BEILSTEIN SYMPOSIUM

Information and Noise: Chemistry, Biology and Evolution Creating Complex Systems

Beilstein Bozen Symposium 2018

5 – 7 June, 2018
Hotel Jagdschloss Niederwald
Rüdesheim, Germany

BEILSTEIN SYMPOSIUM

5 – 7 June 2018
Hotel Jagdschloss Niederwald
Rüdesheim, Germany

The Beilstein-Institut and Open Science

The non-profit Beilstein-Institut is one of the most respected organizations in the communication and dissemination of high-quality information in chemistry. Since 1951, when the foundation was established by the Max Planck Society, we have been fulfilling our mission to support the scientific community by providing high-quality information that is essential for research.

Our role has evolved over the years: from the production of the Beilstein Handbook and Database, to being one of the first open access journal publishers in chemistry, to host of interdisciplinary symposia and supporter of open data initiatives. We believe that free access to scientific research results, giving everyone in the world an equal chance to read and reuse experimental findings and data, is the best way to advance science.

Open Science is a new approach to scientific research. It is based on cooperation and uses new ways to disseminate information and broaden knowledge through digital technologies and new collaborative tools. It aims to make the primary outputs of publicly funded research results – publications (open access) and the research data (open data) – publicly accessible in digital format with no or minimal restriction.

The Beilstein-Institut supports open science and makes the results of its projects freely available to the scientific community as open access publications. This is an essential contribution to the foundation's mission to advance the chemical and related sciences. All journal articles, conference proceedings and videos are open access to allow the worldwide, unhindered sharing and exchange of ideas. This allows scientists, students, educators and the public the opportunity to inform themselves of the latest developments in research and to build on these ideas to further advance scientific knowledge.

Our two platinum open access journals, the *Beilstein Journal of Organic Chemistry* and the *Beilstein Journal of Nanotechnology*, which we fully fund, have no fees for authors or readers. Both journals are produced and managed by the Beilstein Editorial Office team, who work together with a global scientific network of experts that are responsible for the peer review. In 2015, the Beilstein Journals were awarded the DOAJ Seal which recognizes the exceptionally high level of publishing standards and best practices adhering to these journals.

An essential prerequisite for open science data is reporting guidelines and technical standards that provide the framework for the exchange of data from one laboratory to another without technical and textual barriers.

The Beilstein-Institut runs two data standards projects: STRENDA which is concerned with the reporting of enzymology data and MIRAGE with the reporting of glycomics experimental results. Both of which are now widely accepted and acknowledged by the scientific community.

The direct interaction and the exchange of thoughts and ideas between scientists are supported by a program of regularly hosted symposia. These international meetings are organized by the Beilstein-Institut and cover a variety of topics ranging from organic chemistry and biochemistry to nanotechnology and open science as well as interdisciplinary meetings on contemporary topics.

The Beilstein-Institut has been hosting symposia since 1988. Each meeting is always an interesting event with an open result: the Beilstein-Institut provides the framework and the lively and intense exchange of thoughts and ideas of the participants turn it into a memorable and lasting experience. The number of participants is usually limited to around 50 and the program is designed specifically to allow sufficient time for discussions. In some ways the talks can be seen as providing a catalyst for these discussions which often go on into the night and have led to subsequent cooperation projects. The resulting exchange between researchers is the underlying goal of the meeting and gives the Beilstein Symposium their unique character.

Regularly updated information about our symposia is available at www.beilstein-symposia.org.

Upcoming symposia in 2018:

Beilstein Nanotechnology Symposium 2018
Translational Trends in Nanomedicine
17 – 19 September 2018, Rüdesheim, Germany

Scientific Program:
Joerg Lahann, Luis Liz-Marzán, Francesco Stellacci, Molly Stevens

Beilstein Nanotechnology Symposium 2018
Molecular Mechanisms in Tribology
2 – 4 October 2018, Potsdam, Germany

Scientific Program:
Roland Bennewitz and Astrid de Wijn

Beilstein Open Science Symposium 2018
Making Science FAIR
8 – 10 October, 2018, Rüdesheim, Germany

Scientific Program:
Martin G. Hicks and Carsten Kettner

Beilstein Organic Chemistry Symposium 2018

Mechanochemistry: Microscopic and Macroscopic Aspects

13 – 15 November, 2018, Rüdesheim, Germany

Scientific Program:
José G. Hernández

Book of Abstracts

Table of Contents

Overview

When do chemical systems become biological ones? What needs to happen for molecules behaving stochastically to join in networks and cooperate to produce non-random or directed chemical pathways? Biological systems consist of networks of interacting molecules over a large number of time and length scales, and with error tolerance: The larger and more organized the molecules, the more they behave cooperatively. The evolution of biological systems results in interconnected networks optimized for robustness. Such systems are often not the optimal solution, but rather an adjacent one, stable to perturbations. Indeed, before the first genetically regulated ones, such systems had to self-encode into a replicating system. What mechanism led to self-encoding chemistry and was this the seed for biological evolution? This question is perhaps the most important. Finding the first system that is able to evolve is a big challenge.

The first evolving systems started without all the error-correction mechanisms of biology, and chemical reactions do not proceed with 100% yield; they are inherently noisy. Sometimes the reaction produces byproducts, other times, small changes in the conditions lead to changes in products.

Biological systems are also noisy. Noise can be described in terms of apparently undirected activity such as Brownian molecular movement in cells, or even in terms of unspecific, promiscuous enzyme catalysis of chemical reactions involving unusual or uncommon substrates. Information transfer in networks can be facilitated by noise. What is the nature and meaning of the information that we are transferring in chemical and biochemical reactions and what types of noise play a role in signaling and information transfer in biological systems?

Complex molecules found in nature are the results of chemical reactions in biological systems, i.e. living systems. But what is the maximum complexity that can be found abiotically without the use of a biological system and is there a limit to the complexity that biological systems can produce (or humans can understand)? Is the chemical variation of life on earth the most robust form potentially evolvable, or just robust enough? Is it efficient to mimic biological synthesis pathways by means from the organic chemistry toolbox?

Enjoy the Symposium!

Scientific Committee

Lee Cronin
University of Glasgow
lee.cronin@glasgow.ac.uk

Tim Clark
Friedrich-Alexander Universität
Erlangen-Nürnberg
tim.clark@fau.de

Martin G. Hicks and **Carsten Kettner**
Beilstein-Institut, Frankfurt
mhicks@beilstein-institut.de
ckettner@beilstein-institut.de

Registration

All participants must be registered to have access to the conference area.

Participants can ask the organizers for a confirmation of the payment of the conference registration fee. Insurance of participants against accidents, sickness, cancellation, theft, property damage or loss is not covered. Participants are advised to take out adequate personal insurance (see also „Liability and Insurance“).

Participants are responsible for settling their hotel bills directly with the hotel on departure. The total price for participants staying at the Hotel Jagdschloss Niederwald is 617 EUR and includes both accommodation for four nights and the conference package that covers lunches, dinners and coffee breaks as well as admits access to the conference room.

> **Participants not staying at the Hotel Jagdschloss Niederwald are requested to register with the hotel for booking and paying the conference package, i.e. 261 EUR per person.**

Extras, such as drinks, telephone calls etc. are **not** included in the price.

Conference Venue

Both, the conference and lunches and dinners will take place at the conference hotel, i.e.:

Hotel Jagdschloss Niederwald
Jagdschloss Niederwald 1
65385 Rüdesheim
Germany

T +49 (0)6722 - 7106 0
F +49 (0)6722 - 7106 666

www.niederwald.de
jagdschloss@niederwald.de

The hotel offers wireless internet access free of charge. The hotel accepts MasterCard, Visa and EC-Cash (Maestro-Cards).

The Symposium

The symposium will be held from 5 to 7 June, 2018, with the 4th and the 8th for travelling.

The setting and the limited number of participants (max. 50 persons) provide a very convivial atmosphere for the ready exchange of thoughts and ideas.

The scientific program will take place over three days and will

start at 9.00 am on Tuesday, the 5th, and

end in the late afternoon (ca. 5.30 pm) on Thursday, the 7th.

If you wish to extend your stay, please contact the hotel directly.

For the length of the individual talks, please refer to the program. Speakers should allow sufficient time for discussion at the end of their talks (e.g. a 40 min slot includes 30 min talk + 10 min for questions). We will have an LCD projector connected to a Windows PC available.

Presentations of Posters

Poster Exhibition: Tuesday, 5th June, 17.20, Room "Maximilian"

Location of the posters

The Poster exhibition will be placed close to the conference room. Your poster board will be marked with your poster number which is the same in the abstract book.

Poster mounting

Please mount your poster on the 4th June from 4 pm or on the 5th latest by 8.30 am. Your poster will be on display throughout the Symposium. You are asked to remove all poster materials from the board at the end of the meeting otherwise it will be taken down on time and disposed by the organizers. The organizers cannot take any responsibility for this material.

Poster Material

The size of your poster board is 120 x 90 cm (height x width). Hanging material for the poster boards will be provided on-site.

Presentations

The oral poster presentations will take place as indicated in the scientific program. The presentations should not exceed 5 min. You will have 1 min in addition for questions.

Please make sure that you are using the power point template sent out and that you have delivered your final presentation to the organizers in time.

We will have an LCD projector connected to a Windows PC available.

Liability and Insurance

The Beilstein-Institut will not be liable for any accident, theft or damage to property, nor for any delays or modification in the program due to unforeseen circumstances.

Participants and accompanying persons are advised to arrange personal travel and health insurance.

Scientific Program

Monday, 4th June

19.30 Welcome reception

20.00 Dinner

Tuesday, 5th June

09.00	Opening and Introductory Remarks	Martin G. Hicks
	Session Chair: Lara K. Mahal	
09.20	Information / Matter Interplay Conceals Life's Universal Laws	Antoine Danchin
10.00	Macromolecular Crowding is an Important Organizing Principle for Chemical Catalysis Inside Biomolecular Condensates	Santiago Schnell
10.40	Poster Flash Presentation Posters 1 - 4	Riccardo Rao, Johannes Margraf, Eric Fourmentin, Yousef Abul-Haija
11.00	*Coffee Break*	
11.20	Exploring Transitions in Chemical Complexity	Lee Cronin
12.00	Copying vs. Self-assembly: What's the Fundamental Difference?	Thomas E. Ouldridge
12.40	*Lunch*	
	Session Chair: Kepa Ruiz-Mirazo	
13.50	Fundamental Limits on the Thermodynamic Costs of Circuits	David Wolpert
14.30	Semantic Closure Demonstrated by the Evolution of an Universal Constructor Architecture in an Artificial Chemistry	Susan Stepney
15.10	Poster Flash Presentation Poster 5 - 7	Stephanie Colon Santos, David Doran, Wilhelm Boland
15.30	*Tea Break*	
15.50	Exploring the Diversity and Complexity of Glycans in Nature: Not for the Faint-Hearted	Ajit Varki

16.30	How do Proteins Encode their Folded Structures? And, How Might the Folding Code Have Begun?	Ken A. Dill
17.10	*Bio-break*	
17.20	Poster Session	
19.30	*Dinner*	

Wednesday, 6th June

	Session Chair: Susan Stepney	
09.00	Fitness Landscapes of an RNA World	Irene Chen
09.40	Synthetic Genetics: Beyond DNA and RNA	Philipp Holliger
10.20	A miRNA-based Approach Towards Cracking the Glycocode	Lara K. Mahal
11.00	*Coffee Break*	
11.20	In Through the Out Door – Creating Responsive, Dynamic Networks Using Synthetic Replications	Douglas Philp
12.00	Natural Heterotic Computing: ROS-driven Evolution of Environmental Bacteria	Victor de Lorenzo
12.40	*Lunch*	
14.00	*Excursion*	
19.30	*Dinner*	

Thursday, 7th June

	Session Chair: Wilhelm Boland	
09.00	Origin and Effects of 'White Noise' in Cellular Networks	Stefan T. Arold
09.40	G-Protein Coupled Receptors Signaling: Noisy Biological Channels?	Tim Clark
10.20	*Coffee Break*	
10.40	Determinism and Contingency Shape Metabolic Innovation During Symbiogenesis	Juli Peretó
11.20	Systems Biology of Eukaryotic Superorganisms and the Holobiont Concept	Ulrich Kutschera
12.00	*Lunch*	
	Session Chair: Johannes Margraf	
13.30	Creating Evolutionary Feedback Loops	Andrew Ellington
14.10	Morphisms of Reaction Networks	Luca Cardelli
14.50	*Tea Break*	
15.10	Noise-induced Effects in the Dynamics of Gene Regulatory Networks in Single Cells and Tissues	Ramon Grima
15.50	'Information' as a Principle of Organization for Biology: Reinterpreting the Concept to Understand the Complexity of Living Organisms and their Evolutionary Potential	Kepa Ruiz-Mirazo
16.30	Closing Remarks	Martin G. Hicks
19.30	*Dinner*	

List of Posters

The poster presentation includes a short (5 min) oral presentation on Tuesday, 5th June, and the poster session afterwards. The posters will be displayed throughout the entire symposium from Tuesday, the 5th, to Thursday, the 7th June.

Tuesday, 5th June

#1	Nonequilibrium Thermodynamics of Chemical Reaction Networks: the Role of Conservation Laws	Riccardo Rao
#2	Towards a Roadmap of Chemical Space	Johannes Margraf
#3	I2CELL Initiative	Eric Fourmentin
#4	Reactant History Programs the Complexity of Unconstrained Chemical Reactions	Yousef Abul-Haija
#5	Emergence of Constrained Chemical Networks from Unconstrained Reactions	Stephanie Colon Santos
#6	Emergence of Structure and Function from Recursively Programmed Polymers	David Doran
#7	Enhancing Structural Diversity in Terpenoid Biosynthesis: Enzymes, Substrates and Cofactors	Wilhelm Boland

Abstracts

Tuesday

09.20

Information / Matter Interplay Conceals Life's Universal Laws

Antoine Danchin

Hôpital de la Pitiè-Salpetrière
Institute of Cardiometabolism and Nutrition
Paris, France

Biology is often perceived as a collection of weird anecdotes. Attempts to find specific laws that would place life within the realm of physics often fail because investigators see the forest for the trees. Starting from the conjecture that cells are computers making computers we will explore the physico-chemical nature of the "vital force" that has long been the cause of animism or vitalism.

This will ask us to strip biological descriptions from their details to clarify the underlying laws that make cells alive. Highlighting the information of the machine (as opposed to information of the genetic program), we will focus on the role of compartmentalisation and polymerisation associated to the ubiquitous presence of water in shaping what life is.

Back to Program

Tuesday

10.00

Macromolecular Crowding is an Important Organizing Principle for Chemical Catalysis Inside Biomolecular Condensates

Santiago Schnell

University of Michigan Medical School
Department of Molecular & Integrative Physiology
Ann Arbor, MI, United States of America

The physicochemical properties of cellular environments with a high macromolecular content have been systematically characterized to explain differences observed in the diffusion coefficients, kinetics parameters, and thermodynamic properties of proteins inside and outside of cells. However, much less attention has been given to the effects of macromolecular crowding on cell physiology. We present recent findings that shed some light on the role of crowding in various critical cellular processes, paying special attention to its role on biomolecular condensates. Although it is still underappreciated, macromolecular crowding plays a critical role in life as we know it.

Back to Program

Tuesday

Poster #1

Nonequilibrium Thermodynamics of Chemical Reaction Networks: The Role of Conservation Laws

Riccardo Rao, Gianmaria Falasco and Massimiliano Esposito

University of Luxembourg, Complex Systems and Statistical Mechanics, Physics and Materials Science Research, Luxembourg

We formulate a non-equilibrium thermodynamic description for open chemical reaction networks (CN) described by deterministic rate equations. The topological properties of the CN and its conservation laws are shown to play a crucial role. We use them to decompose the entropy production (EP) into a newly identified potential change and two work contributions, one due to time dependent changes in the externally controlled chemostats concentrations and one due to flows maintained across the system by non-conservative forces. In absence of work, the potential is minimized by the dynamics as the system relaxes to equilibrium and its equilibrium value coincides with the maximum entropy principle. Finally, a generalized Landauer's principle holds: the minimal work needed to create a non-equilibrium state is the relative entropy of that state to its equilibrium value (reached in absence of any work). Finally, the theory is extended to CNs described by reaction—diffusion equations as well as stochastic CNs described by chemical master equation.

Back to Program

Tuesday

Poster #2

Towards a Roadmap of Chemical Space

Johannes T. Margraf

Technical University of Munich, Department of Theoretical Chemistry, Garching, Germany

The “chemical space” concept refers to the set of all solids and molecules across compositional and configurational space. In practice, limited subsets of chemical space are usually defined according to some boundary conditions. This can be a trivial task (e.g. for all binary octet semiconductors) or require significant effort (e.g. for all organic molecules up to a certain size).

The goal of the presented work is to understand chemical reactivity through the lens of the chemical space concept. To this end, we have developed methods for the systematic and exhaustive enumeration of reaction intermediates and elementary reaction steps. Unlike previous enumeration efforts (which were focused on stable, drug-like molecules) we obtain an extremely diverse dataset including molecular fragments and (poly-)radical species with an unprecedented coverage of chemical space. We will discuss the use of this data for predicting reaction mechanisms, as well as benchmarking and developing electronic structure and machine-learning methods.

Back to Program

Tuesday

Poster #3

I2CELL Initiative

Eric Fourmentin

Fourmentin-Gilbert Foundation
Noisy le grand, France

Cells, like computers, could be seen as material implementations of Turing machines. From this formalism it is expected that new questions and new approaches will be developed to answer the question “what is life”. Last February, the Fourmentin-Guilbert Scientific Foundation organized an international seminar “From Information to Cells” (I2CELL). This seminar brought together established biologists and computer scientists to discuss the implications of the Turing machine metaphor.

This was the first phase of a larger initiative to foster a research community on using information processing concepts and tools in biology. The next phase will be the launch of a seed award to support experimental validation of testable ideas that exploit the concept of information in biology.

The Fourmentin-Guilbert Foundation is a non-profit organisation whose mission is to foster new concepts in biology

Back to Program

Tuesday

Poster #4

Reactant History Programs the Complexity of Unconstrained Chemical Reactions

Yousef M. Abul-Haija, David Doran, Jan Szymanski, Piotr Gromski, and Lee Cronin

University of Glasgow, WestCHEM, School of Chemistry, Glasgow, United Kingdom

Harnessing unconstrained polymerisation reaction of simple building blocks is of great interest as it allows for exploring the emergence of life-like systems and an understanding of how alternative biologies might be created. Controlling and understanding the ability of unconstrained polymerisation to form both structure and function are particularly challenging because of the tendency to form intractable combinatorial explosions of products. Herein, we investigate how the reactant / reaction history (*e.g.* racemic *vs.* homochiral, and mixing history) might bias the reaction to form products with different complexities, structure and function. The unconstrained condensation reaction of three amino acids (alanine (A), valine (V), aspartic acid (D)) was studied due to their potential ability to form amphiphilic products. We have also developed a complexity index which relates the number of observed products and their mass distribution (generated by mass spectroscopy) to their complexity. The structural and functional differentiation of the products were assessed using different techniques (TEM, CD, esterase activity etc.). Interestingly, we could trace the effect of various reactant history parameters on the emergence of differentiable product distributions in terms of complexity, structure and function without the need for biological machinery.

Back to Program

Tuesday

11.20

Exploring Transitions in Chemical Complexity

Lee Cronin

University of Glasgow
WestCHEM, School of Chemistry
Glasgow, United Kingdom

How can matter transition from the nonliving to the living state? The answer is essential for understanding the origin of life on Earth and for identifying promising targets in the search for life on other planets. Most studies have focused on the likely chemistry of RNA, protein, lipid, or metabolic "worlds" and autocatalytic sets, including attempts to make life in the lab. But these efforts may be too narrowly focused on the biochemistry of life as we know it today. A radical rethink is necessary, one that explores not just plausible chemical scenarios but also new physical processes and driving forces. Such investigations could lead to a physical understanding not only of the origin of life but also of life itself, as well as to new tools for designing artificial biology.

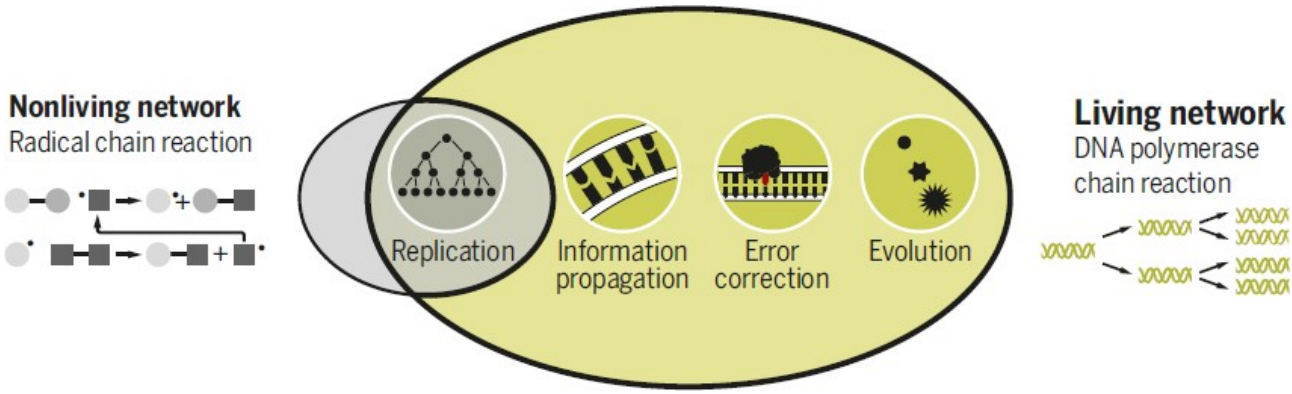

Figure. Comparison of nonliving and living networks. Nonliving and living systems both replicate or copy, but the DNA-based living network allows information propagation, evolution, and error correction. Progress in understanding the origin of life may come from studying how simple chemical networks can transform into living networks.

In this talk I will describe our experimental efforts to explore how random chemistry can become less random over time.

This is an important question and success may shed light on how complex chemical systems could arise comprising complex molecules, systems and architectures similar to those found in biology today. To do this we have developed a new measure of molecular complexity and have been using this as a new guide, that is chemically agnostic, to discover the simplest pathways that might lead to biology.

Back to Program

Tuesday

12.00

Copying *vs.* Self-assembly: What's the Fundamental Difference?

Thomas E. Ouldridge

Imperial College London
Department of Bioengineering
London, United Kingdom

Producing copies of molecular polymers is an essential process within life, occurring during replication, transcription and translation, the three key steps of the central dogma of molecular biology. In such a process, monomer units (*e.g.* nucleotides or amino acids) assemble into a specific sequence determined by the sequence of a template polymer. An apparently related, and also biologically relevant process, is self-assembly. Here, monomer units such as capsid proteins come together to assemble into a well-defined structure (such as a virus capsid).

In recent years, synthetic self-assembling systems of remarkable complexity have been demonstrated using nucleic acid nanotechnology. In the process, important underlying design principles have been identified. However, engineering a synthetic system that produces polymer copies in an autonomous way is much more challenging - suggesting that our understanding of such vital systems is incomplete. In this talk I shall explain the fundamental differences between copying and self-assembly in terms of key aspects of the underlying thermodynamics. These differences impose profound constraints on copy processes, and shape the design space of basic copiers that we might wish to engineer.

Back to Program

Tuesday

13.50

Fundamental Limits on the Thermodynamic Costs of Circuits

David H. Wolpert

Santa Fe Institute
Santa Fe, NM, United States of America

Previous research has derived the minimal heat flow out of any physical system that implements a given computation, *when there are no constraints on how the system operates* — the so-called “Landauer limit”. However common engineered computers use digital circuits to implement computations, as do many biological systems (e.g., gene regulatory networks). Such a circuit's topology introduces constraints on the physical system implementing the circuit. These constraints result in an additional contribution to the minimal work needed to implement the desired computation.

Here we analyze this addition to the minimal required work, which we call “Landauer circuit cost”. We also analyze a second kind of work expended in running a circuit, which we call “mismatch circuit cost'”. This is the extra heat produced if a physical circuit designed to dissipate least heat when run with a distribution q over its inputs is instead run with an input distribution $p \ne q$.

We show that whereas Landauer circuit cost cannot be negative, mismatch circuit cost can be either positive or negative. In fact the total extra heat produced by using a circuit to implement a given computation can be either positive \emph{or negative}. Furthermore, in general different circuits computing the same function have different circuit costs, which leads to the question of how to design a circuit to implement a given computation with minimal heat production (and therefore minimal consumption of free energy).

Back to Program

Tuesday

14.30

Semantic Closure Demonstrated by the Evolution of an Universal Constructor Architecture in an Artificial Chemistry

Susan Stepney

University of York
Department of Computer Science,
York, United Kingdom

I will present a novel computational artificial chemistry system modelled on the von Neumann universal constructor architecture (UCA).

In a UCA, "machines" interact with an abstract description of themselves to replicate by copying the abstract description and constructing the machines that the abstract description encodes. DNA-based replication follows this architecture, with DNA being the abstract description, the polymerase being the copier, and the ribosome being the principal machine in expressing what is encoded on the DNA. This architecture is "semantically closed" in that machine that defines what the abstract description means is itself encoded on that abstract description. Here I will present the results of some computer simulation experiments that show the evolution of the *meaning* of genomic material, allowing the concept of semantic closure and transitions between semantically closed states to be demonstrated through concrete examples.

This talk is based on the published paper available at
http://rsif.royalsocietypublishing.org/content/14/130/20161033

Back to Program

Tuesday

Poster #5

Emergence of Constrained Chemical Networks from Unconstrained Reactions

Stephanie M. Colon Santos and Lee Cronin

University of Glasgow, WestCHEM, School of Chemistry
Glasgow, United Kingdom

Why does life not emerge from complex 'prebiotic' chemical mixtures as a matter of course?

The emergence of abiotic constrained chemical networks has been significantly hindered at the point of transition from complex mixtures and product distributions, into a more highly organized systems. One-pot reaction of simple precursors, such as formamide condensation or the formose reaction, continuously leads to combinatorial explosions in which materials (prebiotic building blocks with sufficient function) are expected to exist, but are in insufficient concentration to self-organise.

Such explosions have been truncated only when specific inorganic surfaces and/or energy sources are employed, and while recursive (cycle-based) experimental models have been discussed extensively as a means to amplify function and promote autocatalysis, they have been explored far less. We set out to explore the effect of recursion on complex chemical mixtures in different mineral environments, as a driver for the development of sustainable dynamic reaction networks.

Through untargeted analysis of the mixtures, we found that the overall number of detected features reduces over cycles, without depleting any of the conventionally targeted products, such as nucleobases and deoxyribose, which were found to form simultaneously under these mild conditions.

Back to Program

Tuesday

Poster #6

Emergence of Function and Speciation from Unconstrained, Recursive Depsipeptide Polymerisation

David Doran, Yousef M. Abul-Haija, Jan Shymanski, Piotr Gromski and Lee Cronin

University of Glasgow, WestCHEM, School of Chemistry
Glasgow, United Kingdom

Living systems are characterised by their ability to sustain chemical reaction networks in far-from-equilibrium states. It is likely that life first arose through a process of continual disruption of equilibrium states in recursive reaction networks, perhaps driven by cyclical environmental changes.

Herein, we report the emergence of structure and function from recursive depsipeptide polymerisation reactions using simple wet-dry cycling of amino acid and α-hydroxy acid monomers. Reactions were kept out of equilibrium by continual dilution of products and replenishment with fresh feedstocks on a range of mineral environments. Recursion imposed a selection pressure and subsequent boundary conditions on products, which may have otherwise been prone to uncontrolled combinatorial explosion.

Product mixtures were screened for their ability to catalyse ester hydrolysis, and demonstrated esterase activity comparable to the biological enzyme α-chymotrypsin. After multiple recursive reaction cycles, differences emerged between mineral environments, demonstrating a form of network-level heredity and speciation.

Back to Program

Tuesday

Poster #7

Enhancing Structural Diversity in Terpenoid Biosynthesis: Enzymes, Substrates and Cofactors

Abith Vattekkatte and **Wilhelm Boland**

Max Planck Institute for Chemical Ecology, Bioorganic Chemistry
Jena, Germany

Currently there are more than 60,000 different terpene metabolites known. Their remarkable chemical diversity can be attributed to the combinatorial biosynthetic chemistry that starts from prenyldiphosphate precursors. The chemical magic begins when one realises that the whole universe of terpenoids is generated by the repetitive use (alkylation) of IDP and DMADP. Besides the numerous single product enzymes from all type of organisms, the recently discovered multiproduct terpenoid cyclases add another structural dimension, as they convert single prenyldiphosphates into a multitude of structurally defined, often even enantiomerically pure products.

For example, incubation of the MtTPS5 enzyme from *Medicago truncatula* with (*E,E*)-FDP provides 27 different sesquiterpenes, all of them chiral and with high optical purity [1]. Furthermore, this enzyme not only accepts (*E,E*)-FDP as a substrate, but also converts (*E,Z*)-FDP into a series of new chiral products, not identical with those derived from (*E,E*)-FDP. While MtTPS5 generated novel and structurally diverse products, other terpenoid synthases from corn plants show a clear preference and higher turnover with either *E*- or *Z*-isomers .

Apart from substrate geometry, variations in specific assay conditions such as assay pH and metal cofactors additionally control the structural diversification. Metal cofactors (Co^{2+}, Mn^{2+}, Mg^{2+}) may control the chain length of prenyldiphosphates in terpenoid biosynthesis [2], but also the product composition of multiproduct terpenoid cyclases. Sometimes even a change in the pH affects the product distribution [3].

In consequence, simple alterations in the cellular environment provide the organism (*e.g.* plant, insect or microorganism) with an enhanced structural plasticity without the need for investing into long-term evolutionary modifications.

This versatility to *ad hoc* modulate product diversity on demand grants the producing organisms, especially immobile plants with access to an enhanced defensive repertoire by simply altering cofactors, pH level and substrate geometry.

References

[1] S. Garms, T. Köllner, W. Boland, A Multiproduct Terpene Synthase from Medicago truncatula generates Cadalane Sesquiterpenes via Two Different Mechanisms (**2010**) *J. Org. Chem.*, 75: 5590-5600.

[2] S. Frick, R. Nagel, A. Schmidt, R.R. Bodemann, W. Brandt, G. Pauls, J. Gershenzon, W. Boland, A. Burse. Metal ions control chain-length specificity of isoprenyl diphosphate synthases: Novel branch point regulation of terpenoid biosynthesis in insects (**2013**) *Proc. Natl. Acad. Sci. USA*, 110: 4194-4199.

[3] A. Vattekkatte, S. Garms, W. Brandt and W. Boland, *Organic & Biomolecular Chemistry*, **2018**, 16, 348.

Back to Program

Tuesday

15.50

Exploring the Diversity and Complexity of Glycans in Nature: Not for the Faint-Hearted

Aniruddha Sasmal[1,2], Zahra Khedri[1,2], Anders Bech Bruntse[1,3], Sandra Diaz[1,2], Nathan Lewis[1,3] and **Ajit Varki**[1,2,4]

University of California, San Diego
[1]Glycobiology Research and Training Center
[2]Department of Cellular & Molecular Medicine
[3]Department of Pediatrics
[4]Department of Medicine
La Jolla, CA, United States of America

Any life-form on earth comprises a complex machinery that has been persistently evolving for optimal function and maximum survival, primarily to assure reproductive success. While the scientific community has made immense progress in understanding these complex processes of life, it is still unclear why life has to be so complex. At the molecular level, all life-forms feature four major types of macromolecules, namely nucleic acids (DNA and RNA), proteins, carbohydrates (glycans), and lipids. These distinct classes of molecules form a vast interconnected network via chemical and physical interactions to generate biological information that governs the development, growth and reproductive success of all living systems. Fully understanding these multi-faceted processes will require inter-disciplinary research and collaborations.

There are many challenges to addressing the interactions of glycans with other biomolecules. Glycans were often ignored due to their structural complexity and non-templated biosynthesis, and the relative lack of simple tools to explore their biology and function. However, all living cell surfaces are covered with a dense and complex layer of glycans. From the evolutionary perspective, the complexity and the heterogeneity of glycan structures make them suitable as the first line of contact with both self and non-self cells.

Furthermore, the linkage and conformational variability in glycans contributes to the structural diversity. Sialic acids are nine-carbon backbone monosaccharides that are predominantly present at the terminal position of the vertebrate cell surface glycans. Due to their conspicuous position, sialic acids play important roles in multiple cellular processes.

To map sialoglycan interactions we take advantage of the high-throughput analysis using a glycan microarray. Our collaboration with the experts from field of chemoenzymatic synthesis resulted in developing a diverse library of sialyltrisaccharides that are found as terminating structures in nature, and these ~200 glycans were applied for screening biomolecular interactions.

To streamline the analysis workflow of the results obtained with glycan-binding proteins, we numerically bar-coded the sialyltrisaccharides using a system that assigns a unique code for individual glycans. Essentially each monosaccharide needs three numbers to encode: the monosaccharide itself, its linkage to the underlying sugar chain, and any modifications. Thus, a tri-saccharide requires 9 digits for encoding it. Looking at known structures we found that a 9 X 9 table was needed to encode various possibilities.

In the course of setting up this coding system, we noted that the theoretical population of sialoglycan trisaccharide sequences is more than 205 million. Filtering out the chemically impossible combinations, the number tentatively dropped two orders of magnitude to 1,359,709 (~10^6 possible combinations) of possible sialyltrisaccharides in nature. While we developed this system for linear trisaccharides, it has not escaped our notice that simply amplifying the calculation to a biantennary branched N-glycan with two terminal sialoglycan trisaccharide sequences would result in squaring of the number of possibilities, giving >10^{12} potential combinations. And with a triantennary branched N-glycan with three terminal sialoglycan trisaccharide sequences there could be >10^{18} potential combinations at a single N-glycan site on a single protein. While all these possibilities likely do not exist in nature, it is clear that sialoglycans can encode enormous diversity.

Further studies will be needed to determine how many of these combinations encode biologically important “information”, and how many represent "noise". In reality, there is probably no such simple dichotomy, it is probably a continuum, also dependent on the genetic, biological, and environmental situation at hand.

Back to Program

Tuesday

16.30

How Do Proteins Encode their Folded Structures? And, How Might the Folding Code Have Begun?

Ken A. Dill

Stony Brook University
Laufer Center for Physical and Quantitative Biology
Stony Brook, NY, United States of America

Two crucial properties of proteins are that they carry information in their sequences and that they fold into unique structures that can perform functions. The folding code has been studied by approximating it as a binary code of hydrophobic (H) and polar (P) monomers.

In recent work, we have found that the HP foldamer model also suggests how longer-chain informational proteins might have arisen from short random sequences.

Back to Program

Wednesday

09.00

Fitness Landscapes of an RNA World

Irene Chen

University of California, Santa Barbara
Department of Chemistry and Biochemistry
Santa Barbara, CA, United States of America

Life likely progressed through an early stage known as the RNA World, in which RNA carried information and also performed catalytic functions for the primitive cell. Understanding the emergence and evolution of the earliest functional RNAs requires knowledge of the relationship between sequence and activity, or the fitness landscape. Although they are poorly understood, knowledge of fitness landscapes is a crucial element for any quantitative prediction of evolution.

I will describe our experimental efforts to map complete fitness landscapes for functional RNA and probe how the protocellular environment would affect these landscapes.

Back to Program

Wednesday

09.40

Synthetic Genetics: Beyond DNA and RNA

Philipp Holliger

MRC Laboratory of Molecular Biology
Cambridge Biomedical Campus
Cambridge, United Kingdom

Synthetic biology seeks to probe fundamental aspects of biological form and function by construction (i.e. resynthesis) rather than deconstruction (analysis). Synthesis thus complements reductionist and analytic studies of life, and allows novel approaches towards fundamental biological questions.

We have been exploiting the synthesis paradigm to explore the chemical etiology of the genetic apparatus shared by all life on earth. Specifically, we ask why information storage and propagation in biological systems is based on just two types of nucleic acids, DNA and RNA. Is the chemistry of life's genetic system based on chance or necessity? Does it reflect a "frozen accident", imposed at the origin of life, or are DNA and RNA functionally superior to simple alternatives.

I'll be presenting recent progress on the development and application of strategies to enable the enzymatic synthesis and reverse transcription and hence replication and evolution of novel synthetic genetic polymers, which we term XNAs. We show that eight different synthetic polymers, based on nucleic acid architectures not found in nature, can also mediate genetic information storage and propagation [1]. Beyond heredity, we demonstrate a capacity for Darwinian evolution by the *de novo* selection of specific ligands (XNA aptamers) and catalysts (XNAzymes) based on entirely synthetic backbones [1, 2]. Thus, key hallmarks of living systems, including heredity and evolution are not limited to DNA and RNA but can be implemented in synthetic polymers and are likely to be emergent properties of polymers capable of information storage.

I'll also be presenting our progress in the engineering and evolution of RNA polymerase ribozymes towards a general polymerase and self-replication capacity We have discovered RNA polymerase ribozymes that are capable of the templated synthesis (i.e. transcription) of another simple ribozyme [3] or RNA oligomers exceeding their own size (>200 nts) [4], a key milestone on the road to self-replication.

References

[1] Pinheiro VB, Taylor AI, Cozens C, Abramov M, Renders M, Zhang S, Chaput JC, Wengel J, Peak-Chew S-Y, McLaughlin SH, Herdewijn P & Holliger P (2012) Synthetic Genetic Polymers Capable of Heredity and Evolution. *Science*. **336**: 341-44.

[2] Taylor AI, Pinheiro VB, Smola MJ, Morgunov AS, Peak-Chew SY, Cozens C, Weeks KM, Herdewijn P & Holliger P. (2015) Catalysts from synthetic genetic polymers. *Nature,* **518**: 427-30

[3] Wochner A, Attwater J, Coulson A & Holliger P (2011) Ribozyme-catalyzed transcription of an active ribozyme. *Science* ; **332** : 209-12.

[4] Attwater J, Wochner A & Holliger P. (2013) In-ice evolution of RNA polymerase ribozyme activity. *Nature Chem.*; **5** : 1011-8.

Back to Program

Wednesday

10.20

A miRNA-based Approach Towards Cracking the Glyocode

Lara K. Mahal

New York University
Biomedical Chemistry Institute, Department of Chemistry
New York, NY, United States of America

Glycans both encode cellular information, such as cell-cell interactions and cell state (Signal), and must avoid being targeted by pathogens (Noise). This leads to a system in which the sugar code (i.e. the glycan motifs controlling function) is hidden within the noisy milieu of larger heterogenous glycan structures. This talk focuses on use of high-throughput analytical methods, including our lectin microarray technology and newly developed miRNA-proxy approach, in tandem with data integration, to decode structure-function relationships in the glycome.

Our work is identifying glycan drivers of biological function including those involved in melanoma metastasis and host-response to pathogens (*e.g.* HIV-1 and influenza), providing a host of new targets for small molecule intervention in these disease states.

Back to Program

Wednesday

11.20

In Through the Out Door – Creating Responsive, Dynamic Networks Using Synthetic Replicators

Douglas Philp

University of St. Andrews
School of Chemistry and EastCHEM
St. Andrews, United Kingdom

The development and deployment of replicating molecular networks can potentially revolutionize materials fabrication at the nanometre scale. Molecular replication can deliver synthetic machinery that is capable of directing its own synthesis and co-operating with other similar systems to create an organized hierarchy. Within this broad objective, the development of efficient protocols that allow replication, organization and emergent behaviour is required. This approach to predetermined dynamic behaviour has been termed [1] “systems chemistry”. We have developed [2] a series of molecular networks that are capable of replication by a variety of different mechanisms. The ability of these individual replicating systems to function as building blocks within more complex reaction networks is related to their ability to selectively bind reagents and accelerate the reactions between them. Kinetic selection based on the autocatalytic or cross-catalytic efficiencies of instruction templates is, however, unlikely to be enough to achieve the goals set out above.

Dynamic covalent chemistry offers an opportunity to develop synthetic protocols that incorporate a degree of error checking through the dynamic and reversible association of the components of a target structure through covalent bonds. The limited number of organic reactions that form covalent bonds and that are also completely reversible under mild conditions hampers the development of this field. The coupling of dynamic covalent reaction networks to replication processes offers an attractive route into reconfigurable reaction systems that are capable of responding to instructional templates.

In this presentation, we will demonstrate that the ability of systems to select and amplify [3] one species from a mixture within closed systems is fundamentally limited.

This limitation exists not only for approaches that exploit [4] thermodynamic selection and also for those that incorporate irreversible processes within a dynamic [5, 6] reaction network.

In order to overcome this barrier, we are developing [7] systems that are capable of exploiting propagating chemical waves (Figure 1), which are mediated by replicating organic structures, as selection tools.

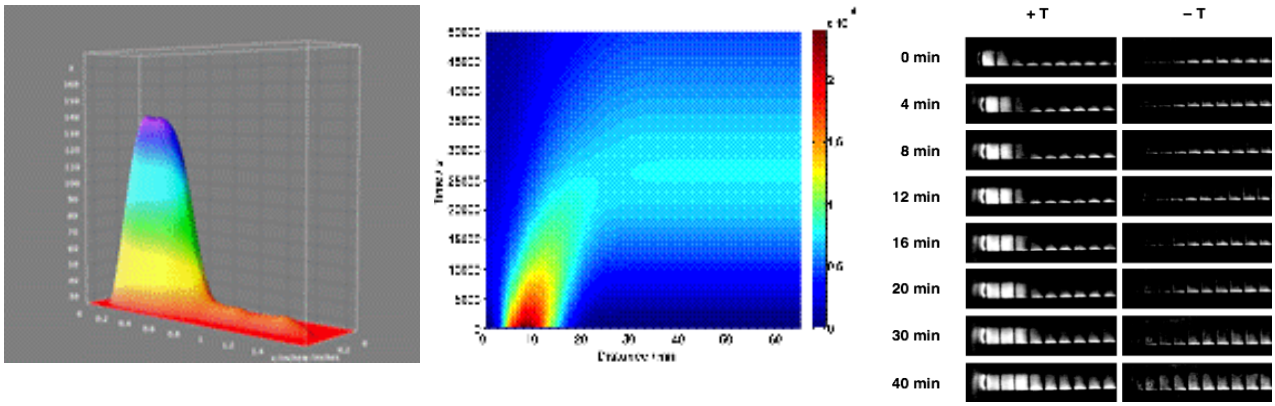

Figure 1

References

[1] (a) M. Kindermann, I. Stahl, M. Reimold, W. M. Pankau, G. von Kiedrowski *Angew. Chem. Int. Ed.* **2005**, 44, 6750. (b) R. F. Ludlow, S. Otto *Chem. Soc. Rev.* **2008**, *37*, 101.

[2] For a review of replicator chemistry, see: T. Kosikova, D. Philp *Chem. Soc. Rev.* **2017**, *46*, 7274.

[3] E. Kassianidis, R.J. Pearson, E.A. Wood, D. Philp *Faraday Discuss.* **2010**, *145*, 235.

[4] (a) V. del Amo, D. Philp *Org. Lett.* **2008**, *10*, 4589. (b) J. E. Richards, D. Philp *Chem. Commun.* **2016**, *52*, 4995.

[5] (a) J. W. Sadownik, D. Philp *Org. Biomol. Chem.* **2015**, *13*, 10392. (b) T. Kosikova, H. Mackenzie, D. Philp *Chem. Eur. J.* **2016**, *22*, 1831.

[6] (a) J. W. Sadownik, D. Philp *Angew. Chem. Int. Ed.* **2008**, *47*, 9965. (b) T. Kosikova, D. Philp *J. Am. Chem. Soc.* **2017**, *139*, 12579. (c) J. W. Sadownik, T. Kosilova, D. Philp *J. Am. Chem. Soc.* **2017**, *139*, 17565.

[7] I. Bottero, J. Huck, T. Kosikova, D. Philp *J. Am. Chem. Soc.* **2016**, *138*, 6723.

Back to Program

Wednesday

12.00

Natural Heterotic Computing: ROS-driven Evolution of Environmental Bacteria

Victor de Lorenzo

Centro Nacional de Biotecnologia, CSIC
Systems Biology Program
Madrid, Spain

The still-evolving 2,4-dinitrotoluene (DNT) pathway of *Burkholderia cepacia* R34 has been studied as a case of emergence of new metabolic capabilities in environmental bacteria. The *dnt* route originated from a precursor naphthalene degradation pathway and the first enzyme (DNT dioxygenase) maintains significant activity towards its earlier substrate. Both *in vivo* reactions and the associated regulatory system mediated by the DntR transcriptional factor indicate that reactive oxygen species (ROS) generated by the faulty (i.e. uncoupled) reaction of the precursor enzymes with DNT elicit genetic diversification. This could in turn ease the solution of the biochemical and physiological problem. When the *dnt* system was transplanted to the genetically tractable background of *Escherichia coli*, mutagenesis caused by endogenously produced ROS was dependent on *rpoS* and *dinB,* and was not accompanied by a general induction of the SOS response.

In addition, analysis of the type of mutations suggested that ROS-triggered genetic diversification was due not so much to misincorporation of 8-oxoguanine as to the lack of fidelity of DNA replication. When the *dnt* operon was inserted in the genome of *Pseudomonas putida* and cells were exposed to DNT, the resulting metabolic ROS did not translate in significantly higher mutagenic rates. Artificially decreasing the intracellular pool of NAD(P)H caused *P. putida dnt+* to acquire a high genetic-diversification regime.

These observations provide a view of evolution as a sort of heterotic computing in which the problem is embodied in the physicochemical frame of the cell and the exploration of the solution space is pushed by its endogenous dynamics.

On this basis, it is plausible that some members of a given microbial community are prone to innovate their metabolic capacities much faster than others while the rest may benefit from such innovation through horizontal gene transfer.

Back to Program

Thursday

09.00

Origin and Effects of 'White Noise' in Cellular Networks

Stefan T. Arold

King Abdullah University of Science and Technology
Computational Bioscience Research Center
Biological and Environmental Sciences and Engineering Division
Thuwal, Kingdom of Saudi Arabia

Ironically, it was the search for the origin of specificity in protein-ligand interactions that has revealed a high degree of promiscuity in many molecular systems, including cellular signal transduction and enzyme-substrate recognition.

I argue that this intrinsic promiscuity necessarily results in a certain amount of noncognate (biologically ‘unwanted’) interactions and interaction products, which create a constant noise on a molecular level. This ‘white noise’ in cellular networks is distinct from the much better-established phenomenon, also called ‘noise’, where stochastic fluctuations in genetic circuits create different individuals amidst a clonal cell population. I will discuss the evolutionary origin and necessity of this ‘white noise’, and how it has shaped cellular networks, giving raise to particular features and constraints for intracellular signal transduction.

Back to Program

Thursday

09.40

G-Protein Coupled Receptors Signaling: Noisy Biological Channels?

Tim Clark

Friedrich-Alexander-Universität Erlangen Nürnberg
Computer-Chemie-Centrum
Erlangen, Germany

G-protein coupled receptors (GPCRs) transmit signals (usually chemical) from outside to inside cells. As membrane proteins, they are inherently hard to crystallize, so that only approximately 45 X-ray structures of GPCRs have been published since the first in 2000. This and other difficulties in experimental GPCR-research mean that classical molecular-dynamics simulations play an unusually important role in the biophysics of GPCRs [1]. The combination of modern supercomputers, software, and simulation protocols [2] has made time-resolved atomistic details of the structures of GPCRs and their mechanisms of action available.

Many questions arise, especially concerning the mechanism of activation of GPCRs. Do partially activated receptors oscillate between active and inactive forms or adopt a static intermediate conformation? Is the mechanism of basal activation (the inherent activity of a receptor without ligand) the same as that of ligand-induced activation? Is moderate basal activity a sign of a noisy receptor? Is there a general mechanism of activation or do different receptors use different mechanisms?

Many fundamental questions need to be answered before we can tackle these questions. For instance, we need to be able to detect the active conformation of a receptor from the atomic coordinates. As the simulations are very expensive, we are making slow but steady progress.

References

[1] T. Clark. G-Protein coupled receptors: answers from simulations. *Beilstein J. Org. Chem.,* **2017**, *13*, 1071-1078 (https://doi.org/10.3762/bjoc.13.106).

[2] N. Saleh, P. Ibrahim, G. Saladino, F. L. Gervasio and T. Clark. An efficient Metadynamics-based Protocol to Model the Binding Affinity and the Transition State Ensemble of GPCR-Ligands. *J. Chem. Inf. Model.,* **2017**, *57*, 1210-1217 (https://doi.org/10.1021/acs.jcim.6b00772).

Back to Program

Thursday

10.40

Determinism and Contingency Shape Metabolic Innovation During Symbiogenesis

Juli Peretó

Universitat de València-CSIC, Institute for Integrative Systems Biology I^{2}SysBio and
Universitat de València, Department of Biochemistry and Molecular Biology
Paterna, Spain

Metabolism is chemistry embodied in the spatial and temporal limits of cells. The evolutionary history of metabolic networks results from the interplay between necessary physico-chemical conditions and historical contingencies. Some metabolic pathways seem less efficient than they could theoretically be. Of course, we refer to those properties that are not determined by thermodynamics or chemical restrictions in cellular systems. These limits impose the boundary of "what is chemically possible" in biology and the naturally evolved biochemical systems represent a subset of that universe. The exploration of the possible is delimited by the chemical reactivity (adaptive or toxic) of the metabolites, accessible not only through the native catalysis but also the promiscuous activity of enzymes as well as non-enzymatic transformations.

As a consequence of the very nature of the evolutionary process, the adopted solutions are not always the best, but simply those that suffice to survive and reproduce. Even in the case of finding an almost optimal solution, circumstances may change and, therefore, cease to be a good solution because we cannot reverse history to look for a better alternative – but this could be artificially achieved by synthetic biology. The co-evolution of species with the environment, including the metabolism of other species, offers notable study cases on how metabolism has evolved with variable doses of opportunism and tinkering.

The emergence of new metabolic pathways by symbiogenesis eloquently speaks about this strategy, in which membrane leakage of metabolites plays a relevant role. Thus, bacterial communities may display metabolic complementation and, in that case, the end product of a pathway is synthesized by the consortium as a whole.

Metabolic modelling allows us the study of the necessary conditions and optimality of metabolic complementation in nutritional, mutualistic associations between insects and intracellular bacteria, and suggests explanations for some remarkable cases of evolutionary convergence in the metabolic arrangements of several insect-bacteria endosymbiosis.

Back to Program

Thursday

11.20

Systems Biology of Eukaryotic Superorganisms and the Holobiont Concept

Ulrich Kutschera[1,2]

[1]The Systems Biology Group Inc., Palo Alto, CA, United States of America,
[2]University of Kassel, Institute of Biology, Kassel, Germany

The founders of modern biology (Jean Lamarck, Charles Darwin, August Weismann etc.) were organismic life scientists who attempted to understand the morphology and evolution of living beings as a whole (i.e., the phenotype). However, with the emergence of the study of animal and plant physiology in the 19th century, this "holistic view" of the living world changed and was ultimately replaced by a reductionistic perspective.

Here, I summarize the history of systems biology, i.e., the modern approach to understand living beings as integrative organisms, from genotype to phenotype. It is documented that the physiologists Claude Bernard and Julius Sachs, who studied humans and plants, respectively, were early pioneers of this discipline, which was formally founded fifty years ago.

In 1968, two influential monographs, authored by Ludwig von Bertalanffy and Mihajlo D. Mesarović, were published, wherein a "systems theory of biology" was outlined. Definitions of systems biology are presented with reference to metabolic or cell signaling networks, analyzed via genomics, proteomics and other methods, combined with computer simulations/mathematical modelling. Then, key insights of this discipline with respect to epiphytic microbes (*Methylobacterium* sp.) and simple bacteria (*Mycoplasma* sp.) are described. The principles of homeostasis, molecular systems energetics, gnotobiology and holobionts (i.e., complexities of host-microbiota interactions) are outlined, and the significance of systems biology for evolutionary theories is addressed.

Based on the microbe-*Homo sapiens*-symbiosis, it is concluded that human biology and health should be interpreted in the light of a view of the biomedical sciences that is based on the holobiont concept.

Back to Program

Thursday

13.30

Creating Evolutionary Feedback Loops

Andrew Ellington

University of Texas at Austin
Center for Systems and Synthetic Biology
Austin, TX, United States of America

Directed evolution can be used to hone the phenotypes of molecules, pathways, and entire organisms. In both directed evolution and natural selection, phenotypes are coupled to the replication of alleles that produce those phenotypes. In nature this coupling (or positive feedback loop) is almost always instantiated via an organism in which the success of the organism and the success of the allele are for the most part completely aligned. The reliance on an organism can make it more difficult to select for molecular, rather than organismal phenotypes; as an obvious example, it can be difficult to select for a thermostable protein in the context of a mesophilic organism.

Artificial systems for directed evolution that do not rely on organisms can be developed in which successful proteins or pathways feedback on the replication of the genes that produce them. We will examine a number of such artificial systems, provide insights into how to craft strong feedback loops between phenotype and replication, and dwell on what pitfalls commonly occur. Contrasting natural (cell-based) and artificial (non-cell-based) directed evolution should assist in understanding how to design or build ever more complex evolutionary systems with intertwined feedback loops.

Back to Program

Thursday

14.10

Morphisms of Reaction Networks

Luca Cardelli

Microsoft Research
Cambridge, United Kingdom

We study morphisms (mappings) between chemical reaction networks that establish structural and functional connections between chemical systems. Such morphisms imply kinetic similarity, and yet their properties can be checked statically on the structure of the networks. In particular we can determine structurally that a complex network *emulates* a simpler network: that is, that it can reproduce the kinetics of the simpler network for all choices of reaction rates and initial conditions of the simpler network. We use this property to relate the kinetics of many common biological networks of different sizes, also relating them to fundamental population algorithms from computing.

The emulation property can be used to map out paths in network space that maintain functionality while increasing complexity, thus highlighting possible evolutionary transitions. It can also be used as a baseline to investigate the effects of noise on systems of different complexity.

Back to Program

Thursday

15.10

Noise-induced Effects in the Dynamics of Gene Regulatory Networks in Single Cells and Tissues

Ramon Grima

University of Edinburgh
School of Biological Sciences
Edinburgh, United Kingdom

Since-cell experiments show that gene expression and regulation is highly noisy. Mathematical models are hence necessary to understand how cells have evolved mechanisms to ensure robust function through the suppression or exploitation of inherent cellular noise.

A key difficulty in studies of this type is the fact that stochastic models of gene regulatory networks are rarely exactly solvable and stochastic simulation is computationally expensive compared to conventional deterministic simulations. In this talk I will summarise our efforts to develop new modelling methodologies which lead to approximate but accurate predictions of the noisy spatial and non-spatial dynamics of gene regulatory systems in a computationally efficient manner.

I will describe how using these methods we have identified or further elucidated various noise-induced phenomena relevant to cellular decision making, rhythmicity of intracellular oscillators, cellular memory and cell-cell communication.

Back to Program

Thursday

15.50

Information as a Principle of Organization for Biology: Reinterpreting the Concept to Understand the Complexity of Living Organisms and their Evolutionary Potential

Kepa Ruiz-Mirazo

University of the Basque Country
Department of Logic and Philosophy of Science / Biofisika Institute
Donostia – San Sebastian, Spain

In this talk I will defend a view in which 'information' should be retrieved and developed as a central concept to account for biological systems. However, unlike many other authors, I will not take it as a primitive coming from physics or chemistry. Instead, information will be proposed as a principle of organization characteristic of more complex systems (not a property that can be ascribed, in any case, to single molecules -- *e.g.*: DNA).

Following this strongly relational conception, grounded on the way in which a collection of molecules 'interpret/translate' functionally what other molecules come to 'signify/represent' in and for the system, I will try to show why this is so fundamental for life. In brief, there is no alternative theoretical construct that can provide us with the variety of insights required to explain the 'hyper-complexity' we encounter in the biological domain.

Living phenomena involve both (i) individual systems carrying out very robust self-(re-)producing dynamics in far from equilibrium conditions (cellular-metabolic ontogenies) and, at a completely different time scale, (ii) populations of those systems undergoing an open-ended process of diversification (eco-evolutionary phylogenies). Without a deep theoretical re-assessment and re-elaboration of the notion of information, specifically tailored for biology, there will be no chance for us to understand how this high 'squared complexity' (physiological and evolutionary) came about during biogenesis and made life, globally speaking, a long-term-sustainable phenomenon on the surface of our planet.

Back to Program