studied opportunistic pathogens known to occupy sites of polymicrobial infection within the cystic fibrosis lung. The ability of P. aeruginosa to outcompete and kill S. aureus under standard laboratory conditions has been well established. However, recent data has shown that in the presence of a metal-sequestering innate immune protein, P. aeruginosa does not elaborate its antimicrobial mechanisms and instead co-exists with S. aureus. I seek to determine the potential benefits that P. aeruginosa gains from a cooperative lifestyle in the presence of S. aureus during infection. Additionally, I have uncovered evidence that S. aureus can outcompete P. aeruginosa under certain conditions. I seek to elucidate the antimicrobial capacity of S. aureus and understand the inherent resistance mechanisms employed by P. aeruginosa under standard laboratory conditions.

- Marvin Whiteley, The University of Texas at Austin, USA.
  Biogeography of in vivo microbial biofilms. Biogeography is the study of the spatial distribution of species within an ecosystem across space and time. The field of microbial ecology has long focused on the micron-scale biogeography and its consequences in polymicrobial communities. For example, studies of the leaf-associated microbiota of plants show that the arrangement of single cells in structured polymicrobial communities is responsible for desiccation tolerance, persistence, and resistance to invading species. The biogeography of human-associated polymicrobial communities, including those in disease, has not been studied to similar depth. While it is now widely accepted that most polymicrobial communities living in natural environments, including the human body, form spatially structured consortia, the mechanisms used by microbes to form these communities is not understood. Here I will discuss recent in vivo evidence supporting this idea using multiple models of infection, and the development of a versatile experimental framework for modulating microbial biogeography on the micron-scale.

- Gerard Wong, University of California Los Angeles, USA
  Memory, surface sensing, and behavior adaptation during the first 20 generations of bacterial

life on a surface. Bacterial biofilms are integrated communities of cells that adhere to surfaces and are fundamental to the ecology and biology of bacteria. The accommodation of a free-swimming cell to a solid surface is more complex than modulation of cell adhesion. We investigate the interplay between motility appendages, molecular motors, hydrodynamics, and exopolysaccharide production near the surface environment using state of the art tools from different fields that are not usually combined, including theoretical physics, community tracking with single cell resolution, genetics, and microbiology. Themes such as surface sensing, multi-generational signaling via secondary messengers, subsequent downstream motility consequences, and the subsequent onset of microcolony organization via interactions between appendages and exopolysaccharides will be discussed.

Poster Abstracts

1. **Understanding the reproducible heterogeneity of T cell populations.**
Donepudi Raviteja and Ramakrishna Ramaswamy,
University of Hyderabad, India, and Jawaharlal Nehru University, Delhi, India.

At population level, the patterns of T cell response for a given infection is highly reproducible. But the mechanism at single-cell level for such reproducibility is not clearly known. Single cell lineage studies showed that naive T cells produce both effector and memory T cells. In-vivo lineage tracing experiments [1, 2] demonstrate that expansion of identical CD8+ T Cells show heterogeneity in both clonal family sizes and marker distribution. In short, one study concluding against the asymmetric division as the solo driver and another suggesting a linear developmental path that progresses from slowly proliferating long-lived to rapidly expanding short-lived subsets. And the reproducibility of the CD8+ T Cells response is ascribed to the population averaging of the seemingly stochastic underlying differentiation fates. However, in vitro experimental evidence does not overwhelmingly support any single developmental pathway. To explore if other types of models will explain the observations better, I, in this work, developed a branching process model at the cellular level, with variedly inherited and stochastically distributed factors and then to build a population. The rules of branching process define the heterogeneous structure of the population and the properties of inheritance of the factors define the way they are distributed between the cells. Branching process model used in this work is the modified cyton model defined in the context of B Cells expansion [3] with two factors, one for propensity to divide (R) and the other for time to die (T), which are

stochastically inherited at each cell division. And the model includes three markers which stochastically inherit at each cell division, but have different rates of accumulation. Preliminary results suggest that population expanded from this model qualitatively fit the experimental results. [1] Gerlach et.al., 2013, Heterogeneous differentiation patterns of individual cd8+ t cells. Science 340, 635639. [2] Buchholz et.al., 2013, Disparate individual fates compose robust cd8+ t cell immunity. Science 340, 630635. [3] Markham et.al., 2010, A minimum of two distinct heritable factors are required to explain correlation structures in proliferating lymphocytes. J. of The Royal Society Interface 7, 1049 1059.

2. **Decision strategies for competing phage infections.**
Vaibhhav Sinha(1,2) and Sandeep Krishna(1),
(1) Simons Centre for the Study of Living Machines, National Center for Biological Sciences, Bangalore; (2) Manipal University, Manipal, India.
Temperate bacterial viruses or phages are interesting predators due to their ability to make a "lifestyle" choice when infecting bacteria. They can either proceed along the lytic pathway, by increasing their numbers in a burst killing the host cell or play a less aggressive strategy and integrate their genome with the host's, ensuring that their numbers increase slowly with each cell division. Several viruses are discovered in this lysogenic state, and even eukaryotic genomes carry evidence of past integration events with viruses. At the level of microbial communities, the phage-bacteria games are diverse and have multiple players. Multiple phages can target the same bacterial cell and can either co-operate or compete. We consider one of the smallest units of such predator-prey communities i.e. two phages, competing for the same bacterial host population. We use the classical E.coli, phage system to do our study. We show that for such kind of viruses, there exists a predictable optimal lysogeny which is the best strategy to play when competing with another phage for getting the larger share of the host population to convert to lysogens.

3. **Rational development of microbial consortia for metabolic engineering.**
Aarthi Ravikrishnan, Smita Srivastava and Karthik Raman,
Bhupat and Jyoti Mehta School of Biosciences, Indian Institute of Technology Madras, Chennai, India.
Microorganisms are ubiquitous and rarely occur in isolation. They always tend to form communities, where they exhibit different types of interactions such as mutualism, commensalism and predation. A consortium enjoys division of labour and provides a wider

scope to leverage the joint metabolic capabilities of the organisms vis--vis a single organism. Although there are several naturally occurring microbial communities, their systematic exploitation through rational design and metabolic engineering has rarely been performed. Consortia have been chosen randomly in the past for carrying out fermentations, particularly in wastewater treatments and fermented food products, but a framework to design a well-defined consortium by exploiting the metabolic diversity is still lacking. Methods to characterise and define consortia for industrial applications is still in infancy. To improve our understanding of these relationships, it is imperative to focus on the development of systems-level modelling oriented towards communities. Towards this end, we have designed an algorithm based on principles from graph theory that can be used for designing industrially useful consortia. This algorithm predicts the potential metabolic interactions between a given set of microorganisms, given the source (s) and the target (s) of interest. Results from the algorithm are used to rank the combinations to determine the best consortium. We applied our algorithm to determine the set of microorganisms that can lead to enhanced bioethanol production while being together in a consortium and also predict the metabolic interactions that happen between these organisms. Currently, we are trying to experimentally verify some of the predictions of our algorithm, by understanding how the microorganisms interact while being together in a consortium. Once established, this algorithm can be used for generating a number of productive consortia for the production of a wide array of compounds from biofuels to pharmaceuticals. This would pave way for systematically analysing and harnessing the full potential of microbial consortia.

4. **Collective motion of Dictyostelium population.**
Trilochan Bagarti and Sitabhra Sinha,
Institute of Mathematical Sciences, Chennai, India.

The Dictyostelium discoideum amoebae population aggregate to form patterns by cyclic adenosine monophosphate (cAMP) signaling. The cAMP molecules are produced by the amoeba in a periodic pattern. The amoeba responds to the increase in cAMP concentration in its neighborhood by producing more cAMP. We present a mathematical model which shows a wide variety of patterns depending on the diffusivity of the cAMP and the mobility of the amoeba.

5. **DIF-mediated intercellular conflict in Dictyostelium discoideum.**
Sonia Kaushik(1), **Krithi Nandimath**(2,3), S. Mahadevan(1) and Vidyanand Nanjundiah(1,2),

(1) Indian Institute of Science, Bangalore; (2) Centre for Human Genetics, Bangalore; (3) University of Wageningen, The Netherlands.

When starved, free-living cells of Dictyostelium discoideum aggregate to form multicellular groups with division of labour. Eventually, some die and form a vertical stalk. The rest become stress-resistant spores on top of the stalk. Along the way the cells release toxic lipid-soluble molecules known as DIF (differentiation-inducing factor). Spore forming efficiencies in inter-strain mixes of D. discoideum show that DIF seems to be used as a signal in the competition between cells to sporulate.

6. **Coupled public goods games.**
Amit Vutha and Shashi Thutupalli,
NCBS-TIFR, ICTS-TIFR, Bangalore, India.

Public-goods dilemmas, and the conditions leading to the maintenance of cooperation are of great interest in biology. However, biologically motivated public- goods games need specific variations. We explore multi-layer games wherein resource production at a given evel is coupled to goods-sharing at another level.

7. **Engineering bacteria for dispersing bacterial biofilms.**
Vihang Ghalsasi and Victor Sourjik,
LOEWE Center for Synthetic and Systems Microbiology, Max Planck Institute of Terrestrial Microbiology, Marburg, Germany.

Biofilms are surface-associated structures formed by bacteria embedded in a self-produced matrix. Biofilms are exceptionally resistant to environmental stress, antimicrobial agents and host immune defense, and combating biofilms has recently become an important research topic. In this work, we present a biologically engineered system that can be applied against a wide range of biofilms formed by pathogenic and non-pathogenic bacteria. This system relies on Escherichia coli (disrupter) strain that was engineered to synthesize and secrete Dispersin B, an enzyme that can hydrolyze poly-N-acetylglucosamine (PGA), a polymer found in the matrix of various bacterial biofilms. We show that the degradation of PGA by the disruptor strain results in the dispersion of the target biofilm. We propose that in the future this simple disrupter module can be combined with other biofilm detection and targeting systems aimed towards the destruction of an existing biofilm.

8. **Novel intracellular compartments in hybrid yeast.**
Ramya Purkanti and Mukund Thattai,
Simons Centre for the Study of Living Machines, National Centre for Biological Sciences, Bangalore, India.
We are interested in the ancient origins of the eukaryotic compartmentalized cell plan. Eukaryotes arose from a prokaryote-like ancestor probably during the global oxygenation event 2.5 billion years ago which evolved into the common ancestor of living eukaryotes dated around 1.8 billion-years ago. The shared features of all extant eukaryotes suggest that this last eukaryotic common ancestor (LECA) was already a complex unicellular organism with quintessentially eukaryotic features: a nucleus, mitochondria, compartmentalized organelles, cytoskeletal machinery, and vesicle traffic. In the absence of any intermediate proto-eukaryotic forms, the challenge is to understand how LECA arose from a prokaryote-like ancestor. The endomembrane system of eukaryotes consists of membrane bound compartments which exchange matter amongst themselves by means of vesicles. To explain their origins, the autogenous theory of compartmentalization has been proposed (Dacks & Field, 2007). Briefly, it states that organellar diversification is caused by the duplication and divergence of compartment's "identity-encoding" genes, an idea which issupported by biophysical models of endomembrane trafficking (Ramadas & Thattai, 2013). We have asked which biological scenario would result in concurrent duplication of the entire set of identity-encoding genes while providing opportunity for loss of cross-interactions. Inter-species hybridization fit the bill. Our study of one such inter-species hybrid, Saccharomyces pastorianus, whose parents diverged apart for 20 million yrs, suggests novelty in endomembrane trafficking of the hybrid in terms of gene regulation and ultrastructural complexity.

9. **Emergence of heterogeneity in a bacterial population.**
Sandeep Miryala and Srinandan C. S.,
Biofilm Biology Lab, School of Chemical & Biotechnology, SASTRA University, Thanjavur, India.
Fluctuating environmental conditions or stochastic gene expression could cause emergence of heterogeneity in a bacterial population. This could also be a bet-hedging strategy of the population. In this study, we observed a pattern of extrapolymeric substance (EPS) producing, non- producing and hyper-swarming cell types of Uropathogenic E.coli (UPEC) colony on Congo red agar (CRA) plate. UPEC is the causative agent in majority of urinary tract infections (UTIs) throughout the world. During infection, persistent, biofilm forming and antibiotic resistant sub-populations emerges and these could be phenotypic or genotypic in nature. We characterized

the sub-populations of the UPEC colony for their other phenotypic traits and the susceptibility towards environmental stresses like the effect of antibiotics, chlorine, heat, etc. The overall bet- hedging strategy of the UPEC population will be discussed.

10. **Evolution of Escherichia coli under prolonged stationary-phase.**
Farhan Ali, Pabitra Nandi, Savita Chib and Aswin Sai Narain Seshasayee,
National Center for Biological Sciences, Bangalore, Karnataka, India.

Microbial habitats are frequently redefined due to uncontrolled environmental factors as well as microbial activity which impose selection pressures on evolution of molecular processes. The interaction between the molecular processes and ecological niche to generate a phenotype is poorly understood. The advent of high throughput technology such as sequencing of entire genomes, system level measurement of gene-expression has offered an opportunity to understand the lifestyle of an organism in its natural ecological context. Starvation is a prevalent state of microorganisms in their natural niche due to intense competition for resources. Starving cultures of Escherichia coli presents a model system to understand the forces of selection operating on organism to optimize their nutrient requirements. E. coli cultured in Luria Bertini (LB), a complex medium which has very low amount of glucose but plenty of other oligosaccharides, smaller peptides and amino acids supports a brief exponential-phase. Extending stationary-phase results in major population crash, however a minority survives for substantially prolonged periods without further supplementation of fresh nutrients. The surviving population becomes the source of genetic diversity from which mutants with increased fitness than the parent are selected and proliferate under non-growth conditions. This phenomenon is known as Growth Advantage in Stationary Phase (GASP) and the mutants are referred as GASP mutants. We have used E.coli GASP model of stationary-phase evolution to identify beneficial mutations that accumulate under prolonged starvation. E.coli strain with rpoS819 GASP allele, a naturally selected variant of stationary-phase sigma factor rpoS was evolved for 28 days under prolonged starvation in lysogeny broth batch cultures. rpoS819 has a 46 base-pair duplication at C-terminal end resulting in functional attenuation. Two colony morphology variants were identified by regular phenotypic screening of independently evolving populations: 1) A colony morphology variant that is characterised as irregular shape with undulate margins. 2) A colony size variant, characterized by small colonies, was first observed at the start of the third week of experiment in two independent population and was coexisting with the regular sized colonies. Genome sequencing of two independent small colony variants has revealed a mutation in rpoC gene. Experiments for genotype to phenotype mapping and ecological relationship underlying the coexistence of colony size variants are in progress. Spectrum of mutations identified by periodic

population genome sequencing provided two key observations: 1) The original 46 base pair duplication in rpoS819 allele reduplicated resulting in a second allele rpoS819_92 in all the replicates. The rpoS819 and rpoS819_92 allele frequencies suggest a competition between them. 2) Multiple alleles of the gene cpdA appeared in four out of the five replicates with a rise in frequency thereafter. CpdA is a cAMP phosphodiesterase that breaks down cAMP. Interestingly, isolated cpdA variants are present in the rpoS819_92 background. Further experiments are in progress to decipher the epistatic relation between these mutations. Strong parallelism at rpoS and cpdA supports previously established observation of RpoS and cAMP role under carbon and energy limitation. The current study will help to narrow the gap in our understanding of how these two players interact to coordinate adaptation to a complex environment such as prolonged stationary-phase.

11. **Dynamics of bacterial communities associated with developmental stages of butterflies and their impact on butterfly fitness.**

Kruttika Phalnikar, Krushnamegh Kunte and Deepa Agashe,
National Centre for Biological Sciences, Bangalore, India.

Bacterial communities associated with insects are known to influence host physiology, dietary niche, immune system, and reproduction. They exist either in the extracellular environment, such as bacteria associated with gut lining or as intracellular symbionts e.g. in ovaries. These bacterial species communicate, compete and cooperate not only within themselves but also interact with the cells of the host insect. Depending on the nature of the interaction between bacteria and host (beneficial, deleterious or neutral), mutualistic or antagonistic associations may arise and evolve between the two. One of the major questions in the field is how these associations influence the assemblage of bacterial communities in insects. Our study focuses on the bacterial communities associated with butterflies. During development, butterflies undergo complete metamorphosis and have four distinct stages egg, larva, pupa and adult. We focus especially on the larval to adult transition in butterflies, which is associated with a drastic dietary switch as well as tremendous physiological change and massive tissue rearrangement including gut tissue, which is a major reservoir of bacterial cells. This transition in diet and physiology in butterflies might alter the nature of host-bacterial association over the course of development. For instance, a bacterial species that is beneficial in the larval stage may not be advantageous for the adult, resulting in distinct bacterial communities across metamorphosis. To test this hypothesis, we analyzed bacterial communities of 8 different butterfly species across developmental stages. In addition, we carried out manipulative experiments to understand the effect of gut

bacteria on fitness of 2 butterfly species and here we present the results for the same.

12. **Hierarchical Prisoner's Dilemma in Hierarchical Public-Goods Game.**
Fujimoto Yuma(1), Sagawa Takahiro(2) and Kaneko Kunihiko(1),
(1) Department of Basic Science and (2) Department of Applied Physics at The University of Tokyo, Japan.
Dilemma in cooperation is one of the major concerns in game theory. In public-goods game, each individual pays a cost for cooperation or not for defection, while receives reward from the collected cost in a group. Thus, defection is beneficial for each individual, while cooperation is beneficial for the group. Now, groups (say, countries) consisting of individual players also play games. To study such a multi-level game, we introduce a hierarchical public-goods (HPG) game in which two groups compete for nite resources, by utilizing costs collected from individuals in each group. From analysis of this HPG game, we found the hierarchical Prisoners Dilemma, in which groups choose defective policy (say armament) as Nash strategy to optimize each groups benefit while cooperation optimizes the total benefit. On the other hand, for each individual within a group, to refuse cost (say tax) is Nash strategy, which, turns to be cooperation policy for group, thus leading to hierarchical dilemma. Here, the reward of one group receives increases with the population, as the collected cost does. In spite of it, we find existence of an optimal group size that maximizes its payoff. Furthermore, when the population asymmetry between the two groups is large, a smaller group will choose cooperation policy (say disarmament), to avoid excessive response from the larger group, which leads to the resolution of the Prisoners Dilemma between the groups. HPG model can be applied to, not only animal society, but conflict-cooperation problem in the multicellularity, that is also discussed.

13. **Functional characterization of Dictyostelium discoideum ammonium transporter using Saccharomyces cerevisiae as surrogate system.**
Asha Densi K P, Revathi S. Iyer, Paike Jayadeva Bhat,
Indian Institute of Technology Bombay, Mumbai, India.
Cellular differentiation in response to nutritional depletion is well studied in Saccharomyces cerevisiae and Dictyostelium discoideum. In S. cerevisiae, depletion of carbon and/or nitrogen induces filamentaion or transition to stationary phase (G0) or sporulation. In D. discoideum, depletion of food source induces unicellular to multicellular transition. A common element that has been shown to

participate in the above processes is ammonium transporter. S. cerevisiae strain lacking ammonium transporter coded by MEP2 is defective in pseudohyphal differentiation. Even though, the deletion of amtA, the ortholgue of MEP2, in D. discoideum shows severe defect in differentiation process, the underlying mechanism is not known. Phylogenetic analysis suggests that, of the ammonium transporters of S. cerevisiae and D. discoideum, AmtA and Mep2 belong to the same family of ammonium transporters. The objective of the study is to functionally characterize amtA by using S. cerevisae as a surrogate system. amtA when present in multiple copies complements mep2 deletion in S. cerevisiae for growth on low ammonia. This complementation is observed when amtA is expressed in multiple copies. Surprisingly, when expressed in single copy amtA fails to complement, suggesting that amtA is not as active as MEP2. Therefore, mutants of amtA that could complement mep2 deletion, when expressed in single copy, were isolated to decipher the mechanism of ammonium transport by AmtA. Further analysis is being carried out to characterize the mutants.

14. **Cooperation, survival and resilience: ecological consequences of heterogeneous metapopulation structure.**

Anurag Limdi(1), Alfonso Perez-Escudero(2), Aming Li(2), Jeff Gore(2)
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While negative frequency dependent selection and population structure are prominently used to explain the evolution of cooperation separately, they have rarely been studied together. Here, we explore the effect of metapopulation structure in a yeast experimental system with cooperators (which produce a public good) and defectors (which don't). Specifically, we focus on the effect of heterogeneouos metapopulation structure, where not all nodes are equivalent and migration between nodes is asymmetric. We find that a star network enhances the fraction of cooperators nearly 2-fold compared to isolated nodes and complete networks, under some parameter regimes. This increase in cooperation is due to a lower density in the side nodes of the network, causednby the asymmetric migration rate. This low density on the side nodes makes star networks less capable of surviving in challenging environments than isolated populations: isolated populations can survive high levels of sustained mortality that are lethal for the star network. Despite this, we find that a star network has greater resilience to temporary perturbations (a salt shock) than isolated populations. These two apparently opposed results can be reconciled: the level of permanent harshness that the network can withstand is given by the side nodes which are the most vulnerable parts of the network. In contrast, the threshold for surviving a temporary perturbation is given by the central node (which has a higher population density and a higher cooperator fraction than isolated nodes), because

it can reseed the side nodes and rescue the whole network. Our results experimentally confirm that heterogeneous networks favor cooperation and demonstrate that ecological communities respond very differently to constantly and transiently harsh environments.

15. **The balance between pro-growth and pro-arrest signals determine the homeostatic control of checkpoint signalling and cell fate.**
Siddharth De, Alessandro Esposito and Ashok R. Venkitaraman,
MRC Cancer Unit, University of Cambridge, UK.
Cellular homeostasis relies upon cell-cycle checkpoints, which, at the single-cell level exhibit stochasticity and non-genetic heterogeneity. The G2 checkpoint monitors DNA damage and prevents it from being carried over into mitosis, but the mechanisms that regulate its enforcement in dividing cells are not well understood. We have combined single-cell imaging with dynamic fluorescence microscopy to investigate this problem. Here, we report that DNA damage triggers an intersection between the ERK signalling pathway and the p53 transcription factor, which regulates cell fate after G2 checkpoint activation. DNA damage activates dynamic changes in the ERK and p53 pathways that exhibit in-phase kinetics. ERK activity alters p53 dynamics but not vice versa. Single-cell imaging reveals that ERK modulation affects cell fate decisions after G2 checkpoint activation. Collectively, our findings reveal cross-talk between growth factor-driven oncogenic pathways, the DNA damage response, and p53, with implications for early oncogenesis, tumour promotion and maintenance of cellular homeostasis

16. **Modelling Phototaxis-Mediated Phenomena in Cyanobacterial Colonies.**
Varuni Prabhakar, Shakti Menon and Gautam Menon,
Institute of Mathematical Sciences, Chennai, India.
Motile micro-organisms respond to a variety of chemical and physical stimuli, including chemical concentrations, pH changes, oxygen, osmolarity and even magnetic fields. Cyanobacteria or 'blue-green alge', are a widely distributed, diverse group of oxygenic photosynthetic gram-negative bacteria that have shown to exhibit phototaxis - motion in response to a light stimulus. In the model cyanobacterium Synechocystis sp. PCC 6803, robust positive phototaxis has been observed as dense finger like projections (over 1-3 days) of cells emerging from a compact colony that are seen to move toward the direction of white light. Other wavelengths of light elicit responses that range from slower moving colony fronts (red light and far-red) to negative phototaxis (blue, UV and high light

conditions). While cells are individually able to sense and respond to light direction, it has been shown that there is likely a social aspect to this phototaxis, since cells form dense aggregates before forming finger like projections. This is believed to be mediated through Type 4 Pili (T4P), that allow cells to attach to other cells. Cell motion is also enhanced in the presence of slime, which the cells produce to facilitate motion across surfaces. Here we present an agent based model for cyanobacterial phototaxis where agents can sense the direction of light and move towards it. To model the T4P we allow agents to attach to and exert forces on other agents in their neighborhood. The individual agents also change the properties of the region they occupy by laying down 'slime'. Thus, agents move as a function of the sensed direction of light, the forces exerted on them by neighboring agents and the 'slime' present at their current location. We show that through this model, we can simulate a variety of phenotypes of collective phototaxis. The model also predicts the nature of collective response in cyanobacterial phototaxis when the direction of the light is abruptly changed and when non-trivial patterns of input light are presented to the colony.

17. **Evolution on Fitness Landscapes.**

Dibyendu Dutta and Supreet Saini,
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Assuming a constant environment and a particular selection pressure, it may be possible to represent the different genotypes an organism may evolve into, as a fitness landscape. The path to the mutant genotype from the original may involve an increase or decrease in fitness. In Darwinian Evolution only fitter organisms get selected and fixed in the population. However, each mutation does not bring forth an additive effect, sometimes the combined effect can be unexpectedly higher, or lower, or neutral, which may be due to epistasis, and molecular pleiotropy. This presents the situation where an organism needs to first acquire mutations that are not the highest in fitness, in order to attain the peak fitness on the landscape. Experiments show that organisms indeed are able to take complicated mutation trajectories to acquire the fitness peaks, for example evolving resistance to a new antibiotic. So, does the optimal trajectory simply emerge by trial and error or do cells possess some sort of compass to help them decide each step? We aim to simulate evolution on different types of fitness landscapes and identify important metrics that allow for navigation on a rugged fitness landscape, and thus reproduce evolution.

18. **Experimental evolution of metabolic dependency in bacteria.**
Glen D'Souza and Christian Kost
Max Planck Institute for Chemical Ecology, Germany; University of Osnabrueck, Germany; EAWAG, Switzerland.
Bacteria frequently lose biosynthetic genes and functions, thus making them dependent on an environmental uptake of the corresponding metabolite. Despite the ubiquity of this genome streamlining, it is generally unclear whether the concomitant loss of biosynthetic functions is favored by natural selection or rather caused by random genetic drift. Here we demonstrate experimentally that a loss of metabolic functions is strongly selected for when the corresponding metabolites can be derived from the environment. Serially propagating replicate populations of the bacterium Escherichia coli in amino acid-containing environments revealed that auxotrophic genotypes rapidly evolved in less than 2,000 generations in almost all replicate populations. Moreover, auxotrophs also evolved in environments lacking amino acids yet to a much lesser extent. Loss of these biosynthetic functions was due to mutations in both structural and regulatory genes. In competition experiments performed in the presence of amino acids, auxotrophic mutants gained a significant fitness advantage over the evolutionary ancestor, suggesting their emergence was selectively favored. Interestingly, auxotrophic mutants derived amino acids not only via an environmental uptake, but also by cross-feeding from coexisting strains. Our results show that adaptive fitness benefits can favor biosynthetic loss-of-function mutants and drive the establishment of intricate metabolic interactions within microbial communities.

19. **Ecological-evolutionary feedback in evolved lineages of Pseudomonas fluorescens.**
Chhavi Chawla(1) and Paul Rainey(1,2),
(1) NZIAS, Massey University, Auckland; (2) Max Planck Institute for Evolutionary Biology, Plön, Germany.
Evolution of cooperation is hypothesized to be the very first step in the evolution of multicellularity and so the understanding of it becomes important; however, it presents a problem; natural selection rewards selfish behavior; yet, in nature, cooperation is apparently common. Assortment between cooperating types has been identified as the underlying mechanism behind theories for the evolution of cooperation. However, the theories fail to acknowledge frequency (evolutionary) and density (ecological) dependent nature of interactions, capable of generating co-evolutionary interactions. In this regard the feedback between ecology and evolution (eco-evo feedback) is of likely importance. In a previous long-term evolutionary experiment, a rudimentary life cycle was established

in model bacterial populations between a cellulose producing, group living cooperator type, termed WS, and a solitary, free living cheater type, termed SM. I believe that the eco-evo feedback is likely to have occurred on the WS-SM interactions. The aim of my study was to identify the presence of the feedback in the evolved lineages. I compared the evolutionary dynamics and population dynamics on the interactions between WS and SM. I also report the joint influence of evolutionary and population dynamic patterns via ecospace diagrams of the ancestor and evolved lineages. The results showed that the interactions between WS and SM are both frequency and density dependent and the interplay of the two factors suggest the presence of the eco-evo feedback.

20. **Novel microfluidic platform to control and investigate cell community behaviour using portable microscopy.**

Rudra Vaswata Roy Choudhury(1), Dr. Sunil Laxman(2), Dr. Anil Prabhakar(1),
(1) Indian Institute of Technology Madras; (2) inStem, NCBS-TIFR Bangalore.

Varied nutrient stimuli might lead to varied cell responses, thereby affecting the behaviour of cell communities. We design and demonstrate a novel Lab-on-chip platform which provides a convenient technology to examine the different cellular responses to varied nutrient conditions. The platform consists of a microfluidic device, which can control nutrient gradient in multiple chambers, where colonies of cells are maintained. It could be used to study single cell as well as cell community responses to different nutrients and micro-environmental conditions. The device is augmented to a portable microscopy platform which enables imaging of live cells, and thus provides a mean to study growth behaviour of cell colonies in effect to key nutrient conditions. The microscope consists of cost-effective and easily available optical and electronic components and thus provides a platform for analyzing micro cell communities (including small microbial or mammalian cell colonies) under diverse, controlled environmental conditions.

21. **Interplay of synergy and redundancy in a two-step cascade information transmission motif.**

Ayan Biswas and Suman K. Banik,
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To better respond to the physio-chemical changes in its environment, it is important for a living system to harness useful information and process it with significant accuracy. For this purpose, living species have developed optimized architechtural complexity over the evolutionary timescale thereby attaining better adaptation skills. Information theory provides sophisticated techniques to

address this problem efficiently and identifies the governing physical principles. We have utilized a stochastic framework to describe the dynamics of different interacting biochemical species forming a two-step cascade (TSC) motif. Application of Linear Noise Approximation to the set of Langevin equations involving Gaussian random variables which represent involved biochemical species, provides analytical expressions for the second moments which are ingredients for calculating mutual information (MI). The formalism of Partial Information Decomposition using these MI terms quantifies the net synergy which predicts whether the source variables are capable of synergistically provide information about the target variable or not. The analysis reveales signatures of both synergy and redundancy, the later arising out of Markovian property. Another important finding of this study is that redundancy in information transmission can indeed empower fidelity of the signaling pathway. Reference : Ayan Biswas and Suman K. Banik, Phys. Rev. E 93, 052422 (2016).

22. **Stability, efficiency and reproducibility in microbial communities with trophic layers.**
Akshit Goyal(1), , Sandeep Krishna(1,3), Sergei Maslov(2) and Kim Sneppen(3),
(1) Simons Centre for the Study of Living Machines, NCBS-TIFR; (2) Department of Bioengineering, University of Illinois at Urbana-Champaign; (3) Center for Models of Life, Niels Bohr Institute, University of Copenhagen, Denmark.

Research on microbial communities has expanded into several avenues: both experimentally and theoretically. While they remain good systems to study cooperation and competition in populations, we believe that there is a lack of simple phenomenological models that explain some overarching themes in the field. We believe these to be of three broad kinds: stability, efficiency and reproducibility (parallelism) among similar communities. Here, we constructed a class of simple abstract models of microbial communities with trophic layers. We believe such models capture temporal trends about the stability and efficiency of certain classes of communities (such as those used in wastewater treatment) that are often seen to undergo rapid turnovers and succession, as well as to talk about rarefaction studies where areas are sampled for new species.

23. **Metabolic Regulation of Fungal Morphogenesis.**
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Institute for Stem Cell Biology and Regenerative Medicine, Bangalore, India.

Unicellular organisms employ multiple strategies to adapt to changing environments around them. Once such strategy deployed unicellular organisms is the ability to form complex multicellular communities. During this transition from a unicellular form to a multicellular community which is often reversible, cells usually undergo division of labor wherein different cells of the community perform distinct specialized functions. This process of Cellular specialization is critical for the survival of these multicellular complex communities. Fungal morphogenesis is one such process wherein fungal cells can reversibly switch from a sessile unicellular state to numerous types of facultative multicellular forms including biofilms (liquid medium), rugose mats (solid medium) hyphal/pseudohyphae, flocculation etc. to name a few. These morphogenetic changes allows the fungi to quickly adapt to varying environmental conditions and even thrive in them. For example, Candida albicans, an opportunistic pathogen that causes a variety of human infections can reversibly switch between its yeast like form (non-pathogenic) and its hyphal form (pathogenic) when it enters into a vertebrate host. Several studies have shown that this morphogenesis is crucial for C. albicans to cause successful infections in a host. Candida glabrata has recently emerged as the second leading cause of infective candidiasis and forms robust biofilms on both biotic as well as abiotic surfaces to cause persistent infections. Pathogenic isolates of C. glabrata forms rugose mats on solid surfaces compared to the smooth colonies formed by the non-pathogenic isolates. Although many genes involved in these morphogenetic behaviors are known, we lack an understanding of the driving principles behind such behavior. We hypothesize that specific metabolic demands of these aforementioned fungal pathogens in a particular host niche are primary determinants of fungal morphogenesis, with key metabolic events determining the ability to switch to complex communities. Saccharomyces cerevisiae can serve as an excellent model for understanding these metabolic regulations of fungal morphogenesis as it can reversibly switch from a single-cell form to multiple distinct types of complex communities under specific nutrient conditions. These complex communities formed by S. cerevisiae show spatial organization, morphological differences, and can survive harsh environmental conditions. Such features in S. cerevisiae includes flocculation, biofilm formation, and invasive or pseudohyphal growth of cells. We therefore propose to address this hypothesis by using biofilms with rugose morphology (BRM) and pseudohyphal formation as outputs of fungal morphogenesis. Our initial findings show that S. cerevisiae can form robust BRMs when grown at low glucose conditions, in contrast to the uniform, smooth colonies they form when glucose is abundant. We also have discovered gluconeogenesis to be a critical process for this morphogenetic change since the deletion of the gene encoding a key gluconeogenic enzyme, PCK1 (Phosphoenol pyruvate carboxykinase) completely abrogates the BRM phenotype. We also observe that the availability of free amino acids are critical for

the formation of biofilms with rugose morphology.

24. **With a little help from my friends: Does high relatedness favour the evolution of metabolic cross-feeding?**

Samir Giri and Christian Kost,
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Metabolic cross-feeding interactions, in which two or more bacterial species exchange costly metabolites, are very common in bacterial communities. Evolutionary theory predicts cooperating organisms should favour genealogically related individuals over non-kin. Whether or not the relatedness among two bacterial lineages to engage in cooperative cross-feeding interactions remains elusive. Previous work of our laboratory has shown that cooperative cross-feeding interactions rapidly evolved between two Escherichia coli genotypes that were auxotrophic for two different amino acids. Evolved auxotrophic consortia displayed significantly increased consortium-level fitness relative to derived populations of metabolically autonomous, prototrophic cells. Moreover, derived auxotrophic consortia showed an extensive degree of phenotypic diversity, formed multicellular clusters and a significantly improved growth relative to the ancestor. The main objective is to unravel how the relatedness among coevolving auxotrophic genotypes affects the evolution of cross-feeding interactions. To address this issue, pairs of auxotrophic genotypes will be set up within the same and between different bacterial species and experimentally coevolved to compare their propensity to engage in cooperative cross-feeding interactions. The expected results will provide unprecedented insights into the role relatedness plays for the evolution of cross-feeding among different bacterial genotypes and may thus help to explain the widespread distribution of such interactions in nature.

25. **Microenvironmental regulation of intra-tumor heterogeneity.**

Sandeep Kumar and Shamik Sen,
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Heterogeneity within single tumor population referred as intra-tumor heterogeneity has been observed in many experimental studies and has been implicated in development of multi-drug resistance, increased cancer aggressiveness, and metastasis organotropism.

Understanding the mechanism(s) that induces this heterogeneity can significantly improve our understanding of cancer progression and that knowledge can be used to identify novel cancer drugs and therapies. However, due to involvement of multiple length/time scale processes and complex cell-cell and cell-surrounding interactions, it is very difficult to study the emergence of intra-population heterogeneity within tumor population in purely experimental framework. To address this, we are using multi-scale computational modeling approach augmented with experimental studies to understand the emergence of phenotypical heterogeneity like heterogeneity in cell size/shape, migration, and, its implication in cancer metastasis. Specifically, we are using cellular Potts model (CPM) and cellular automata (CA)-based in silico study to understand how remodeling of extracellular matrix (ECM) as observed during cancer progression can alter the tumor population composition. During this meeting, I would like to discuss about some of our recent findings where we are studying how the confinement geometry, cell-cell adhesion and cell migration can cause the emergence of intra-tumor heterogeneity. I will also discuss about some of the relevant experimental observations pertaining to populations of HT-1080, MCF7 and MDA-MB-231 cells.

26. **Positive effects of natural within-group diversity on spore productivity of social bacteria.**
Samay Pande and Gregory J. Velicer,
Institute for Integrative Biology, ETH Zurich, Switzerland.

Myxococcus xanthus is a predatory soil bacterium that exhibits vegetative growth and multicellular fruiting body development as two distinct life history stages. It was previously demonstrated that genetically heritable social variation within fruiting bodies is common. However, factors that affect the maintenance of such natural within-group variation remain unknown. We tested the effects of within-group diversity on both total-group and individual-strain spore productivity using eight representative isolates derived from a single natural fruiting body. Interestingly, total productivity of chimeric populations containing all eight isolates was higher than expected from monoculture controls. Further analyses suggest that chimerism does not stimulate total productivity by affecting just one or two isolates, but rather a majority of the eight isolates respond positively to chimerism. We also tested for pair-specific interactions by performing all possible pairwise-mixes. In these experiments, positive responses to mixing were more common than negative ones. Finally, we show that positive effects of mixing several isolates on total group productivity are specific to isolate sets that derive from the same fruiting body group, whereas effects of chimerism on total productivity among isolates from different fruiting bodies were negative, and increasingly so as a function of mean distance between the soil sites from which fruiting bodies

were derived. Our study shows that chimerism among distinct but closely related individuals from the same natural social-group can enhance the absolute fitness of a majority of group members. These studies also show the importance of incorporating information on spatial locations of individuals for analyses of interactions.

27. **Swarming in Pseudomonas aeruginosa: Why and how?**
Shubham Joge, Ayushi Mishra, Muhammad Ameen and Varsha Singh,
Department of Molecular Reproduction, Development and Genetics, Indian Institute of Science.
Bacteria have been traditionally regarded as solitary individuals in a planktonic phase. In the past few decades it has increasingly become clear that many cells can come together to form multi cellular communities in the face of competition, predation and other unknown factors to ensure survival of the species. One such multi cellular community is called biofilm. This is a surface associated aggregate of mostly sessile cells covered in matrix of secreted exopolysaccharides. Swarming population of bacteria is a quorum dependent community but comprises motile bacteria that show rapid and coordinated movement over semisolid surfaces. Pseudomonas aeruginosa (PA) is a ubiquitous environmental organism that is also an opportunistic human pathogen in immune compromised individuals with cystic fibrosis, and in burn wounds or diabetic foot ulcers. When solitary, PA can swim, twitch or slide, but swarms or forms biofilm when in a community and has reached quorum. The swarming patterns of PA comprise dendrites which branch at regular intervals reminding one of fractal patterns. Since no two species of swarming bacteria produce similar patterns, we are motivated to understand if motives and mechanisms of swarming are distinct in these bacteria. Using PA as a model swarming bacterium, we use both genetic and modelling approaches to understand the why and how of swarming.

28. **Clustering in sequences.**
Rahul Siddharthan and **Ankit Agrawal**,
The Institute of Mathematical Sciences, Chennai, India.
A new way of clustering for high-throughput sequencing which divides the sequences into clusters. And these clusters can be analyzed for particular properties.

29. **microRNAs regulate neural specificity and organization during planarian brain regeneration.**
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The unique capacity of planarians to regenerate their central nervous system provides an opportunity to investigate mechanisms critical for adult neurogenesis. The brain regeneration in planaria is mediated by tightly orchestrated spatiotemporal regulation of gene expression critical for multiple aspects of neurogenesis. However, the mechanisms crucial for gene regulation essential for brain regeneration are largely unknown. Multiple studies have identified microRNAs as key regulators of gene expression essential for diverse cellular processes in metazoans. Here, we report a novel role of miR-124c in regulating axon guidance, organization of brain and photoreceptors in regenerating planaria. Albeit highly conserved in metazoans and thought to regulate neural differentiation, the role of the miR-124 family in neural wiring and brain organization is not known. Our study shows that miR-124c is expressed on day 3 post-amputation in the anterior regenerating tissue of the planarians. We demonstrate its critical role in regulating key pathways such as axon guidance and planar cell polarity, essential for accurate neural patterning and neural growth during anterior regeneration. The animals with miR-124c KD showed ectopic expression of chat+ and mispatterned, reduced expression of gad+, th+ neurons suggesting that miR-124c plays a pivotal role in the specification and organization of neuronal subtypes in the planarian brain. Our study identified notch and the genes essential for axon guidance and planar cell polarity as direct targets of miR-124c. We also showed that miR-124c regulate slit-1, a gene required for axon guidance, by modulating the Notch pathway. Together, our results reveal a novel role for miR-124c in regulating axon guidance cues and the planar cell polarity pathway. This is essential for precise neural growth and wiring, which is necessary for the regeneration of both functional brain and photoreceptors.

30. **Regulation of lipid homeostasis maintenance by Drosophila hemocytes.**

Shaarvari Bhat, Saurabh Patil, Sukanya Madhwal and Tina Mukherjee,
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Hemocytes govern various functions such as immune response, tissue remodeling, wound healing amongst others. A multitude of signaling mechanisms regulate the development of hemocytes, Notch signaling being one of them. Notch signaling pathway plays a crucial role in many critical functions that include cell fate specification, stem and progenitor cell development, cell survival and cell death. Interestingly in addition to these functions, ongoing studies in our lab has shown that notch signaling in the hemocytes respond to the nutritional cues. To understand this further, we perturbed notch in the hemocytes and we found that, mainly lipid homeostasis in the organism is compromised. Our study aims to decipher the mechanism by which Notch signaling in the hemocytes

is responsible for maintaining lipid homeostasis.

31. **Long range dispersal and its consequences in a laboratory predator-prey system**
Shashi Thutupalli, Sravanti Uppaluri, George Constable, Corina Tarnita, Simon Levin, Howard Stone and Clifford Brangwynne,

The ecological and evolutionary dynamics of populations are shaped by the strategies they use to produce and utilize resources. However, our understanding of the interplay between the genetic and behavioral factors driving these strategies is limited. Here we report on a C. elegans-E. coli (worm-bacteria) experimental system in which the worm foraging behavior leads to a redistribution of the bacteria, resulting in a growth advantage for both organisms, similar to that achieved via farming. We show experimentally and theoretically that the increased resource growth represents a public good that can benefit all other consumers, regardless of whether they are producers or not. Mutant worms that cannot farm bacteria benefit from farming by other worms in direct proportion to the fraction of farmers in the worm population. At the same time, the population dynamics of the bacteria is significant affected due to their long range spreading : we explore these consequences in the contexts of diversity, competition and spread of evolutionary novelties.

32. **Cell commitments to division during yeast metabolic cycles explained by a "frustrated bistability" model.**
Sunil Laxman(1) and Sandeep Krishna(2),
(1) Institute for Stem Cell Biology and Regenerative Medicine and (2) National Centre for Biological Sciences, Bangalore, India.

Under continuous glucose limited growth, budding yeast (S. cerevisiae) spontaneously undergo robust oscillations in oxygen consumption. During these oscillations, over half the yeast genome is periodically expressed, specifying a temporally separated orchestration of numerous processes and leading to distinct phases of growth, cell division and quiescence-like states. We now understand that the entry into growth and division hinges upon an increase in a central metabolite, acetyl CoA, derived from glucose metabolism. However, it remains unclear how only a sub-set of cells in the population enter into growth and cell division, and how these oscillations are maintained stably and indefinitely as long as these nutrient limited conditions persist. We attempt to understand these oscillations

using the notion of "frustrated bistability". Here, we posit that the cells can be in two stable states, either growing/dividing or quiescent. However this bistability is destabilised by the accumulation of intracellular nutrients (likely acetyl CoA) when most cells are quiescent. We show using mathematical models that this mechanism is sufficient to trigger oscillations. This is a work in progress and we're exploring the space of such models, but we should be able to make testable predictions about how the oscillations would be affected as we change parameters such as the influx rate of nutrients, the density of cells, etc. Our preliminary models already suggest that communication between cells is necessary for these oscillations.