MEETING REPORT

Birds of different feathers flock together

Cooperation and collaboration in *Ropalidia* wasps, evolution and computation, the role of metabolism in generating multicellularity, communication strategies in starlet flocks and social networks, evolution of *C. elegans* as a model organism, phylogenetic networks, relationship between phenotype and genotype.... what holds these disparate phenomena together such that it seemed worthy of being discussed on the same platform on the same day?

Scientists at the National Centre for Biological Sciences (NCBS), Bengaluru, playfully experimented with the serious subject of the Interface of Biology and Theoretical Computer Science, between the 19th and 21st of December 2016. In the year that gave Nobel Prize in Chemistry to work on molecular machines, the Simons Centre for Study of Living Machines at NCBS supported the gathering to discuss the list of topics in the above paragraph.

The first day focused on populations and communication. In the plenary session, Raghavendra Gadagkar of the Indian Institute of Science (IISc), Bengaluru explored the process of delineating and unveiling the intricate interrelationships between members of *Ropalidia* wasp colonies. How does the queen manage to maintain order in the colony? What determines which member will become queen if the existing queen is removed? What are the parameters that determine the extent of collaboration, cooperation and conflict within and outside the colony? What kind of experiments can we devise to examine such issues? What are the limits of our present understanding? Addressing such questions, on the basis of over 40 years of experiments and experiences, he also titillated the audience with further questions, reserving their answers for later discussions with interested individuals.

In stark contrast to Gadagkar's experimental prodding of nature to elicit answers, Nisheeth Vishoi, a computer scientist at EPFL, Switzerland, drew parallels between the processes of evolution and the life cycle of HIV. The replicative cycle of HIV not only acts as a model for evolutionary processes, the understand-

ing allows application in drug design. He then gave a brief background on computer algorithms and presented concepts related to Markov chains, networks and flows – concepts that can deal with widely disparate biological phenomena such as convergence of traits during evolution and behaviour of the slime mold, *Physarum*.

As if to find a middle ground in the approaches used by biologists and theoretical computer scientists, Sunil Laxman, from inStem Bengaluru, introduced the concept of metabolic pathways and networks in biology. He referred to the well-known process of the development of complex multicellularity in unicellular Dictyostelium amoebae in response to starving, and its relationship to metabolic pathways and networks. Sunil also explained the recent understanding of switching to the Glucose phosphate shunt pathway in *Saccharomyces* yeast. The switch involves the use of glucose to generate trehalose sugars along with changes in the way fats are metabolized. And, interestingly, the change in metabolism of individual cells leads to clearly visible structural patterns at a gross level, in a population of the microorganism in a petri dish.

Arnab Bhattacharya, IISc, Bengaluru, examined complex patterns that emerge in space and time in a large population. What is the minimum conditions needed for the emergence of coherence in large numbers of a species? How does local communication impact long range order? He explained the principle of social network graph where mutual influences can either enhance or eliminate differences, and at times, even polarize them.

By lunch time, there was enough food for thought. The patterns of collaboration between scientists of diverse backgrounds to uncover the commonalities under the veil of differences – how will they emerge?

In the first session of the afternoon, Marie-Anne Felix, ENS Paris, sketched out the different strategies used by scientists to understand evolution. Phylogenetic reconstructions assumed genetics and evolution but did not incorporate the findings from genetics, except in recent

times, when genomic data and the technologies to deal with such data became available. Even now the processes that are involved in evolution are not examined. Investigations into the differences in the developmental processes of closely related species of nematodes, such as *C. elegans* and *C. briggsae*, may provide insights about the divergences of species, she said. As an example, she presented studies on the mutations in six loci that control the development of the cells that form the vulva. She underlined the differences in the impact of these mutations on the development in both the species.

Daniel Gusfield, a computer scientist at UC Davis, remarked on the reconstruction of phylogenetic trees from a totally different perspective. The emergence of sexual reproduction and consequent recombinations form a web, interconnecting members of a population. Considering evolution only as a tree of life will not give us the true picture, unless we understand this network formed by recombination, he said. From a purely combinatorics point of view, he analysed the evolution of a stretch of genetic material that undergoes recombination and demonstrated the effect of networks in evolution.

Fyodor Kondrashov, Centre for Genomic Regulation, Barcelona, presented the results of experimental assays of the genotype to phenotype connection, using the Green Fluorescent Protein as the model. More broadly, the interplay of genes that generate the segments of an insect body was playfully dissected by Fyodor, generating chuckles and laughter from the audience.

The formal meeting for the day ended on this note. But after a short break, it resumed, next to the dining facilities, instead of in the auditorium.

Mukund Thattai, NCBS, Bengaluru, started with listing some primary issues under two heads: biology and theoretical computer sciences. On a green board, he started with listing a few points such as biological phenomena and the tools for tackling the problems in computer sciences. He elicited the perceptions of people belonging to different disciplines about those who are following the other,

the differences in attitudes, the difficulties with terminologies, the need to build bridges, the strategies for doing it – he filled up a green board with points harvested from the participants. This, in a way, tied up the diverse topics discussed during the day and prepared the participants to the topics coming up in the next two days.

The food for thought continued in small groups along with food on dinner tables.

The second day focused on molecules and information. The plenary lecture was on the science of information: Case studies from DNA and RNA assembly, by David Tse of Stanford. He pointed out that, behind the stupendous feat of deciphering the DNA sequences of whole genomes, there are the ideas of Shannon and of Turing. Sketching the first principles in theory, he explained the problem sequencing small sequences of DNA generated by restriction enzymes from a genome and then attempting to reconstruct the whole genome by piecing together the available bits of information. It is like a jigsaw puzzle that does not have an accompanying picture for reference, he said. Lack of adequate overlap between the sequences, multiple copies of the same gene pose problems. He presented some of the strategies used in overcoming these problems.

The DNA sequence data would have solved the problem of reconstructing RNA sequence data, if not for the introns – sequences that do not code for amino-acids – in between sequences that do, said David. He presented strategies for generating RNA sequences and the tools developed by his lab to face the challenges.

Garud Iyengar, Columbia University, presented his work on Cellular Information Processing. He briefly described the mathematical formalisms required to describe complex cellular processes. He presented a mathematical model of processes, starting from the binding of a ligand to a receptor on the cell surface, to the downstream amplification of the signal and the processes set off in response to these signals. He also dealt with the way one cell signals to the next, using glycan moieties. He presented the required mathematical representations that are simple enough to derive meaningful experimental strategies.

When a ligand attaches to a receptor, there are changes in their three dimensional conformation which allows work to be done by the protein. It is not that the whole protein structure is changed. There is a shear band within the protein and the changes are localized there. Tsvi Tlusty, Institute for Basic Science, Ulsan, narrated numerical experiments where a part of the protein is attached. At high frequencies the protein acts like a spring. But at low frequencies it becomes a soft viscous flow. Wet lab methods have a limitation. He explained the methods to identify the shear band using modelling techniques.

Leelavati Narlikar, a computer scientist at National Chemical Laboratory, Pune, shifted our attention to stretches of DNA where there are promoters that initiate transcription. Are there common motifs in the promoter regions? To extract answers to the question she resorted to computer techniques that not only matched the sequences against each other, but also learned from the process. Through this technique her team was able to identify motifs that would otherwise escape human notice. Leelavati's methods to identify the regulatory architectures of promoter regions using unsupervised learning might have applications in other homologous areas in biology.

The concert played by the regulatory processes is responsible for an embryo developing into an adult. From an undifferentiated ball of stem cells, the process leads to highly differentiated tissues. Jyotsna Dhawan, a cell and developmental biologist at Centre for Cellular and Molecular Biology, Hyderabad, talked about the way in which muscle tissue regenerates damaged cells. Some cells that were quiescent in the tissue start differentiating and replace damaged cells. The quiescent cells can be provoked to divide and the process of differentiation depends on local controls. If these controls are lost or tampered with, these cells act like cancer. The pathways from stem cells to division, differentiation, quiescence and death are not linear, but branched and cyclic.

To understand the complexity of such collective dynamics is not easy. Shashi Thutupalli, NCBS, Bengaluru, examined some specific properties of collective dynamics: synchronization of behaviour. Using studies on simple physical models, he demonstrated how collective behaviour can also be either unsynchronized or synchronized, in phase or out of phase. There are also phases where chimera states appear: some members of the group may be synchronized whereas others may be unsynchronized. The chimera can also go into oscillations where the in-phase and out-of-phase may switch back and forth. Such behaviours are seen in biological systems. For example, the left and right brain of a sleeping dolphin goes through switching between synchronized and asynchronized electrical activities.

Timothy Saunders, from the Mechanobiology Institute in Singapore, spoke about how cells use mechanical cues during the growth and development of embroys. He focused on the fruitfly embryo, and examined how cells in highly curved portions of the embryonic tissue were able to address the competing requirements of tissue rigidity and flexibility. Cells solved this puzzle by taking on different shapes in different parts of the tissue, and making use of topological tricks known as T1 transitions.

The plenary lecture by Upinder Bhalla, NCBS, Bengaluru, on the third day, was on sequence recognition in molecules and networks. While coding for the sequence of amino acids in a protein uses a spatial sequence, coding in neurons takes on a temporal sequence. The sequential inputs from different clusters of neurons through various dendrites on a neuron are not easily seen by the human eye because they are hidden in the very large numbers of dendrites firing at any moment in the brain. But having uncovered the phenomena using pattern recognition algorithms, he worked out the consequences at cellular levels, in terms of the release of Calcium ions: waves of chemical reactions that either amplify or nullify the progress to the firing of a neuron. And this happens in behavioural time scales, he pointed out. With inputs from mathematical modelling, computer programing and wet lab results, he demonstrated that it is possible to solve what was not solvable using only the techniques of biology.

Santosh Vempala, of the Georgia Institute of Technology, a computer scientist, marvelled at the brain. To present his understanding of computation in the brain, he quickly explained the basic information processing in neurosciences and provided a computer science perspective. His goal was to build up a new grammar for the basic operations performed by the brain, whether simple or complex. This project is in its infancy, and will take a massive collaboration

between neuroscientists and computer scientists, to push forward.

Venkat Ramaswamy, NCBS, Bengaluru, presented his work on creating an Axiomatic Theory for neural computation. He started with some preliminary axioms and proceeded to show that the theorems derived from these axioms put neurosciences on a firm theoretical footing.

Manoj Gopalkrishnan, Indian Institute of Technology Bombay, pointed out that a chemical reaction is equivalent to a computation. For example, a reaction proceeding to equilibrium is equivalent to an optimization programme for free energy. He proposed an algorithmic biology that can form the basis for explaining the evolution from molecules to intelligence.

A panel discussion at the end of the meeting dealt with questions such as how to keep the interface between biology and theoretical computer sciences going, what kind of curriculum is needed to build up the manpower that is required to build the bridges between the two disciplines, how can such a curriculum be practically imparted, etc... And that tied up the points that Mukund Thattai had initiated at the end of the first day.

Though the birds that assembled were of different feathers and they all had their own songs, both the colours and the sounds somehow harmonized. And it became a fugue where mathematics, information sciences, computer sciences, genetics, developmental physiology, neurosciences, ethology and ecology merged. Some notes from theoretical linguistics could have made the music richer and merrier, one could not help thinking.

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OPINION

Groundwater management and achieving equity by direct transfer of electricity subsidy: a workable option

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The policy decision to provide free or subsidized electricity has been a key driver for widespread groundwater exploitation in India. Groundwater utilization has immensely enhanced crop productivity and employment generation, which has led to poverty reduction and rural prosperity. To boost rural development in the 1970s, state government, initially began unmetered electricity supply for irrigation, which is still being continued in different states as part of their rural development policy. Policy planners and administrators are now faced with the challenge to design and implement a workable mechanism to manage the ever-growing complexity of groundwater – energy nexus. Groundwater extraction has already surpassed sustainable utilization limits in most parts of India. Also, the water table is going down at an alarming rate, with continuous deterioration in quality. Consequently, chasing rapidly declining water table has become too costly for small and marginal farmers, thus aggravating disparity among the farming groups.

In Karnataka, groundwater depletion has forced farmers to drill up to depths of 200 to 300 m, costing about Rs 2.5–3.0 lakhs for a successful bore-well. Moreover, due to increasing interferences between wells, now bore-wells last only for 2–6 years. Bore-well failures cause huge economic setbacks for small and marginal farmers with no resources to drill another bore-well. Incurring loans for drilling another bore-well may backfire if the attempts are unsuccessful.

In Karnataka, there are 2.26 million electrically operated irrigation pump sets (EOIP). The numbers are increasing at an annual growth rate of 4.3%. This means an addition of 70,000 new pump sets per year, which also increases electricity demand. Presently, the agriculture sector in Karnataka is the largest consumer of electricity with 16,788 million units, which is 35.83% of total consumption of the state[1]. Electricity consumption for irrigation is increasing at a rate of 8% per annum, posing stiff challenges in an electricity-deficient state. Karnataka meets 20% of its demand by short-term power purchases. Marginal and small farmers constitute 76.4% of the total farm families in the state, among whom 17.8% use EOIP sets. Medium and large farmers constitute 23.6%, among whom 26% use EOIP sets. Further, marginal and small farmers own 64%, and medium and large farmers have 36% of total EOIP sets in Karnataka. Skewed ownership of irrigation facility is evident from the fact that every irrigated small farm-holder (<2 ha) and large farm-holder (>4 ha) uses 1.36 and 1.90 units of EOIP respectively. On an average, per irrigation pump set, every small and large farm-holder irrigates 0.7 and 7.3 ha respectively.

Assuming that all farmers own pump sets of the same horse power, draw water from the same depth and follow the same cropping pattern, the inequality among farmers can be understood using the extent of irrigated area as a proxy for estimating the amount of electricity consumed by small and large farm holders. Total area irrigated by small farm-holder is, on an average, 1.4 ha whereas it is 9.1 ha for the large farm-holder. This implies that every large farm-holder uses nearly seven times more power than the small farm-holder. Yet this may be a conservative estimate ignoring the fact that most plantations are owned by large farm-holders, who require continuous irrigation at specific intervals. Therefore, the resource-rich farmers enjoy greater