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Centre for the Study of Living Machines

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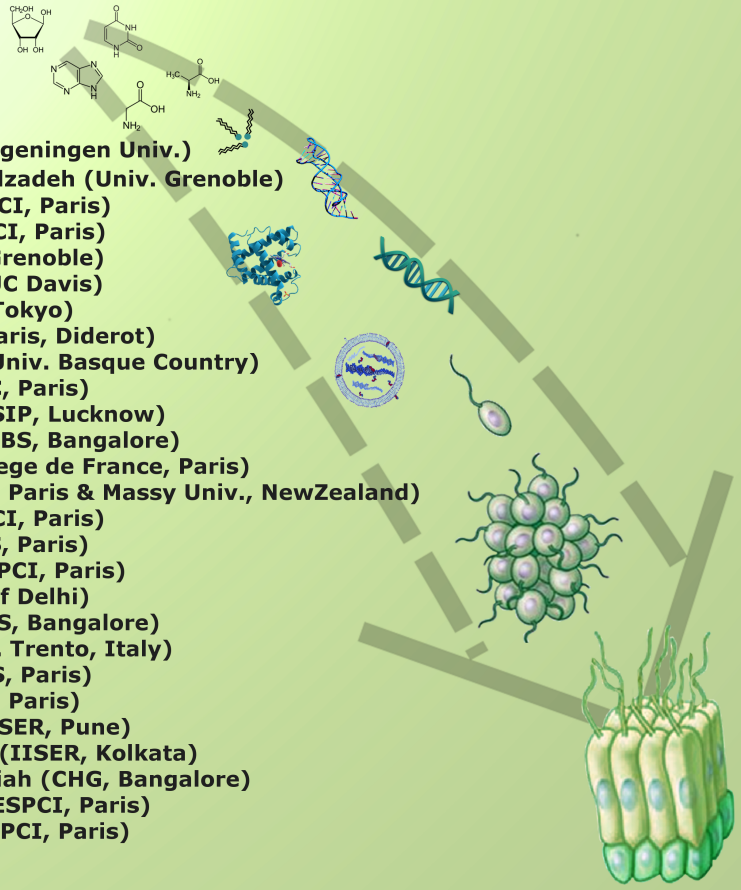
Emergence and evolution of biological complexity

(From the origins of life to multicellularity)

4-6th February, 2017, NCBS Bangalore

Registration deadline, 15th November, 2016



Speakers

Arjan de Visser (Wageningen Univ.)
Bahram Houchmandzadeh (Univ. Grenoble)
Clément Nizak (ESPCI, Paris)
David Lacoste (ESPCI, Paris)
Ivan Junier (Univ. Grenoble)
James Griesemer (UC Davis)
Jim Cleaves (ELSI, Tokyo)
Julien Derr (Univ. Paris, Diderot)
Kepa Ruiz-Mirazo (Univ. Basque Country)
Martin Weigt (UPMC, Paris)
Mukund Sharma (BSIP, Lucknow)
Mukund Thattai (NCBS, Bangalore)
Olivier Rivoire (College de France, Paris)
Paul Rainey (ESPCI, Paris & Massy Univ., NewZealand)
Philippe Nghe (ESPCI, Paris)
Rémi Monason (ENS, Paris)
Sandeep Ameta (ESPCI, Paris)
Sanjay Jain (Univ. of Delhi)
Shachi Gosavi (NCBS, Bangalore)
Sheref Mansy (Univ. Trento, Italy)
Silvia DeMonte (ENS, Paris)
Simona Cocco (ENS, Paris)
Sudha Rajamani (IISER, Pune)
Supratim Sengupta (IISER, Kolkata)
Vidyanand Nanjundiah (CHG, Bangalore)
Yannick Rondelez (ESPCI, Paris)
Zorana Zeravcic (ESPCI, Paris)

Organizers

Clément Nizak (ESPCI, Paris), Philippe Nghe (ESPCI, Paris), Sandeep Ameta (ESPCI, Paris), Sandeep Krishna (NCBS, Bangalore), Sudha Rajamani (IISER, Pune)

Contact:
Email: complexity@ncbs.res.in
Website: https://www.ncbs.res.in/events/evolution-biological-complexity

Contents

WiFi and Phone Numbers

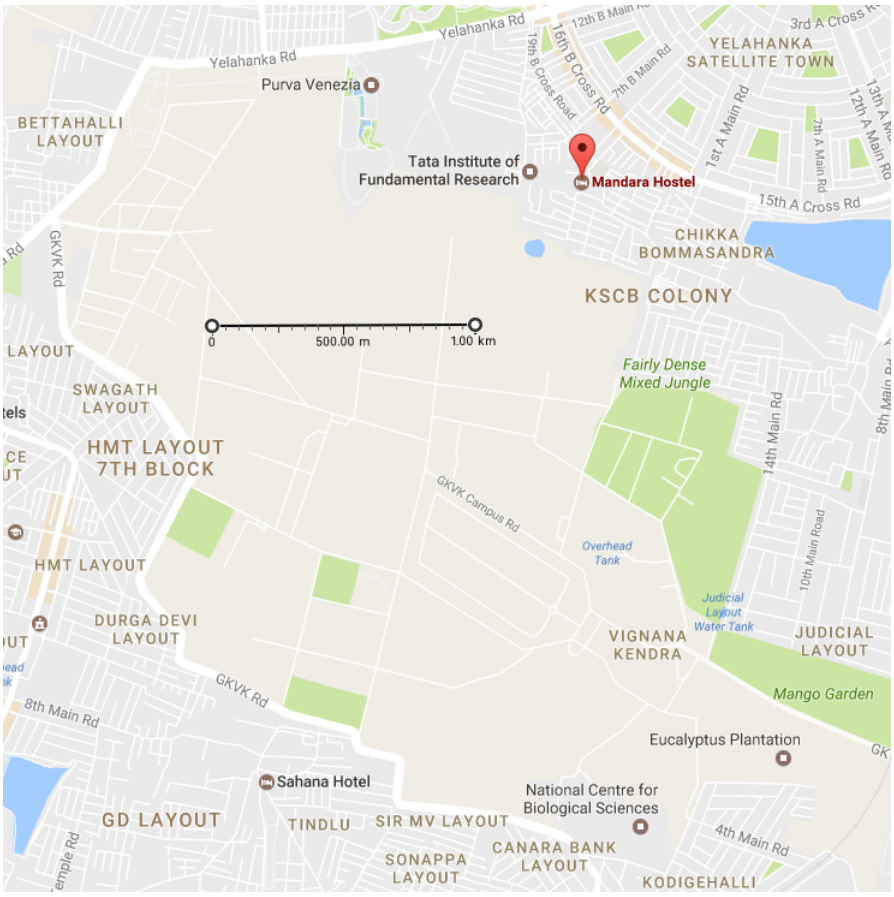
1 WiFi

1. Use your Eduroam login if you have one, or,
2. Connect to 'NCBS Hotspot'
   Open any page on your browser – it will display a short form
   Upon submitting the form you will receive an activation email
   Open that email and click on the link within to get 24hr Internet access

2 Important phone numbers

1. NCBS reception:
   +91 80 23666001/6002/6018/6019
   +91 80 67176001/6002/6018/6019
   (from within NCBS you only have to dial the last four digits)
2. Meetings Office Executives:
   Bhavya S +91 9742992541 or +91 9740329317
   Bhavya R +91 9844593831
3. Sandeep Krishna: +91 8722211882

Transport to/from NCBS housing campus (Sugandhi and Mandara)



Some of you are staying at the NCBS housing campus (‘Mandara hostel’ on google maps, at top of the map above), and some of you on the NCBS main campus (’National Centre for Biological Sciences’ on google maps, at bottom of the map above)

For speakers, there are NCBS cars to bring you back and forth whenever you want. Please call the NCBS reception if you do not find a car waiting for you at the housing campus.

For participants, special shuttles for the meeting will run at the following times:

From NCBS housing campus (Sugandhi and Mandara) to NCBS: 08:00, 08:15, 08:30, 08:45, 09:00, 09:15am
From NCBS to the NCBS housing campus (Sugandhi and Mandara): 20:30, 21:00, 21:30

If you miss these shuttles, there are also the regular shuttles and buggy trips between the campuses at the following times (this information is also listed on https://www.ncbs.res.in/shuttle_trips)

Shuttle timings between NCBS and Mandara

Weekdays		**Sunday**	
from **NCBS**	from **Mandara**	from **NCBS**	from **Mandara**
08:00 AM	07.30 AM	09:00 AM	08.30 AM
09:00 AM	08.30 AM	10:30 AM	09.30 AM
10:00 AM	09.30 AM	08:30 PM	06.00 PM
05:45 PM	10.30 AM	10:00 PM	09.30 PM
08:30 PM	06.05 PM	11:00 PM	10.30 PM
10:00 PM	09.30 PM	02:00 AM	12.00 AM
11:00 PM	10.30 PM		
12:30 AM	11.30 PM		
01:30 AM	01.00 AM		

Buggy timings between NCBS and Mandara

from **NCBS**	from **Mandara**
07:45 AM	08.00 AM
08:30 AM	08.45 AM
09:00 AM	09.15 AM
09:30 AM	09.45 AM
10:30 AM	10.45 AM
11:15 AM	11.30 AM
01:00 PM	01.45 PM
02:00 PM	02.30 PM
03:00 PM	03.30 PM
06:00 PM	06.15 PM
06:30 PM	06.45 PM
07:00 PM	07.15 PM
08:00 PM	08.15 PM

Map of main NCBS campus

Schedule

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

	Feb 4, Sat	**Feb 5, Sun**	**Feb 6, Mon**
08:15-09:00	Breakfast		
09:00-09:30	Breakfast+Registration		
09:30-10:00	Registration continues Opening remarks at 9:50	Zorana Zeravcic	Ivan Junier
10:00-10:30	Julien Derr	Kepa Ruiz-Mirazo	Bahram Houchmandzadeh
10:30-11:00	Flash talks: Lorenz Keil, Manoj Gopalkrishnan	Olivier Rivoire	Flash talks: Mrudula Sane, Md. Zahid Kamal
11:00-12:00	Tea/coffee/posters		
12:00-12:30	David Lacoste	Arjan de Visser	James Griesemer
12:30-13:00	Flash talks: Niraja Bapat, Karsten Kruse	Yannick Rondelez	Mukund Thattai
13:00-14:00	Lunch		
14:00-15:00	Poster Session		
15:00-15:30	Sheref Mansy	Shachi Gosavi	Silvia De Monte
15:30-16:00	Sanjay Jain	Simona Cocco	Mukund Sharma
16:00-16:30	Sandeep Ameta	Rémi Monasson	Vidyanand Nanjundiah
16:00-16:30	Supratim Sengupta	Tea/coffee/posters	Tea/coffee/posters
17:00-18:00	Tea/coffee/posters	Tea/coffee/posters	Tea/coffee/posters
18:00-19:00	Keynote: Jim Cleaves	Keynote: Martin Weigt	Keynote: Paul Rainey
19:00-19:30	Free/Discussion time	Free/Discussion time	Free/Discussion time
19:30-21:00	Beverages & Dinner		

Detailed schedule for Saturday, 4 Feb, 2017		
	08:15-09:00	Breakfast
	09:00-09:50	Breakfast + Registration
	09:50-10:00	Opening remarks
Chair: Arati Ramesh (NCBS, Bangalore)	10:00-10:30	Julien Derr, Emergence of complexity in the RNA world
	10:30-10:45	Lorenz Keil, Microthermal approaches to the origin of life
	10:45-11:00	Manoj Gopalkrishnan, A proposal for open-ended evolution in silico
	11:00-12:00	Tea/coffee/posters
Chair: Philippe Nghe (ESPCI, Paris)	12:00-12:30	David Lacoste, Kinetics and thermodynamics of reversible polymerization
	12:30-12:45	Niraja Bapat, Enzyme-free prebiotic reactions and their implication for early information transfer
	12:45-13:00	Karsten Kruse, Unbounded growth patterns of reproducing, competing polymers – similarities to biological evolution
	13:00-14:00	Lunch
	14:00-15:00	Poster session
Chair: Sudha Rajamani (IISER Pune)	15:00-15:30	Sheref Mansy, Prebiotic synthesis of iron-sulfur peptides
	15:30-16:00	Sanjay Jain, Emergence of complexity in prebiotic chemical evolution: Some mathematical models
	16:00-16:30	Sandeep Ameta, Autocatalytic RNA replicators in origin of life
	16:30-17:00	Supratim Sengupta, Perspectives on the origin of the standard genetic code
	17:00-18:00	Tea/coffee/posters
Chair: Sudha Rajamani (IISER Pune)	18:00-19:00	Jim Cleaves, The chemical space of life
	19:00-19:30	Free/Discussion time
	19:30-21:00	Beverages & Dinner

Detailed schedule for Sunday, 5 Feb, 2017		
	08:15-09:00	Breakfast
	09:00-09:30	Breakfast + Registration
Chair: Shashi Thutupalli (NCBS, Bangalore)	09:30-10:00	Zorana Zeravcic, Spontaneous emergence of self-replicating cycles with colloidal spheres
	10:00-10:30	Kepa Ruiz-Mirazo, Grasping the core of biological complexity: autonomy and open-ended evolution
	10:30-11:00	Olivier Rivoire, Informations in models of evolving populations
	11:00-12:00	Tea/coffee/posters
Chair: Kavita Jain (JNCASR, Bangalore)	12:00-12:30	Arjan de Visser, Exploring the evolvability of an antibiotic resistance enzyme
	12:30-13:00	Yannick Rondelez, Parameter landscapes for artificial reaction-networks
	13:00-14:00	Lunch
	14:00-15:00	Poster session
Chair: Clément Nizak (ESPCI, Paris)	15:00-15:30	Shachi Gosavi, Non-folding factors that modulate folding energy landscape
	15:30-16:00	Simona Cocco, Maximum entropy modeling of protein families: What lattice proteins teach us
	16:00-16:30	Rémi Monasson, Selective and entropic forces on immunostimulatory motifs in viruses and non-coding RNA
	16:30-18:00	Tea/coffee/posters
Chair: Clément Nizak (ESPCI, Paris)	18:00-19:00	Martin Weigt, Bridging multiple scales in the coevolution of interacting proteins
	19:00-19:30	Free/Discussion time
	19:30-21:00	Beverages & Dinner

Detailed schedule for Monday, 6 Feb, 2017		
	08:15-09:00	Breakfast
	09:00-09:30	Breakfast + Registration
Chair: Aswin Seshasayee (NCBS, Bangalore)	09:30-10:00	Ivan Junier, Coordination of transcription in bacteria: What do we know?
	10:00-10:30	Bahram Houchmandzadeh, Neutral aggregation in genome space
	10:30-10:45	Mrudula Sane, How does bacterial GC content evolve?
	10:45-11:00	Md. Zahid Kamal, Evolution of interactome complexity of survivin, a hub in protein interaction network
	11:00-12:00	Tea/coffee/posters
Chair: Sunil Laxman (InStem, Bangalore)	12:00-12:30	James Griesemer, Beyond the rock (genome-centrism) and the hard place (self-organization): Breaking dichotomies of biological systems thinking
	12:30-13:00	Mukund Thattai, Possible and impossible cells
	13:00-14:00	Lunch
	14:00-15:00	Poster session
Chair: Ramray Bhat (IISc, Bangalore)	15:00-15:30	Silvia De Monte, The evolution of collective function in multicellular assemblages
	15:30-16:00	Mukund Sharma, Darwin's dilemma and enigma & evidence of precambrian life
	16:00-16:30	Vidyanand Nanjundiah, Self-organisation and social selection lie behind the complexity of Dictyostelid life cycles
	16:30-18:00	Tea/coffee/posters
Chair: Philippe Nghe (ESPCI, Paris)	18:00-19:00	Paul Rainey, Origin of multicellularity
	19:00-19:30	Free/Discussion time
	19:30-21:00	Beverages & Dinner

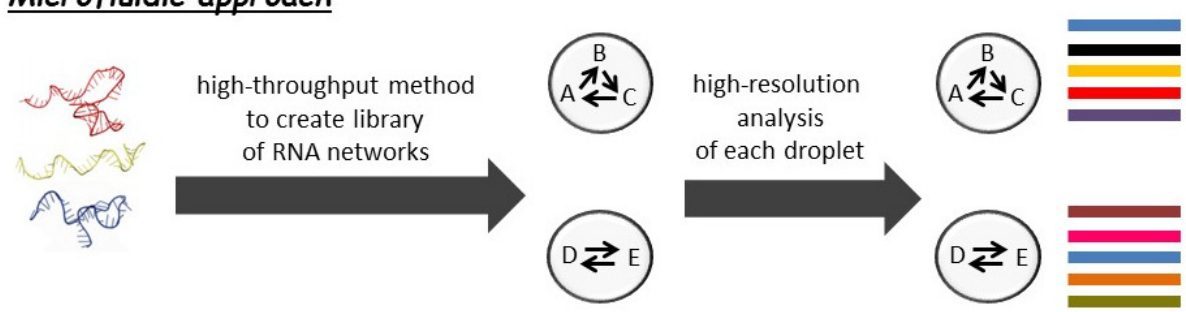
Talk Abstracts

Autocatalytic RNA Replicators in Origin of Life

Sandeep Ameta

ESPCI, Paris

Self-assembly must have been an intriguing feature of prebiotic molecules to generate first life-like scenarios on Earth. Both small molecule-based chemical systems as well as RNA are shown to possess self-assembly properties to generate more complex prebiotic-relevant products[1,2]. Recent works has shown how small RNA fragments of *Azoarcus* group I intron spontaneously self-assemble to form fully-functional ribozymes in a co-operative and autocatalytic fashion[3,4], overcoming the hurdle of error-catastrophe in a pure replication-based origin-of-life system[5,6]. In the current project, we are exploiting these self-assembling RNA fragments to study complex autocatalytic RNA networks with an ultimate goal of demonstrating Darwinian-like evolution. To this end we have developed a high-throughput experimental set-up by combining droplet-microfluidics[7,8] with next-generation sequencing where we can study RNA networks in each droplet at an unprecedented resolution.



We selected few sub-sets of RNA fragments from *Azoarcus* group I intron ribozyme system based on different network parameters[9,10] to generate a diverse RNA network library using droplet-microfluidics. This library will be evaluated for the relation between network topology and 'fitness'. Having established a good relation between network topology and fitness, these topologies will be further evaluated for information retention and transfer in such rudimentary RNA networks.

1. Deamer, D., Singaram S., Rajamani S., Kompanichenko V., Guggenheim S., Philos. Trans. R. Soc. Lond., B, Biol. Sci., 361, 2006.
2. Higgs P. G., Lehman N., Nat. Genet., 16, 2015.
3. Hayden, E. J., Lehman, N., Chem. Biol., 13, 2006.
4. Vaidya, N., Manapat M.L., Chen I. A., Xulvi-Brunet R., Hayden E.J., Lehman N., Nature, 491, 2012.

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6. Kun, A., Santos, M., Szathmary, E., Nat. Genet., 37, 2005.
7. Ryckelynck, M., Baudrey S., Rick C., Marin A., Coldren F., Westhof E., Griffiths A.D., RNA, 21, 2015.
8. Matsumura S., Kun A., Ryckelynck, M., Coldren F., Szilagyi A., Jossinet F., Rick C., Nghe P., Szathmary E., Griffiths A.D., Science,354, 2016.
9. Nghe P., Hordijk W., Kauffman S.A., Walker S. I., Schmidt F. J., Kemble H., Yeates J. A. M., Lehman N., Mol. BioSyst., 11, 2015.
10. Jain S., Krishna S., Proc. Natl. Acad. Sci. USA, 98, 2001.

The Chemical Space of Life

Jim Cleaves

ELSI Tokyo Tech

Terrestrial organisms share a great deal of biochemical composition and organization, for example in the use of the canonical ribonucleotides, deoxyribonucleotides, amino acids, and cofactors and in the form of the very nearly universal genetic code. However, it is now known from a few natural and laboratory-engineered examples that some fundamental aspects of biochemistry can be altered or augmented. For example alternative amino acids and nucleobases are used by some free-living organisms or have been experimentally incorporated into others. We have explored, using graph theory-based computational techniques, the chemical space of possible isomers of nucleosides (the building blocks of nucleic acids), alpha-amino acids (the building blocks of proteins) and the components of the reverse tricarboxylic acid cycle (a fundamental carbon-fixation pathway). For these compound classes, there are thousands to billions of possible isomers or compounds which are chemically similar. This raises numerous fundamental questions: what type and how many unnatural substitutions can be substituted into modern organisms? What selection pressures may have guided nature's "choice" of components? Is biochemistry an optimal solution to life's function, or could it perhaps have been otherwise, or be otherwise elsewhere? Answers to these questions could help us design new forms of biology, detect alien or "shadow" biologies, and understand how our own form of biology came to be as it is.

Effect of Presence of Co-solutes on Enzyme-free Copying Reactions

Niraja Bapat

IISER, Pune

Nonenzymatic propagation of the genetic information would have been a crucial step during the origin of life on prebiotic Earth. It has been observed that the addition of non-cognate nucleotides during nonenzymatic replication stalls the process and also leads to a cascade of mismatches after the initial erroneous addition. However, these studies were carried out in a chemically simpler environment, which might not be a true representative of prebiotic milieu. Here we report, the effect of presence of Poly Ethylene Glycol (PEG) and double chain surfactant lipid as co-solutes on enzyme-free template directed copying reactions using 5'-imidazolides. We observed that the rate of primer extension was slowed down in the reaction involving addition of a 'matched' purine monomer.

Moreover, combined use of PEG and lipid led to an even greater decrease in the extension rates in such reactions. We also observed that reactions involving the addition of a mismatched monomer across the non-cognate template base, were not notably affected. This resulted in elevated frequency of incorrect additions, specifically against 'C' and 'U' template bases. This is critical to consider as rate of addition of correct or incorrect monomers would potentially have had important consequences for the accuracy of enzyme-free reactions, in a putative RNA world. Our results suggest direct implications for efficient replication of functional nucleic acid sequences in a complex prebiotic milieu.

Maximum Entropy Modeling of Protein Families: What Lattice Proteins Teach Us

Simona Cocco

ENS, Paris

Massive sequencing techniques make available ever-increasing numbers of protein sequences. A fundamental problem is to extract structural and functional information from those sequence data, and to identify sequences sharing common structure and/or function (corresponding to a given family). I will review how statistical physics tools can be helpful to model the (wide) distribution of sequences in a family, and how maximum-entropy approaches allow us to infer the 'energetic' parameters of models from the sequence data. The inferred models provide information on the three-dimensional structures of the proteins, and could be useful to design new, artificial proteins sharing the features common to the family. I will address more conceptual questions about the validity of the maximum-entropy approaches on synthetic data corresponding to lattice-based proteins, which are controlled albeit 'realistic' models of proteins.

The Evolution of Collective Function in Multicellular Assemblages

Silvia De Monte

ENS, Paris

Modeling the evolution of collective properties, such as for instance cooperative behaviour, has mainly focused on the effect of individual actions on fitness within groups, and much less on the mechanisms through which such groups formed in the first place or perpetuated. In this talk I will address a general mechanism of physical interaction – adhesion – in its evolutionary consequences, and as a determinant of evolutionary changes in the structure and function of groups of cells. I will discuss the adaptive evolution of adhesiveness, as measured by a quantitative trait. Under general conditions, this trait can evolve towards higher values, entraining a change in the group structure of the population, together with group performance. An interesting consequence of specifying the mechanism of group formation is the possibility of accounting for cells that remain ungrouped. I will show that even though they are excluded by definition from selection on group-level properties, such cells can play an important role in the early stages of the emergence of cellular collectives.

Emergence of Complexity in the RNA World

Julien Derr
Univ. Paris Diderot

During the origin of life, the biological information of nucleic acid polymers must have increased to encode functional molecules (the RNA world). Ribozymes tend to be compositionally unbiased, as is the vast majority of possible sequence space. However, ribonucleotides vary greatly in synthetic yield, reactivity and degradation rate, and their non-enzymatic polymerization results in compositionally biased sequences.

While natural selection could lead to complex sequences, molecules with some activity are required to begin this process. Was the emergence of compositionally diverse sequences a matter of chance, or could prebiotically plausible reactions counter chemical biases to increase the probability of finding a ribozyme?

After discussing the issues of defining and measuring complexity in the context of the RNA world, I will detail the results of a study of ours considering Shannon entropy concepts:

Using simulations, we showed that template-directed ligation and high concatenation rates counter compositional bias and shift the pool toward longer sequences, permitting greater exploration of sequence space and stable folding. We verified experimentally that unbiased DNA sequences are more efficient templates for ligation, thus increasing the compositional diversity of the pool. Our work suggests that prebiotically plausible chemical mechanisms of nucleic acid polymerization and ligation could predispose toward a diverse pool of longer, potentially structured molecules. Such mechanisms could have set the stage for the appearance of functional activity very early in the emergence of life.

Finally, I will compare this study to the litterature and discuss prospects.

Exploring the Evolvability of an Antibiotic Resistance Enzyme

Arjan de Visser
Laboratory of Genetics, Wageningen University, Wageningen, The Netherlands

Evolution is inherently stochastic due to chance events, such as mutations, but not fully random due to deterministic consequences of natural selection and developmental constraints. A better understanding of the factors and conditions that increase the predictability of evolution may help to control the evolution of unwanted phenotypes, such as antibiotic-resistant pathogens. I will present results from evolution experiments with the notorious antibiotic resistance enzyme, TEM-1 β-lactamase, in the presence of third-generation cephalosporin cefotaxime. We use both *in vitro* (only TEM) and *in vivo* (TEM + host) evolution experiments to address the effect of population size on the tempo and mode of adaptation. The results from *in vitro* experiments show greater adaptive heterogeneity, with higher maxima, in small relative to large populations, as well

as indirect effects of TEM expression on the fitness of others than the producer. In the *in vivo* experiments we find no adaptive benefit for small populations, but differential effects from population size on the repeatability of different mutation classes: large populations show more parallel SNPs and indels, while small populations show more parallel large-scale chromosomal changes. We hypothesize that this divergent result derives from clonal interference benefitting lower-rate, but larger-benefit SNPs and indels.

A Proposal for Open-ended Evolution In Silico

Manoj Gopalkrishnan

IIT Bombay

Darwinian evolution on earth has taken primordial self-replicating systems to the manifold sophisticated forms of life that inhabit our planet today. Sophisticated agents in an ecosystem force each other to become even more sophisticated by competing for resources, and by literally feeding on each other. We are attempting to get to the heart of the algorithmic ideas that allow open-ended evolution by building a software system with similar feedback loops as nature, hoping to see more and more sophisticated behavior the longer it is run.

Our animals are decision trees which compete for resources by making predictions on a bit-string environment of which they themselves are also a part. The survivors pass on their strategies to progeny with variation. The bit-string environment dynamically reflects the changing composition, and increasing sophistication, of the population. As the population becomes more sophisticated, the animals find themselves challenged with an environment that has become harder to predict. We hope this will force an unbounded ratcheting-up of sophistication. To test whether our system is indeed able to increase in sophistication, we challenge it with a machine learning problem, and find promising initial results.

Non-folding Factors That Modulate Folding Energy Landscapes

Shachi Gosavi

NCBS, Bangalore

The chemistry of the same amino-acid sequence ensures both protein folding and protein function (defined in the broadest sense and includes binding and activity, post-translational modifications, protein localization, etc.). Amino acids that have been conserved to aid these non-folding effects are also present while folding and modulate the folding energy landscape in a variety of ways. I will give a few examples of such effects, how they can be detected through protein folding simulations and how they aid in understanding the design of natural proteins.

Beyond the Rock (Genome-Centrism) and the Hard Place (Self-Organization): Breaking Dichotomies of Biological Systems Thinking

James Griesemer
University of California, Davis

Understanding the complexity of biological systems is often portrayed in terms of a dichotomy between systems as designed or evolved and requiring inputs of energy, information, structure, or control from outside versus systems as self-organizing or self-assembling which lack or are independent of such requirements. Is order costly because of this design input or free because spontaneously organized out of noise or chaos? In this presentation of some very preliminary ideas, I explore a way of breaking out of this dichotomy in terms of dynamical transformations that are not exactly designed or programmed nor merely seeded or triggered. I call such systems "scaffolded" and suggest they display their own mode of complexity. Scaffolded developmental systems require inputs from outside only in the sense that the concept of "system" already requires heuristic idealization of inside and outside such that scaffolds are recognized as coming from outside rather than within. Scaffolds are not mere triggers or seeds, nor are they (typically) full-blown genomes in structure, function or inheritance. They join and become active participants in developmental systems, but can have quite different properties than the genomes sometimes said to program or serve as software for cellular hardware. In the talk, I plan to briefly touch on two modes of systems thinking, make some brief remarks on complexity, organization, and emergence, introduce the concept of developmental scaffolding and an associated account of biological reproduction, and finally to mention two applications of the perspective: a way of thinking about the complexity of complex life cycles and the idea that scaffolding can be a fitness modulator of developmental reaction norms.

Neutral Aggregation in Genome Space

Bahram Houchmandzadeh
Univ. of Grenoble

Complex patterns observed in nature can be due random, neutral events. For example, individuals randomly moving, reproducing and dying will tend to agglomerate and form high density clusters even in the absence of attractive interactions or habitat heterogeneity. We show that a similar phenomenon occur in the genome space: genes subject to random mutations, reproduction and death will also agglomerate and form clusters in the genome space, even in the absence of selection. The amplitude of this neutral clustering depends on the population size, sequence length and mutation rate through a very simple relation.

1. PHYSICAL REVIEW E 95, 012402 (2017) https://hal.archives-ouvertes.fr/hal-01377505v2

Emergence of Complexity in Prebiotic Chemical Evolution: Some Mathematical Models

Sanjay Jain

Department of Physics and Astrophysics, University of Delhi, India

Two puzzles that are part of the origin of life problem will be discussed. One, how did a complex chemical organization emerge on the prebiotic Earth, and two, how did large molecules consisting of hundreds of monomers first arise? Mathematical models of artificial chemistries that provide speculative solutions to these two questions will be described. The dynamics of auto-catalytic sets plays an important role in both.

Coordination of Transcription in Bacteria: What Do We Know?

Ivan Junier

CNRS & Université Grenoble Alpes, TIMC-IMAG, Grenoble, France

Coordination of gene transcription allows cells to continuously adapt their molecular content to varying environmental conditions. The mechanisms at the core of this basal coordination yet remain to be understood with, in particular, the puzzling observation in all bacteria studied so far, of a majority of operons that are not directly regulated by transcription factors (TFs). In this talk, I will present a framework that aims at identifying specific domains of transcriptional coordination in any bacterium. It is based on the identification of conserved domains of proximal genes (synteny segments) in a thousand bacterial genomes. Within these synteny segments, which extend beyond the operon scale, the basal coordination of operons appears to be independent of the action of TFs and sigma factors. Instead, in-depth analyses in well-studied model organisms call for a mechanism of facilitated co-transcription, according to which the transcription of an operon mechanically enhances the transcription of adjacent operons.

1. Junier, I., & Rivoire, O. (2016) Conserved Units of Co-Expression in Bacterial Genomes: An Evolutionary Insight into Transcriptional Regulation. PLoS ONE, 11(5), e0155740. http://doi.org/10.1371/journal.pone.0155740
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Evolution of Interactome Complexity of Survivin, a Hub in Protein Interaction Network

Md. Zahid Kamal

National Centre for Cell Science, Pune

There is little room, if any, for the argument against the continuous increase in biological complexity during evolution. However, while the increase in complexity at the morphological and anatomical level of organisms is evident and easily acceptable, same can't be said at the molecular level. What kind of changes at the molecular level accompanies increased complexity at organismal

level; do the molecules themselves become more complex? Non-existence of good correlation between genome-size and complexity of organisms strongly pointed towards the possibility that organism complexity might be related to size of the interactome. Findings such as epistasis being the major force in evolution also support such possibility. The best way to increase interactome-size, without paying additional cost of increasing genome-size, is to employ same molecule in many more (new) interactions. I am investigating such possibilities using survivin, a hub protein in protein-protein interaction network. My study suggests that survivin has increased its number of interactions in higher organisms without increasing number of binding interfaces; surprisingly it does so while decreasing its molecular size.

Microthermal Approaches to the Origin of Life

Lorenz Keil

LMU, Munich

All known living systems are built around information stored in RNA and DNA. To protect this information against molecular degradation and diffusion, the second law of thermodynamics imposes the need for a non-equilibrium driving force. We have shown that heat gradients across sub-millimetre sized pores can drive an accumulation, replication, and selection of ever longer molecules, implementing all the necessary parts for Darwinian evolution [1]. We show that heat gradients can also form pH gradients of at least 1-2 units. Here, individual species of a buffer solution exhibit an increase in concentration at the bottom, in which the accumulation of the proton acceptor is mostly stronger compared to the proton donor. As a result, the protonation at the bottom locally reduces the oxonium ion concentration and forms a pH gradient. This finding opens the door for various reaction pathways to the origin of life that involve subsequent pH changes [2]. We also found that laminar thermal convection can efficiently drive an RNA-catalyzed form of polymerase chain reaction. The laminar convection offers a variety of temperature cycle conditions for bulk material. The RNA polymerase ribozyme replicates short RNA strands up to 10 nucleic acids, thus enabling the propagation of information in a natural environment and the absence of proteins [3].

[1] M. Kreysing et al., Nat. Chem. 7, 203-208 (2015)

[2] M. W. Powner et al., Nature 459, 239-242 (2009)

[3] D. P. Horning and G. F. Joyce, PNAS 113, 9786-9791 (2016)

Unbounded Growth Patterns of Reproducing, Competing Polymers–Similarities to Biological Evolution

Karsten Kruse

Univ. of Geneva

Since the origin of life the interplay between reproduction, variation, and selection has been driving the emergence of new species. The evolution of the Earth's biosphere appears to innovate unceasingly instead of coming to a stall. Here, we introduce a model system of linear molecules where new polymers appear by spontaneous ligation. The polymers proliferate following a template-based mechanism. Our combined experimental and theoretical study shows that for sufficiently rapid autocatalysis the reproduction process selects particular lengths–while ever longer polymers emerge. We suggest similarities to biological evolution.

Kinetics and Thermodynamics of Reversible Polymerization

David Lacoste

ESPCI, Paris

Biological systems make extensive use of reversible polymerization: peptides are assembled from amino-acids, actin filaments are assembled from G-actin and glucans (carbohydrates) are assembled from monosaccharides. In this talk, inspired by a recent experimental study on the metabolism of glucans, we study the self-assembly of such polymers from the point of view of non-equilibrium thermodynamics. We first consider a closed system in which polymers dynamically evolve towards equilibrium where detailed balance is satisfied and the entropy is maximum. We then consider open systems, in which the polymers are in contact with chemostats, characterized by fixed concentrations of polymers of a given length. In accordance to a general theoretical result, we find new dynamic regimes when the number of chemostats is larger than the number of conservation laws of the chemical network. We will then discuss extensions of this framework for the self-assembly of polymers which carry information in their sequence.

1. Kinetics and thermodynamics of reversible polymerization in closed systems, S. Lahiri, Y. Wang, M. Esposito, and D. Lacoste, New J. Phys., 17, 085008 (2015)
2. Glucans monomer exchange dynamics as an open chemical network, R. Rao, D. Lacoste and M. Esposito, J. Chem. Phys., 143, 244903 (2015).

Prebiotic Synthesis of Iron-Sulfur Peptides

Sheref S. Mansy

Univ. of Trento

Iron-sulfur clusters are ancient cofactors that play a fundamental role in metabolism and may have impacted the prebiotic chemistry that led to life. However, it is unclear whether iron-sulfur clusters could have been synthesized on the early Earth. Here we outline one potential way in which iron-sulfur clusters could have been synthesized on the surface of prebiotic Earth through

mechanisms highly similar to the metallochaperone pathways found in extant cellular life. [2Fe-2S] and [4Fe-4S] clusters coordinate to and are stabilized by a wide range of thiolate containing tripeptides in aqueous solution, and the assembly of iron-sulfur cluster-peptide complexes can take place within model protocells. Duplications of the tripeptides to hexa- and dodeca-peptides leads to increased stability and altered redox activity, suggesting a path from short, prebiotically plausible peptide sequences to ferredoxin-like polypeptides. In fact, the spacing of cysteines arising from such duplication events is highly similar to that of ferredoxin. Our experiments suggest that iron-sulfur clusters may have formed easily on early Earth, facilitating the emergence of an iron-sulfur cluster dependent metabolism.

Selective and Entropic Forces on Immunostimulatory Motifs in Viruses and Non-coding RNA

Rémi Monasson

ENS, Paris

An approach to quantify the interplay of entropic and selective forces on nucleotide organization is introduced and applied to the genomes of single-stranded RNA viruses and non-coding RNAs overexpressed in cancer cells. We first consider the case of influenza and HIV viruses. We find viruses altering their dinucleotide motif use under selective forces, with these forces on CpG dinucleotides growing stronger in influenza the longer it replicates in humans. For a subset of genes in the human genome, many involved in antiviral innate immunity, the forces acting on CpG dinucleotides are even greater than the forces observed in viruses, suggesting that both effects are in response to similar selective forces involving the innate immune system. In a second time, we consider a set of noncoding RNAs (ncRNAs) abundantly transcribed within tumors as opposed to normal tissue. We show that those ncRNAs are subject to forces similar to pathogen-associated RNA. For instance, the tumor-associated human satellite repeat II (HSATII) is enriched in motifs containing CpG dinucleotides in AU-rich contexts that most of the human genome and human adapted viruses have evolved to avoid. A key subset of these ncRNAs functions as immunostimulatory self-agonists and directly activates cells of the mono-nuclear phagocytic system to produce pro inflammatory cytokines. The innate response in tumors may partially originate from direct interaction of immunogenic ncRNAs expressed in cancer cells with innate pattern recognition receptors, revealing a previously unidentified danger-associated function to a set of dark matter repetitive elements.

1. A Quantitative Theory of Entropic Forces Acting on Constrained Nucleotide Sequences Applied to Viruses, B. Greenbaum, S. Cocco, A. Levine, R. Monasson, Proc. Natl. Acad. Sci. USA 111, 5054-5059 (2014)
2. Distinguishing the Immunostimulatory Properties of Non-coding RNAs Expressed in Cancer Cells. A. Tanne, L. Muniz, A. Puzio-Kuter, K. Leonova, A. Gudkov, D. Ting, R. Monasson, S. Cocco, A. Levine, N. Bhardwaj, B.Greenbaum, Proc. Natl. Acad. Sci. USA 112, 15154-15159 (2015)

Self-organisation and Social Selection Lie Behind the Complexity of Dictyostelid Life Cycles

Vidyanand Nanjundiah

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Aggregative multicellularity is found in all major groups of eukaryotes except one. In a striking example of convergent evolution, the underlying life cycles involve single cells that collaborate to form fruiting bodies, occasionally with reproductive division of labour. In the best studied case, that of the Dictyostelids (cellular slime moulds), multicellular complexity can be viewed in two ways. On the one hand, it is a product of spontaneous self-organisation. On the other hand, it is the evolutionary outcome of competition between stressed cells to survive and reproduce. The talk will attempt to integrate these two points of view. It will be argued that individual-level selection, acting in a social, and therefore interactive, context, makes it possible for genetically heterogeneous cooperative groups to co-exist stably in the long term.

1. Nanjundiah and Sathe, Integr Biol 3: 329–342, 2011; Saçlioğlu et al., J Biosci 39(2): 177–189, 2014.

Origin of Multicellularity

Paul Rainey

ESPCI, Paris and Massey Univ., New Zealand

The evolution of multicellular life from unicellular predecessors marks a Major Evolutionary Transition that underpins the emergence of biological complexity. Cooperation is central to the process, however the means by which the earliest groups of cells maintained integrity in the face of destructive cheating types is unclear. One idea posits cheats as a primitive germ line in a life cycle that facilitates group reproduction. I will describe an experiment in which simple cooperating lineages of bacteria were propagated under a selective regime that rewarded collective-level fecundity. Collectives reproduced via life cycles that either embraced, or purged, cheating types. When embraced, the life cycle alternated between phenotypic states. Selection fostered inception of a developmental switch that underpinned the emergence of collectives whose fitness, during the course of evolution, became decoupled from the fitness of constituent cells. Such development and decoupling did not occur when groups reproduced via a cheat-purging regime. The findings capture key events in the evolution of Darwinian individuality during the transition from single cells to multicellularity. If time permits, I will discuss new results arising from continuation of the core experiment with modification to explore the evolution of cancer and a potential resolution of Peto's paradox.

Informations in Models of Evolving Populations

Olivier Rivoire

College de France, Paris

I will present some simple models of evolutionary dynamics in fluctuating environments for which the adaptive value of different modalities of acquisition

and transmission of information can be compared. The models lead to generalizations of well-known quantities of information theory and provide a bridge between population genetics and stochastic control. I will discuss two applications of these models to rationalizing the diversity of biological phenomena: one pertaining to the multiplicity of modes of inheritance and the other to the multiplicity of immune strategies.

Parameter Landscapes for Artificial Reaction-Networks

Yannick Rondelez

ESPCI, Paris

Complexbehaviors can be produced -or controlled- by networks of simple elementsconnected in precisely organized larger systems. At the biochemical level, this is exemplified by impressive biologicalphenomena such as genetic regulation, morphogenesis, or the immune system, allcontrolled solely by dedicatedchemical reaction networks.

We are experimentally "universal" *in vitro* chemistries based on synthetic DNA oligonucleotides, that can be used to build dissipative, non-linear reaction network of any topology. This is because the identity ofthe nodes (the molecular compounds) canalways be found as short DNA strands.

However,the dynamic behavior of a network is controlled not only by its topology/structure,but results from the interplay with the dynamical properties of each individualelement. These individual properties may be difficult to accessor to to tune. What is then potential of a given chemical reactionnetwork in terms of dynamical function?

By compartmentalising reaction network in minute droplets, we interrogate the relationships betweenlocal features and global behaviors of man-made molecular programs in a high throughputformat.

Grasping the Core of Biological Complexity: Autonomy and Open-ended Evolution

Kepa Ruiz-Mirazo

University of the Basque Country, Spain

In this talk I will briefly present a theoretical framework to understand biological complexity that is based on two key ideas: autonomy and open-ended evolution. I will argue that biology requires a conceptual integration between two very different traditions, associated to apparently alternative approaches to life, physiology and evolutionary thinking, and exploring the relationship between those two key ideas, and how they may be implemented by real chemical systems, will surely contribute to the task. Furthermore, I will hold that the best arena to tackle this conceptual problem is the 'origins-of-life' research field, which should therefore become a central area of investigation in the natural sciences. We will never fully grasp biological complexity until we find out how it came about – or, more generally, how it may come about.

How Does Bacterial GC Content Evolve?

Mrudula Sane
NCBS, Bangalore

Bacterial genome GC content varies from ∼13% to 75% GC. Understanding the source and maintenance of this variation is important for understanding the evolution of codon usage bias and protein-coding sequences. Both neutral processes (like mutation) and selective processes (environmental selection) are thought to shape GC content. One environmental factor, nitrogen-limitation, is thought to select for AT-rich genomes. We hypothesized that if this is true, over evolutionary time scales genomes with an underlying GC→AT mutational bias would have a selective advantage over the wild-type under nitrogen-limitation. Our data suggest that under nitrogen-limitation, mutants with altered mutational biases vary in initial fitness, suggesting that under selection, these mutants would have different probabilities of becoming fixed in the population. We find that a mutant with a GC→AT bias does not have a fitness advantage over WT, but a mutant with an AT→GC bias has 30% higher fitness compared to the WT in nitrogen limitation, in a 24-hour competition. We find that the GC→AT biased mutant has a selective advantage over WT in rich media. This suggests that under nitrogen limitation, a GC→AT biased mutant would only rise to high frequencies under genetic drift. When evolved under genetic drift, these mutants show the expected whole genome mutational biases and mutation rates. We therefore now have expectations for what mutational biases arise under genetic drift, and we are currently evolving mutants with biased mutational spectra under environmental conditions implicated in GC content evolution to understand whether the spectrum of mutations fixed under selection is different from that observed under drift.

Perspectives on the Origin of the Standard Genetic Code

Supratim Sengupta
IISER, Kolkata

The standard genetic code (SGC) which provides a recipe for protein synthesis emerged nearly 4 billion years ago, prior to the appearance of the Last Universal Common Ancestor (LUCA) of all living organisms. The emergence of the SGC is one of the major transitions in evolution since it marks the transition from a plausible RNA world to a world of DNA and proteins. In this talk, I will highlight some of the challenges associated with understanding the origin of the genetic code and critically re-examine one of the primary theories of code-origin by using simulations of a finite population model of code-sequence co-evolution. I will then show how the effect of horizontal transfer of genetic elements across leaky protocells may have significantly facilitated the emergence of innovations in biological information encoding, which eventually culminated in the establishment of a universal and optimized genetic code.

Darwin's Dilemma and Enigma & Evidence of Precambrian Life

Mukund Sharma

Birbal Sahni Institute of Palaeosciences, Lucknow, India

More than 150 years ago, while propounding the theory of evolution, Darwin was perplexed with sudden appearance of complex life forms and body plans in the Cambrian sedimentary successions. Although he was aware of the vast sedimentary successions underlying the Cambrian Period, both in terms of geological age (¿541 million years ago) and thickness of the rock records (thousands of kilometres), yet the fossil records of pre-Cambrian Era were unknown to the world. It was an enigma to the *explorer Darwin*. He, therefore, argued if the theory of evolution was correct there ought to be signatures of gradual evolution of complexity in character states and body plans in the geological records. Unable to explain the 'Cambrian Explosion' of animal life in terms of his theory of evolution, he categorically expressed this dilemma in his famous book 'the Origins of Species'.

Even today the sudden appearance of eumetazoans with varied body plans in the Cambrian is a matter of heated debate. Palaeontologists and molecular biologists both are attempting to resolve this conundrum. Recent state of this dilemma is presented and enigmatic life forms recorded from Precambrian sedimentary successions are discussed. Some enigmatic fossil entities are also demonstrated which await suitable explanation. Complexities are not only manifested in metazoans but also noted up to certain degree in metaphytes. Palaeontological records of both metaphytes and metazoa are highly incomplete and any reconstruction in the evolutionary theory is always constrained by these limitations. Application of bio-medical engineering tool to understand and reconstruct plausible complex life entities from piecemeal evidence present in the nature is also demonstrated. The chain of global discoveries in the Ediacaran Period (635-541 million years before present) provides multiple lines of evidence of complex life forms. Radial, bilateral and asymmetric symmetry were noted in Ediacaran assemblage of Australia (570-545 million years before present). Radial symmetry, known since beginning of the biosphere, got another dimension in the form of bilateral symmetry in the Ediacaran Period. Discovery of putative fossil bilaterian embryos known from 580 million years old Daushantuo Formation of China (Chen et al., 2000, PNAS 97(4): 4457- 4462) suggest that evolutionary history of bilaterian forms could extend many million years deeper in the Precambrian times. Distinct cleavage patterns, such as spiral, radial, and syncytial, observed in extant animals certainly help understand the evolutionary steps adopted by the animal world in geological history. Advent of similar complexities in forms and functions are also noted in plants such as among the simplest cell harnessing light energy conversion mechanism by early bacteria to cyanobacteria to eukaryotes to multicellular grade organization. Report of multicellular eukaryotic macroscopic fossils from Lantian Formation, China (579-565 Ma) suggests that Marinoan glaciation drove the macroscopic multicellularity (Yuan et al., 2011, Nature 470: 390-393).

Gigantism is another route adopted by a few prokaryotes several times in the geological history, the reason for which is yet to be established. Based on the observations on the morphology of few other problematic macrofossils, it

is difficult to assign them to any extant forms or lineage. Such forms are considered as failed experiments of the Nature in the biological world. But despite this breadth of experimentation by nature in early multicellularity, no organ grade differentiation in embryophytes/plant forms could be established in pre Ediacaran world. Complexity in terms of diagnostic cell division at some stage of their life cycle and co-ordinated inter cellular signalling are known from pre Ediacaran records. It is yet to be established which lineages formalized such a habit (ontogenetically and ecologically). The presentation highlights the studies from Indian sedimentary successions and provides evidence of these complex forms.

Possible and Impossible Cells

Mukund Thattai

NCBS, Bangalore

Cells are the smallest complete units of self-replication, and all life is made up of them. It is becoming clear that cells are best studied as informational and computational units, not just physical machines. Many of the questions of interest to cell biologists into the general category of "how is this or that aspect of a cell encoded in its genome?" But the connection between molecules and phenotype is complex: cells are irreducible, and must be understood as a whole. I will discuss questions that arise in the study of membrane traffic: the logistics system that moves cargo between different parts of a cell. Surprisingly, many important issues can be phrased as well-posed abstract problems, whose analysis leads to experimentally testable predictions. I will close with our recent experimental work on the evolution of Saccharomyces carlsbergensis, the yeast that makes lager beer.

Bridging Multiple Scales in the Coevolution of Interacting Proteins

Martin Weigt

UPMC, Paris

Understanding protein–protein interactions (PPI) is central to our understanding of almost all complex biological processes. Computational tools exploiting rapidly growing genomic databases to characterize PPI are therefore urgently needed. Such methods should address multiple scales of PPI: (i) Between two interacting proteins, which residues are in contact across the interfaces? (ii) Inside a genome, which specific proteins interact and which do not? (iii) On evolutionary time scales, which protein-protein interactions are actually conserved across thousands of species? Statistical inference methods like the Direct-Coupling Analysis (DCA), have recently triggered considerable progress in using sequence data to connect these different scales, thereby helping to assemble quaternary protein structures and to predict conserved interactions between proteins. Besides evident bioinformatic applications in structural and systems biology, these methods help to deepen our understanding of the patterns of co-evolution between interacting proteins in general.

Spontaneous Emergence of Self-replicating Cycles with Colloidal Spheres

Zorana Zeravcic
ESPCI, Paris

Biological systems are a source of inspiration for creating a new paradigm for material synthesis. This paradigm aims to design materials that can self-replicate, while providing functionality such as catalysis of multiple reactions. Ultimately, tuning the parameters of such systems would allow the possibility of evolving materials with either designed or unexpected properties by carrying out cycles of mutation and selection. Even though these ideas seem removed from realization in the laboratory, recent experimental advances in coating colloidal-scale objects with specific glues, like complementary DNA strands, have suggested theoretical models in which the possibilities of these ideas can be explored in a controlled way. I will describe our ongoing work on exploring these ideas through theory and computer simulations.

Poster Abstracts

1 A Computational Model of Large-scale Nuclear Architecture

Ankit Agrawal, Nirmalendu Ganai, Surajit Sengupta, Gautam Menon
The Institute of Mathematical Sciences, Chennai

Active matter models describe a number of biophysical phenomena at the cell and tissue scale. Such models explore the macroscopic consequences of driving specific soft condensed matter systems of biological relevance out of equilibrium through micro-scale 'active' processes. In this poster we describe how active matter models can be used to study the large-scale properties of chromosomes within the nuclei of human cells in interphase. We show that polymer models for chromosomes that incorporate inhomogeneous activity reproduce many general, yet little understood, features of large scale nuclear architecture. These include: (i) the spatial separation of gene-rich, low-density euchromatin, predominantly found towards the centre of the nucleus, vis a vis. more peripheral, gene poor and denser heterochromatin regions, (ii) the differential positioning of individual gene-rich and gene-poor chromosomes, (iii) the formation of chromosome territories as well as (iv), the weak size dependence of the positions of chromosome centres-of-mass relative to the nuclear centre that is observed in some cell types. Such structuring is induced purely by the combination of activity and confinement and is absent in thermal equilibrium. We describe a systematic exploration of active matter models for chromosomes, indicating how our model can be generalized to study variations in chromosome positioning across different cell types. The approach described in this poster provides a quantitative, first-principles description of the non-equilibrium physics that underlies large-scale nuclear architecture.

2 High Glucose Uptake Rate in the Hotspring Biota of Ladakh, India

A.H. Ansari, Shamim Ahmed, V.K. Singh, Mukund Sharma, Yogesh Kumar
Birbal Sahni Institute of Palaeosciences, Lucknow

This study measures the in-situ glucose uptake rate by hotspring biota at the two different hotspring sites with different temperatures and pH. For that, we used ^{13}C labelled glucose as a substrate to spike in the gas-tight incubation bottles with the slurry from hotspring site. These incubation bottles were incubated for 0, 1, 2, 3, 4 hours and incubation were terminated on completion with $HgCl_2$. Centrifugation isolated the particulate matter from these incubation bottles and which then dried. The dried particulates were crushed with an agate mortar, and their $\delta^{13}C$ were measured on MAT-253 by combustion method. $\delta^{13}C$ of Panamik and Puga hotspring biota were -9.1‰ and -11.7‰ respectively. With

the uptake of ^{13}C labelled glucose, the maximum isotopic value in Panamik reached to 2472‰ at the end of the second hour. Similarly, the uptake of ^{13}C labelled glucose at Puga Hotspring site reached a maximum value of 4365‰ at the third hour. This infers an unknown intracellular constraint instead time on glucose uptake in hotspring biota. These isotopic values were used to calculate the uptake rate at the two hotspring site which was found dependent upon temperature of the Hotspring. At Panamik and Puga hotspring site uptake rate of the ^{13}C labelled glucose were 3.7 to 96.5 and 13.6 to 163.4 mmole g^{-1} dry weight. It reveals that even at very high-temperature thermophiles are capable of running their metabolic machinery perhaps faster than biota do at standard temperature and pressure.

3 Effect of Presence of Co-solutes on Enzyme-free Copying Reactions

Niraja V. Bapat, Sudha Rajamani
Indian Institute of Science Education and Research (IISER), Pune, India

Nonenzymatic propagation of the genetic information would have been a crucial step during the origin of life on prebiotic Earth. It has been observed that the addition of non-cognate nucleotides during nonenzymatic replication stalls the process and also leads to a cascade of mismatches after the initial erroneous addition. However, these studies were carried out in a chemically simpler environment, which might not be a true representative of prebiotic milieu. Here we report, the effect of presence of Poly Ethylene Glycol (PEG) and double chain surfactant lipid as co-solutes on enzyme-free template directed copying reactions using 5'-imidazolides. We observed that the rate of primer extension was slowed down in the reaction involving addition of a 'matched' purine monomer. Moreover, combined use of PEG and lipid led to an even greater decrease in the extension rates in such reactions. We also observed that reactions involving the addition of a mismatched monomer across the non-cognate template base, were not notably affected. This resulted in elevated frequency of incorrect additions, specifically against 'C' and 'U' template bases. This is critical to consider as rate of addition of correct or incorrect monomers would potentially have had important consequences for the accuracy of enzyme-free reactions, in a putative RNA world. Our results suggest direct implications for efficient replication of functional nucleic acid sequences in a complex prebiotic milieu.

4 Kinetics and Thermodynamics of Information-carrying Polymers

Alex Blokhuis, David Lacoste, Philippe Nghe
ESPCI, Gulliver; ESPCI, LBC

The RNA-world hypothesis posits that life started with populations of RNA that increased in complexity. So far, research on the first stages of the RNA-world has been focused on 'decorated' addition-fragmentation chemistry. We derive a consistent and general stochastic thermodynamics framework for information-carrying polymers. With this framework, we highlight that various nonequilibrium conditions can be employed for nonequilibrium polymerization and that energetically neutral recombination reactions can also be used to this effect. In addition, we find thermodynamic bounds for the speed of exploration of

sequence space, which forces us to reconsider current paradigms in prebiotic models.

5 Insects are Clever in Combating the Microbial Pathogens, Successfully Thrive and Continuously Evolve in the Ever Changing World

C. Ravi

Department of Zoology, Thiagarajar College Madurai - 625 009, India

Insects are ubiquitous and inhabit almost all environments except the marine ecosystem. Their ecological role is very important and without insects, life is very difficult in this planet. Insects are highly evolved and developed various adaptation strategies to counter the challenges being posed by the environment and pathogens. Most of the insects interact with the soil hence it is continuously exposed to various pathogens. Though evolution is very complex, the defense mechanisms of insects are comparatively simple yet very powerful. The resistance starts by avoiding the pathogens itself; they have an aversion towards the pathogens and their sensory systems are highly evolved thereby gives a wonderful shield to them. In addition to that, the hard cuticle prevents the entry of pathogens into the body of insects. However, the crafty pathogens gain entry into the body of insects where the immune system comes into act. The internal organs of insects float in the hemolyph pool where the pathogens are neutralized mostly by the antimicrobial peptides enzymes and other proteins. The insects have also developed unique biochemical pathways to hostage and destroy the pathogens. The adaptive immune system is not much developed hence there is no memory also. Nevertheless, the insects are combating the microbial pathogens, successfully thrive and continuously evolve in the ever changing earth. The article tries to explore the complexity in the evolution and adaptation of the immune system in insects.

6 On the Evolution of tRNA Modifying Enzymes and Their Impact on Bacterial Genome Evolution

Gaurav D Diwan, Saurabh Mahajan, Deepa Agashe

NCBS, Bengaluru

Bacterial translation involves the recognition of 61 sense codons on mRNAs bytransfer RNA (tRNA) molecules. However, all bacteria possess only a subset of thepossible 61 cognate tRNA molecules, which should prevent them from decoding all the codons used in protein-coding genes. This discrepancy is overcome by non Watson-Crick base pairing between a specific tRNA and multiple codons, achieved by chemical modication of the first base of the tRNA anticodon by modifying enzymes. Together, multiple tRNA modifying enzymes may allow bacteria to carry fewer tRNA genes, and to use all codons in their genome despite a limited tRNA pool. Both these possibilities have major implications for the evolution of bacterial genomes and the genetic code.We tested these hypotheses by analysing genomes of $\sim$1100 bacterial species. We determined the tRNA gene content of these bacteria and mined their proteomes for the presence of all reported modifying enzymes. Finally, we determined the

effective tRNA content of each species by factoring in the presence of modifying enzymes. We find that only a few tRNA modifying enzymes are ubiquitous in the bacterial phylogeny. Gammaproteobacteria have the largest repertoire of modifying enzymes, whereas Actinobacteria have very few modifying enzymes. We speculate that Actinobacteria lack several modifying enzymes because they use 'undecoded' codons very rarely, compared to other bacteria. More generally, we also find that although tRNA modifying enzymes allow for cognition of a wider set of codons, some codons do not have cognate tRNA molecules. Interestingly, these codons are typically rarely used, and we speculate that they may be translated (inefficiently) by near-cognate tRNAs. Alternatively, the recognition of these codons may depend on as yet undiscovered tRNA modifying enzymes. Contrary to our hypothesis, some bacteria have a very limited tRNA set as well as very few modifying enzymes. Most of these bacteria are animal endosymbionts or pathogens and have undergone rapid genome reduction that may account for the loss of multiple genes, including tRNAs and modifying enzymes. Their dependence on the host translation machinery may potentially explain their surprisingly limited decoding capability. Overall, our results suggest that tRNA modifying enzymes may help explain the observed variability in bacterial codon use and tRNA pools. Notable exceptions to the role of modifying enzymes include cases of massive genome reduction in endosymbionts and pathogens.

7 Development of Metabolic Pathway in Kluveromyces marxianus using RNAseq Data for Efficient Production of Biofuels

Varshit Dusad

IIT Kharagpur

Understanding biological complexity has been challenging exercises for biologists, physicists, and mathematicians alike. Deciphering in multicellular organisms is more difficult than unicellular organisms. However, the exercise is really fruitful if it can elucidate new properties about an industrial relevant organism like Kluveromyces marxianus, a yeast whose importance is recently recognized, as a potential microbial factory to produce biofuels. It is readily used as a host for metabolic engineering and recombinant protein production due to numerous benefits in comparison to Saccharomyces cerevisiae like thermotolerance and growth in many variety of sugars. Some The genome sequence has been annotated for this organism. We will use RNAseq data from wet lab experiments and analyze it through reconstructing pathway maps, enrichment statistics, reporter metabolites, and a flux simulation model to understand its genome-scale response in different conditions suitable for the production of biofuels in an integrative systems biology manner. Previous studies have emphasized the role of subcellular localization in the transcriptomic responses which agrees with our predictions. The final objective of this study is to derive key insights about metabolic pathways of Kluveromyces marxianus to develop a roadmap for efficient biofuel production.

8 Testing the Formation and Stability of Protocellular Vesicular Systems in Prebiotically Relevant Scenarios

Manesh Joshi, Sudha Rajamani
IISER Pune

Geothermal volcanic pools situated in Kamchatka peninsula (Russia) and Bumpass Hell (California, USA) have been studied in the context of a potential environment for the emergence of life on the early Earth. The highly acidic conditions of such geothermal pools, however, are thought be challenging for the formation and survival of the first protocells. On the contrary, the water samples collected from hot springs at Ladakh (India) showed alkaline pHs, ranging from 8-8.5. Therefore, it would be pertinent to know whether these conditions provide a better alternative for the emergence of first protocellular entities, one of the crucial steps for the evolution of early life. As a first step to understanding whether spontaneous assembly of vesicles is possible in aforementioned scenarios, we tested for the formation of mixed fatty acid vesicles that are thought to have formed the first protocells. We also evaluated their stability over several dehydration-rehydration cycles at elevated temperatures as these are thought to have assisted in the non-enzymatic polymerization of mononucleotides. The outcome of this experiment would help in better understanding of the potential candidature of lipids as a key element in the emergence of life on the prebiotic Earth.

9 Evolution of Interactome Complexity of Survivin, a Hub in Protein Interaction Network

Md. Zahid Kamal
National Centre for Cell Science, Pune

There is little room, if any, for the argument against the continuous increase in biological complexity during evolution. However, while the increase in complexity at the morphological and anatomical level of organisms is evident and easily acceptable, same can't be said at the molecular level. What kind of changes at the molecular level accompanies increased complexity at organismal level; do the molecules themselves become more complex? Non-existence of good correlation between genome-size and complexity of organisms strongly pointed towards the possibility that organism complexity might be related to size of the interactome. Findings such as epistasis being the major force in evolution also support such possibility. The best way to increase interactome-size, without paying additional cost of increasing genome-size, is to employ same molecule in many more (new) interactions. I am investigating such possibilities using survivin, a hub protein in protein-protein interaction network. My study suggests that survivin has increased its number of interactions in higher organisms without increasing number of binding interfaces; surprisingly it does so while decreasing its molecular size.

10 Microthermal Approaches to the Origin of Life

Lorenz Keil, Friederike Möller, Michael Kieß, Christof B. Mast, Dieter Braun
LMU Munich, Systems Biophysics, Amalienstrasse 54, 80799 Munich, Germany

All known living systems are built around information stored in RNA and DNA. To protect this information against molecular degradation and diffusion, the second law of thermodynamics imposes the need for a non-equilibrium driving force. We have shown that heat gradients across sub-millimetre sized pores can drive an accumulation, replication, and selection of ever longer molecules, implementing all the necessary parts for Darwinian evolution [1].

We show that heat gradients can also form pH gradients of at least 1-2 units. Here, individual species of a buffer solution exhibit an increase in concentration at the bottom, in which the accumulation of the proton acceptor is mostly stronger compared to the proton donor. As a result, the protonation at the bottom locally reduces the oxonium ion concentration and forms a pH gradient. This finding opens the door for various reaction pathways to the origin of life that involve subsequent pH changes [2].

We also found that laminar thermal convection can efficiently drive an RNA-catalyzed form of polymerase chain reaction. The laminar convection offers a variety of temperature cycle conditions for bulk material. The RNA polymerase ribozyme replicates short RNA strands up to 10 nucleic acids, thus enabling the propagation of information in a natural environment and the absence of proteins [3].

[1] M. Kreysing et al., Nat. Chem. 7, 203-208 (2015)

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[2] D. P. Horning and G. F. Joyce, PNAS 113, 9786-9791 (2016)

11 Is DNA Cytosine Methylation a Deliberate Bacterial Strategy to Introduce Consequential Mutations?

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Epigenetic modifications play a key role in gene regulation and in recognition of self DNA in bacteria. In-spite of their positive role in cell survival, modifications like cytosine methylation incur a mutational cost. Cytosine methylation, specifically 5-methylcytosine (5mC), is prone to hydrolytic deamination which leads to C $\rightarrow$ T and G $\rightarrow$ A transitions. Here, we first study the abundance of mutagenic cytosine methylation target motifs and show that bacteria like *Vibrio cholerae* might use motif avoidance as a strategy to minimize the mutational effect of deamination of methylated cytosine. Second by performing SNP analysis on whole genome sequence data from *Vibrio cholerae* patient isolates we show a) high abundance of cytosine methylation-dependent mutations in the cytosine methylation target motif RCCGGY, b) 95% of these C $\rightarrow$ T and G $\rightarrow$ A transitions in the coding region lead to non-synonymous substitutions and c) many of these transitions are associated with membrane proteins and are implicated in virulence. Thus, our SNP analysis of *V. cholerae* genomes implicates

the role of cytosine methylation in generating genotypic diversity with adaptive potential.

12 Collective Motility of Multiple Asters in Simulations

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Microtubules (MTs) and molecular motors (MMs) are an essential component of the eukaryotic cytoskeleton, with self organizing properties that result in emergence of cellular and sub-cellular patterns. Asters are radial arrays of MTs that function as microtubule organizing centers in the cells, involved in vital cellular processes such as cell division, motility, cellular transport and positioning of organelles. They can form self-organized patterns such as bipolar structures formed by heteromeric plus- and minus-ended motors motors[1], and produce centripetal movement by diffusible tetrameric minus-ended motors, reproducing observations in meiosis I of mouse oocytes[2]. In this study, we aim to examine patterns that emerge from the collective behavior of multiple asters and different motor types in the confined geometry. We have explored the regimes in which the motility of multiple asters exhibit disordered, directed or ordered motion. We model multiple asters confined in a circular geometry with different combinations of diffusible clustering dyneins and kinesin-5 motors. Preliminary results show random, pulsating and correlated motion of multiple asters in some scenarios. We quantify the observed motility regimes based on order parameters used for swarming motions as described by Viscek. In future, we aim to examine the effect of cortical and central localization of motors and their effect on coherent movement of the multiple asters. Such collective motion could also have implications for acentrosomal spindle assembly and centrosome motility in synctial cells.

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13 Logics for Algorithmic Chemistry

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Early work on theories of biological organization included the Algorithmic Chemistry project started by Walter Fontana. Though Fontana's early work based Algorithmic Chemistry on lambda calculus, in later work Fontana and Leo Buss report numerous problems with this approach. Central to their concerns was the inadequacy of the framework for modeling more complex phenomena at the biological level. The expressive limitations of the framework are a function of the logic on which it is based, so the more complex the phenomena, the more expressive the underlying logic needs to be. Accordingly, many alternative algorithmic chemistries have been developed, including refinements of those based on lambda calculus. In this paper, I address whether those refinements are enough to avoid Fontana and Buss's original criticisms. I then

propose a way to move forward with a chemistry-first approach to algorithmic chemistry development. A procedure is given by which a practicing scientist may select a framework best suited for their task, rather than continually amending a single fixed framework to extend its applicability beyond the expressive limitations of its logic.

14 Origins of Stochasticity of Cell Size, Interdivision Time and Growth Rate in Bacteria

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Recent single cell experiments have led to the observation of probability distributions ofcell sizes, interdivision times and growth rates in isogenic populations of bacteria. We have created simple non linear autocatalytic chemical models which include a division machinery that are successful at explaining a variety of features of the available data like the 'adder' property (adding a fixed amount of volume in a generation) that follows as an emergent property of the growth-division process. Using analytical methods we also show that a single microscopic parameter completely specifies the coefficient of variations of the macroscopic quantities viz. cell sizes (at birth and division), added volume and interdivision times. Through such simple models we have tried to provide a unified understanding of the origin of the complex correlations and relationships between macroscopic physiological quantities in populations of bacteria.

15 Investigating the Functional Relevance of Kinesin-3/UNC-104 Degradation at Synapses

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Kinesins are molecular motors that aid in microtubule based transport of cargo in the anterograde direction i.e. away from the nucleus. When not in use, there is increasing evidence to support auto-inhibition of these motors that may prevent futile ATP consumption. This mechanism has also been shown to be important for recycling Kinesin-1 motors once transport is complete.

A previous study from our lab has shown that Kinesin-3/CeUNC-104 in contrast is degraded in neurons at synapses. The physiological relevance of degradation as opposed to recycling is currently not known. One of the ways in which we are trying to address this question is by observing the consequences when the degradation of motor does not occur. A possible hypothesis could be that motor levels have to be maintained below a threshold at synapses to prevent self-activation and resulting competition between oppositely moving motors.

16 Microsimulation of Chemotaxis: Detailed Tracking of Each Bacterium in a Population

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Chemotaxis mechanism helps bacteria swim towards nutrients using temporal nutrient gradient. The primary purpose of chemotaxis is to search and acquire food which is achieved using Michaelis-Menten Kinetics. Short term memory of the history of nutrients sensed helps the chemotactic bacteria to bias its walk towards nutrient rich sources and the functional form of the memory has been quantified through experiments. In very low nutrient concentration noise might disrupt the sensing and efficient chemotaxis. Although nutrient acquisition is at the core of chemotactic movement, it has not been quantified so far. Inspired by agent-based models that are used in health and traffic modeling, we introduce a microsimulation method which tracks each individual bacterium in a population precisely using noisy sensing, Michaelis-menten absorption kinetics, memory dependent bias in the random walk, and cell division. We start with a population of 105 chemotactic bacteria and allow it to divide to 2.5×10^6 bacteria in 8 hours and study the nutrient uptake advantage ofchemotaxis compared to the memoryless random walk.

17 Potential Influence of Encapsulation in the Evolution of RNA Based Cellular Life

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The concept of RNA world is solely based on the ability of RNA to act both as a catalyst and a storage house of genetic information. However, functional evolution of RNA would have been a rare mutational events unless there is some favorable factor that enhanced the overall activity of related nucleotide sequences dedicated for a particular function. Here we show that encapsulation of RNA in a protocell was in fact beneficial for the evolutionary progress of RNA based cellular life. We found that encapsulation lowers the K_D value of various RNA aptamers irrespective of the membrane composition. Besides, confinement size produces a significant role. Our initial experimental evidence show that both structural change and increased local concentration of the reactants in encapsulated condition could be responsible for the activity enhancement.The concept of RNA world is solely based on the ability of RNA to act both as a catalyst and a storage house of genetic information. However, functional evolution of RNA would have been a rare mutational events unless there is some favorable factor that enhanced the overall activity of related nucleotide sequences dedicated for a particular function. Here we show that encapsulation of RNA in a protocell was in fact beneficial for the evolutionary progress of RNA based cellular life. We found that encapsulation lowers the K_D value of various RNA aptamers irrespective of the membrane composition. Besides, confinement size produces a significant role. Our initial experimental evidence show that both structural change and increased local concentration of the reactants in encapsulated condition could be responsible for the activity enhancement.

18 How Does Bacterial GC Content Evolve?

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Bacterial genome GC content varies from ∼13% to 75% GC. Understanding the source and maintenance of this variation is important for understanding the evolution of codon usage bias and protein-coding sequences. Both neutral processes (like mutation) and selective processes (environmental selection) are thought to shape GC content. One environmental factor, nitrogen-limitation, is thought to select for AT-rich genomes. We hypothesized that if this is true, over evolutionary time scales genomes with an underlying GC→AT mutational bias would have a selective advantage over the wild-type under nitrogen-limitation. Our data suggest that under nitrogen-limitation, mutants with altered mutational biases vary in initial fitness, suggesting that under selection, these mutants would have different probabilities of becoming fixed in the population. We find that a mutant with a GC→AT bias does not have a fitness advantage over WT, but a mutant with an AT→GC bias has 30% higher fitness compared to the WT in nitrogen limitation, in a 24-hour competition. We find that the GC→AT biased mutant has a selective advantage over WT in rich media. This suggests that under nitrogen limitation, a GC→AT biased mutant would only rise to high frequencies under genetic drift. When evolved under genetic drift, these mutants show the expected whole genome mutational biases and mutation rates. We therefore now have expectations for what mutational biases arise under genetic drift, and we are currently evolving mutants with biased mutational spectra under environmental conditions implicated in GC content evolution to understand whether the spectrum of mutations fixed under selection is different from that observed under drift.

19 Protein Secretion Machinery in a Model Filamentous fungus

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Protein secretion is a fundamental biological process involved in immune response, cellular communication and cellular homeostasis. In eukaryotes the traffic of proteins destined for extracellular space are processed, packaged and delivered via an intricate network spanning several organelles. From a biotechnological perspective, elucidating this protein secretion machinery in filamentous fungi is critical for development of hypersecretion strains for novel enzymes. Towards this goal we have reconstructed the protein secretion system in the model filamentous fungus *Neurospora crassa*. Our reconstruction pipeline involved a combination of functional genomics tools and literature curation. This effort led to assignment of function to several proteins of unknown function. Subsequent analysis of next generation RNA-seq and Chip-seq data within the context of the reconstructed network shed new insights on the regulation of the protein secretion system in Neurospora crassa. In summary our integrative analysis provides a systems perspective on the protein secretion machinery in *Neurospora crassa*.

20 Effect of Changing Codon Bias of a Gene on Fitness of Methylobacterium extorquens

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The selection pressures that shaped codon usage in genomes have long been a mystery. Most organisms show a codon bias i.e. they tend to use some codons more frequently than others that code for the same amino acid and this bias varies across organisms. Previous studies have shown that changing the codon bias of a gene can have a negative impact on fitness, possibly due to decreased mRNA and protein levels. Multiple possible mechanisms like tRNA-codon imbalance, ribosome pausing and altered mRNA secondary structure have been hypothesized to lead to decreased protein levels and thus lower fitness. We are studying the fitness effects of changing the codon bias of two genes, *mauA* and *mtdA* in *Methylobacterium extorquens*. These two genes are part of a pathway for the utilization of molecules with single carbon atoms (for example, methylamine and methanol), and are highly expressed by the cell. Changing codon usage in these genes is expected to impact fitness only when the bacterium is growing on methylamine as the sole carbon source. Fitness data of changing codon bias of *fae*, another gene in this pathway is available from a previous study in the lab. By comparing the fitness effects of changing codon bias across genes from the same pathway, we can determine if there exist any broad patterns that point to the causes that led to the origin and maintenance of this complexity in codon usage.

21 Unbounded Growth Patterns of Reproducing, Competing Polymers–Similarities to Biological Evolution

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Since the origin of life the interplay between reproduction, variation, and selection has been driving the emergence of new species. The evolution of the Earth's biosphere appears to innovate unceasingly instead of coming to a stall. Here, we introduce a model system of linear molecules where new polymers appear by spontaneous ligation. The polymers proliferate following a template-based mechanism. Our combined experimental and theoretical study shows that for sufficiently rapid autocatalysis the reproduction process selects particular lengths–while ever longer polymers emerge. We suggest similarities to biological evolution.

22 A Proposal for Open-ended Evolution In Silico

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Darwinian evolution on earth has taken primordial self-replicating systems to the manifold sophisticated forms of life that inhabit our planet today. Sophisticated agents in an ecosystem force each other to become even more sophisticated by competing for resources, and by literally feeding on each other. We are attempting to get to the heart of the algorithmic ideas that allow open-ended evolution by building a software system with similar feedback loops as nature, hoping to see more and more sophisticated behavior the longer it is run.

Our animals are decision trees which compete for resources by making predictions on a bit-string environment of which they themselves are also a part. The survivors pass on their strategies to progeny with variation. The bit-string environment dynamically reflects the changing composition, and increasing sophistication, of the population. As the population becomes more sophisticated, the animals find themselves challenged with an environment that has become harder to predict. We hope this will force an unbounded ratcheting-up of sophistication. To test whether our system is indeed able to increase in sophistication, we challenge it with a machine learning problem, and find promising initial results.

23 Autocatalytic RNA Replicators in Origin of Life

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Self-assembly must have been an intriguing feature of prebiotic molecules to generate first life-like scenarios on Earth. Both small molecule-based chemical systems as well as RNA are shown to possess self-assembly properties to generate more complex prebiotic-relevant products[1,2]. Recent works has shown how small RNA fragments of *Azoarcus* group I intron spontaneously self-assemble to form fully-functional ribozymes in a co-operative and autocatalytic fashion[3,4], overcoming the hurdle of error-catastrophe in a pure replication-based origin-of-life system[5,6]. In the current project, we are exploiting these self-assembling RNA fragments to study complex autocatalytic RNA networks with an ultimate goal of demonstrating Darwinian-like evolution. To this end we have developed a high-throughput experimental set-up by combining droplet-microfluidics[7,8] with next-generation sequencing where we can study RNA networks in each droplet at an unprecedented resolution.

We selected few sub-sets of RNA fragments from *Azoarcus* group I intron ribozyme system based on different network parameters[9,10] to generate a diverse RNA network library using droplet-microfluidics. This library will be evaluated for the relation between network topology and 'fitness'. Having established a good relation between network topology and fitness, these topolo-

gies will be further evaluated for information retention and transfer in such rudimentary RNA networks.

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