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THE ROYAL SOCIETY

DISCUSSION MEETING ON

The chemical origins of life and its early evolution

Monday 21 and Tuesday 22 February 2011

Organised by Professor David Lilley FRS and Professor John Sutherland

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The chemical origins of life and its early evolution

Monday 21 – Tuesday 22 February 2011

Organised by Professor David Lilley FRS, University of Dundee and Professor John Sutherland, MRC Laboratory of Molecular Biology, Cambridge

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11.40	Discussion	**16.00**	Discussion	**11.30**	Discussion	**16.00**	Discussion
11.50	**Martin Hanczyc** Metabolism and motility in prebiotic structures	**16.15**	**Joe Piccirilli** Crystal structure of the class I ligase ribozyme	**11.45**	**Robert Pascal** Energy flows, metabolism, and translation	**16.15**	**Marina Rodnina** Evolutionary optimization of speed and accuracy of ribosome decoding
12.20	Discussion	**16.45**	Discussion	**12.15**	Discussion	**16.45**	Discussion
12.30	LUNCH	**17.00**	CLOSE	**12.30**	LUNCH	**17.00**	CLOSE

The chemical origins of life and its early evolution

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Synopsis

How did life begin on the planet, and how did metabolic and genetic processes evolve at an early stage? Did this generate an RNA-based form of life, and how did this evolve into the present protein-based life? Researchers from a wide variety of disciplines will discuss possible mechanisms whereby biology emerged from chemistry, and subsequently evolved.

Monday 21 February 2011

9.00 Welcome by Mr Stephen Cox CVO, Executive Director, Royal Society

9.05 Introduction by Professor David Lilley FRS, University of Dundee

Session 1 – Prebiotic chemistry: setting the stage

Chair Professor John Sutherland, MRC Laboratory of Molecular Biology, Cambridge, UK

9.20 Serpentinite and the dawn of life

Professor Norm Sleep, Stanford University, USA

Hydrothermal vents above serpentinite produce chemical potential gradients of aqueous and ionic hydrogen and thus provide a very attractive venue for the origin of life. This environment was most favourable before the Earth's massive CO_2 atmosphere was subducted into the mantle. Thermophile to clement conditions persisted for several million years while atmospheric pCO_2 dropped from ~25 bar to below 1 bar. The ocean was weakly acid pH ~6, and a large pH gradient existed for nascent life with pH 9 to11 vent fluids. Total CO_2 in water was significant so the vent environment was not carbon limited as in the modern ocean. Phosphorus and Fe(II) were somewhat soluble. This epoch occurred well before the earliest record of surface rocks ~3.8 billion years ago; by then photosynthetic life teemed on the Earth and the oceanic pH was the modern value of ~8. Serpentinite existed by 3.9 Ga, but older rocks that might retain evidence of its presence have not been found. The mantle of the Earth sequesters extensive evidence of Archaean and younger subducted biological material. There has been no systematic search of mantle-derived rocks for such evidence of life in the Hadean or conversely Hadean abiotic conditions.

9.50 Discussion

10.00 RNA – prebiotic product, or biotic invention?

Professor John Sutherland, MRC Laboratory of Molecular Biology, Cambridge, UK

A true understanding of biology must include knowledge of its chemical origin, and comprehending the chemical events that gave biology its foundations – cellular format, the central dogma, the genetic code – is therefore a fundamental aspect of natural science. We are interested in uncovering

prebiotically plausible syntheses of the informational, catalytic and compartment–forming molecules necessary for the emergence of life. We have previously demonstrated the constitutional self-assembly of pyrimidine ribonucleotides from mixtures of simple building blocks, and we are now exploring similar 'systems chemistry' approaches to the purine ribonucleotides, and ways of assembling RNA from these ribonucleotides with regiocontrol of the internucleotide phosphodiester linkage. Success or not in these ventures will go some way to answering the question posed in the title to this presentation.

10.30 Discussion

10.40 Tea/coffee

11.10 Probing the puzzle of 'Original Syn'

Professor Donna Blackmond, The Scripps Research Institute, USA

Highly enantioenriched precursors to RNA are synthesized from achiral and prochiral source molecules through a sequence of physical and chemical amplification processes in which the evolving asymmetry is derived solely from a small initial imbalance of amino acid enantiomers. This work provides a prebiotically plausible rationalization for the single-handedness of biological molecules prior to the emergence of self-replicating informational molecules and endorses the suggestion of Budin and Szostak [1] that both physical and chemical processes played essential roles prior to the emergence of evolved biochemical capabilities.

References

[1]Budin, I., Szostak, J.W., Expanding Roles for Diverse Physical Phenomena During the Origin of Life, *Annu. Rev. Biophys*. 2010. *39*:245–63.

11.40 Discussion

11.50 Metabolism and motility in prebiotic structures

Dr Martin Hanczyc, University of Southern Denmark, Denmark

Easily accessible, primitive chemical structures produced by self-assembly may produce self-moving agents able to sense the environment and move with purpose. These would constitute the first examples of life on earth, even more primitive than simple bilayer vesicle structures. A few examples of simple chemical systems will be presented that self-organize to produce oil droplets capable of movement, environment remodeling, and chemotaxis. These chemical agents are powered by an internal chemical reaction based on the hydrolysis of an oleic anhydride precursor or on the hydrolysis of HCN polymer, a prebiotic chemistry. Such motile agents would be capable of finding resources while escaping equilibrium, and sustaining themselves while retaining a chemical memory of their past actions. These primitive agents would thus be capable of temporal evolution.

12.20 Discussion

12.30 Lunch

Session 2 – Self-assembled vesicles
Chair Professor Fritz Eckstein, Max-Planck Institute for Experimental Medicine, Germany

13.30 Did life emerge from messy mixtures or purified prebiotic products?
Professor Jack Szostak, Massachusetts General Hospital/Harvard Medical School, USA

The accumulation of pure, concentrated chemical building blocks, from which the essential components of protocells could be assembled, has long been viewed as a necessary but extremely difficult step on the pathway for the origin of life. However, recent experiments have shown that surprisingly complex chemical mixtures can in some cases lead to simpler sets of reaction products than are obtained from more restricted sets of reactants. Similarly, model protocell membranes composed of certain mixtures of simple amphiphilic molecules have superior physical properties (e.g. high thermostability and permeability) than membranes composed of single, homogeneous amphiphiles. Moreover, membrane self-assembly under simple and natural conditions gives rise to heterogeneous mixtures of large multilamellar vesicles, which are predisposed to a robust pathway of growth and division that does not work for the nominally simpler small, monodisperse, and unilamellar vesicles. Might a similar relaxation of the constraints on building block purity and homogeneity actually facilitate the difficult problem of nucleic acid replication? Several arguments suggest that mixtures of monomers and short oligonucleotides may facilitate the chemical copying of polynucleotides of sufficient length and sequence complexity to allow for the emergence of the first nucleic acid catalysts. The question of the origin of life may become less daunting once the constraints of overly well-defined laboratory experiments are appropriately relaxed.

14.00 Discussion

14.15 Aminoacylation, transacylation and peptide synthesis facilitated by a pentaribonucleotide, GUGGC
Dr Mike Yarus, University of Colorado, USA

Given the difficulty of synthesis for congeners of RNA under geochemical conditions, the smallest nucleotide structures which are catalytic or hosts for biochemistry are of particular interest. I will review the reactions of GUGGC, which, when supplied with aminoacyl adenylate and GCCU, makes a manifold of about twenty products (including GCCU-amino acid, GCCU-peptide and GCCU-2′, 3′ dipeptide). Thus some basic reactions of translation would be attained as soon as minute amounts of short oligoribonucleotides became available. Nucleotide ribose itself seems sufficient to some of these chemical group transfers; thus even this very simple chemical platform could have been unexpectedly useful in evolving a primitive translation apparatus.

14.45 Discussion

15.00 Tea/coffee

15.30 General acid-base catalysis in the nucleolytic ribozymes
Professor David Lilley FRS, University of Dundee, UK

The nucleolytic ribozymes are a group of five natural RNA species that catalyze site-specific cleavage and ligation reactions. We have made an extensive analysis of the catalytic mechanism of the VS ribozyme, supporting general acid-base catalysis by nucleobases. In the cleavage reaction a guanine acts as general base to deprotonate the 2′O nucleophile, while an adenine acts as general acid to protonate the 5′O leaving group. This is supported by functional group substitution, and the pH dependence of the reaction rate for the natural and modified RNA.

Although possessing totally different folds, the functional elements of the VS and hairpin ribozymes are topologically and mechanistically very similar if not identical. The hairpin ribozyme also appears to act by general acid-base catalysis using adenine and guanine nucleobases. The other nucleolytic ribozymes appear to use the same mechanism. Four of the five use guanine as general base. But they have diversified to employ hydrated metal ions and even small molecules in their catalytic mechanisms. By contrast, the larger ribozymes seem to have adopted a different, metalloenzyme, catalytic strategy.

16.00 Discussion

16.15 Crystal structure of the class I ligase ribozyme

Professor Joseph Piccirilli, University of Chicago, USA

All models of the RNA World era invoke the presence of ribozymes that can catalyze RNA polymerization. The class I ligase ribozyme selected in vitro 15 years ago from a pool of random RNA sequences catalyzes formation of a 3',5'-phosphodiester linkage analogous to a single step of RNA polymerization. Recently the three dimensional structure of the ligase has been solved in complex with U1A RNA binding protein and independently in complex with an antibody fragment. The RNA adopts a tripod arrangement and appears to utilize a two-metal ion mechanism similar to proteinaceous polymerases. I will discuss structural implications for engineering a true polymerase ribozyme and describe the use of the antibody framework both as a portable chaperone for crystallization of other RNAs and as a platform for exploring steps in evolution from the RNA World to the RNA-Protein World.

16.45 Discussion

17.00 Close

Tuesday 22 February 2011

Session 3 – The RNA world. RNA catalysis
Chair Professor David Lilley FRS, University of Dundee, UK

9.00 Ribozymes and riboswitches
Professor Scott Strobel, Yale University, USA

The recently identified *glmS* ribozyme revealed that RNA enzymes, like protein enzymes, are capable of using small molecules as catalytic cofactors to promote chemical reactions. Flavin mononucleotide (FMN), S-adenosyl methionine (SAM), adenosyl cobalamin (AdoCbl) and thiamine pyrophosphate (TPP) are known ligands for RNA riboswitches in the control of gene expression, but are also catalytically powerfully and ubiquitous cofactors in protein enzymes. If RNA, instead of just binding these molecules, could harness the chemical potential of the cofactor, it would significantly expand the enzymatic repertoire of ribozymes. We will present several riboswitch structures and speculate on how these cofactors might have been employed by ribozymes in the prebiotic RNA World or may still find application in modern biology.

9.30 Discussion

9.45 Ribonuclease P
Professor Sidney Altman, Yale University, USA

The gene coding for the RNA subunit of RNase P is essential in all free living organisms. The RNA subunit, itself, is an enzyme and, from its evolutionary tree, we can infer that it is a very ancient molecule. The specificity of this enzyme is that it cleaves other RNA molecules at the junction of single stranded and the 5' end of double stranded regions of RNA. One can infer that this molecule was very useful in an ancient world in cleaving long pieces of RNA, that must have contained hairpin regions in it, into shorter molecules with the capability of different functions from the longer parent. Today, the specificity of the enzyme can be utilized in designing drug therapies.

10.15 Discussion

10.30 Tea/coffee

11.00 Use of a coenzyme by the *glmS* ribozyme-riboswitch suggests primordial expansion of RNA chemistry by small molecules
Dr Adrian Ferré-D'Amaré, Fred Hutchinson Cancer Research Center, USA

The *glmS* ribozyme-riboswitch is the first known example of a naturally-occurring catalytic RNA that employs a small molecule as a coenzyme. Binding of glucosamine-6-phosphate (GlcN6P) activates self-cleavage of the bacterial ribozyme. As the ribozyme is part of the mRNA encoding the metabolic enzyme GlcN6P-synthetase, cleavage leads to negative-feedback regulation. GlcN6P binds in the active site of the ribozyme where its amine functions as a general acid and electrostatic catalyst. The ribozyme is pre-folded but inactive in the absence of GlcN6P, demonstrating it has evolved strict dependence on the exogenous small molecule. The ribozyme showcases the ability of RNA to co-opt non-covalently bound small molecules to expand its chemical repertoire. Analogue studies demonstrate that some molecules other than GlcN6P, such as L-serine (but not D-serine), can function as weak activators. This suggests how coenzyme use by RNA world ribozymes may have led to evolution of proteins. Primordial cofactor-dependent ribozymes may have first evolved to bind their

cofactors covalently. If amino acids were used as cofactors, this could have driven the evolution of RNA aminoacylation. The ability to make covalently bound peptide coenzymes may have further increased the fitness of such primordial ribozymes, providing the selective pressure for the invention of translation.

11.30 Discussion

11.45 Energy flows, metabolism, and translation

Dr Robert Pascal, University of Montpellier, France

Thermodynamics provides an essential approach to understand how living organisms survive in an organized state despite the second law. Exchanges with the environment constantly produce large amounts of entropy compensating for their own organized state. In addition to this constraint on self-organization, the free energy delivered to the system, in terms of potential, is essential to understand how a complex chemistry based on carbon has emerged. Accordingly, the amount free energy brought about in discrete events must reach the strength needed to induce chemical changes in which covalent bonds are reorganized. The consequence of this constraint will be scrutinized in relation with both the development of a carbon metabolism and that of translation. Amino acyl adenylates involved as aminoacylation intermediates of the latter process reach one of the higher free energy levels found in biochemistry, which may be informative on the range in which energy was exchanged in essential early biochemical processes. The consistency of this range with the amount of energy needed to weaken covalent bonds involving carbon may not be accidental but the consequence of the above mentioned thermodynamic constraints, which could be useful in building scenarios for the emergence and early development of translation

12.15 Discussion

12.30 Lunch

Session 4 – Emerging from the RNA world
Chair Dr Venki Ramakrishnan, Medical Research Council, UK

13.30 The RNA origin of transfer RNA aminoacylation and beyond
Professor Hiroaki Suga, The University of Tokyo, Japan

Aminoacylation of tRNA is an essential event in the translation system. Although in the modern system protein enzymes play the sole role in tRNA aminoacylation, in the primitive translation system RNA molecules could have catalyzed aminoacylation onto tRNA or tRNA-like molecules. Even though such RNA enzymes thus far are not identified from known organisms, in vitro selection has generated such RNA catalysts from a pool of random RNA sequences. Among them, a set of RNA sequences, referred to as flexizymes, discovered in our laboratory are able to charge amino acids onto tRNAs. Significantly, flexizymes allow us to charge a wide variety of amino acids, including those of non-proteinogenic, onto tRNAs bearing any desired anticodons, and thus enable us to reprogram the genetic code at our will. This lecture summarizes the evolutionary history of flexizymes and also the most recent advance in manipulating translation system in the integration with flexizymes.

14.00 Discussion

14.15 Mistranslation and its control by tRNA synthetases
Professor Paul Schimmel, The Scripps Research Institute, USA

Aminoacyl tRNA synthetases are ancient proteins that interpret, or translate, the genetic material in all life forms. The synthetases are thought to have appeared during the transition from the RNA world to the theatre of proteins. In the first step of protein synthesis, they establish the rules of the genetic code, whereby each amino acid is matched with a tRNA that is cognate to the amino acid. Mistranslation occurs when an amino acid is attached to the wrong tRNA and subsequently is misplaced in a nascent protein. These errors of translation have been shown to be toxic to bacteria and mammalian cells, and to lead to heritable genetic changes. Some evidence suggests that the greatest challenge for Nature has been the mistranslation of serine for alanine. The severity of the problem is seen with the tiny amounts of mistranslation of serine for alanine that cause severe neuropathologies in the mouse. To minimize serine-for-alanine mistranslation, powerful selective pressures developed to correct errors of translation through a special editing activity that is imbedded within alanyl-tRNA synthetases (AlaRSs). This editing activity removes serine that has been misattached to alanine tRNAs. However, the problem of serine-for-alanine mistranslation is so acute that a separate, genome-encoded fragment of the editing domain of AlaRS is distributed throughout all 3 kingdoms of the Tree of Life. This fragment - known as AlaXp - is ancient and redundantly provides editing activity to prevent serine from being incorporated into proteins at positions reserved for alanine. Thus, a reiterative process that uses both the editing activities of AlaRS and of AlaXp is designed to prevent misincorporation of serine. Detailed x-ray structural and functional analysis has shed light on the reasons why the problem of serine-for-alanine mistranslation is universal, and on the selective pressures that engendered the appearance of AlaXp's at the base of the Tree of Life.

14.45 Discussion

15.00 Tea/coffee

15.30 A vestige of an RNA apparatus with ribozyme capabilities embedded and functions within the modern ribosome

Professor Ada Yonath, Weizmann Institute of Science, Israel

Ribosomes, the universal cellular machines, possess spectacular architecture accompanied by inherent mobility, allowing for their smooth performance as polymerases that translate the genetic code into proteins. Composed of RNA moieties, the site for peptide bond formation (PTC) is located within a universal internal symmetrical region connecting all of the remote ribosomal features involved in ribosomal functions. The elaborate architecture of this region positions ribosomal substrates in appropriates stereochemistry for peptide bond formation, for substrate-mediated catalysis, and for substrate translocation. The high conservation of the symmetrical region implies its existence irrespective of environmental conditions and indicates that it may represent an ancient RNA machine. Attempts for proving this assumption will be discussed.

16.00 Discussion

16.15 Evolutionary optimization of speed and accuracy of ribosome decoding

Dr Marina Rodnina, Max Planck Institute for Biophysical Chemistry, Germany

The speed and accuracy of protein synthesis are fundamental parameters for understanding the fitness of living cells, the quality control of translation, and the evolution of ribosomes. The error frequency of translation of an mRNA codon by a near-cognate aminoacyl-tRNA is close to 10^{-3} *in vivo* and *in vitro*. The selectivity is predominantly due to the differences in rates of forward reactions of GTP hydrolysis and peptide bond formation for cognate and near-cognate reactions, while the intrinsic affinity differences between cognate and near-cognate codon-anticodon complexes are not utilized for tRNA discrimination. Thus, the ribosome appears to be optimized towards high speed of translation at the cost of fidelity. Competition with near- and non-cognate ternary complexes reduces the rate of GTP hydrolysis in the cognate ternary complex, but does not appreciably affect the rate-limiting tRNA accommodation step. Thus, the GTP hydrolysis step is crucial for the optimization of both the speed and accuracy, which explains the necessity for the trade-off between these two fundamental parameters of translation.

17.00 Close

Please note: The discussion meeting closes at 5pm and we ask that all participants vacate the building promptly.

Organiser, speaker and chair biographies

Professor Sidney Altman, Yale University, USA (Speaker)
Sidney Altman's undergraduate work was in physics. Later he worked on mutagenesis of phage T4 before he became involved in tRNA biogenesis and mutagenesis. He discovered a radioactive pure precursor and subsequently RNase P. The purification and characterization of RNase P took his attention for several years. Recently he has been involved in a putative drug therapy involving the use of RNase P in vivo. Altman has been chair of his department at Yale University and Dean of Yale College. He is a member of the National Academy of Sciences, the American Philosophical Society and a Nobel Laureate in Chemistry (1989)

Professor Donna Blackmond, The Scripps Research Institute, USA (Speaker)
Donna G Blackmond has held professorships in the US, Germany, and the UK. In 2010 she moved from Imperial College London to The Scripps Research Institute in La Jolla, California. Professor Blackmond's research focuses on kinetic and mechanistic studies of asymmetric catalytic reactions as well as investigations of the phase behavior of chiral molecules. Professor Blackmond received the 2009 Royal Society of Chemistry Award in Physical Organic Chemistry. She was awarded a Royal Society Wolfson Research Merit Award in 2007 and an Arthur C. Cope Scholar Award from the Organic Chemistry Division of the American Chemical Society in 2005. In 1998 she received the Max-Planck-Society's Award for Outstanding Women Scientists. She has been a Woodward Visiting Scholar at Harvard University (2002-2003) and a Miller Institute Research Fellow at University of California, Berkeley (2003).

Professor Fritz Eckstein, Max-Planck Institute for Experimental Medicine, Germany (Chair)
Professor Fritz Eckstein received his Ph. D. in chemistry from the University of Bonn in 1960. He then completed postdoctoral work at University of Toronto (1960-62) and Harvard University, Dept. of Chemistry, with Prof. R. B. Woodward (1962-63) before working at the Max-Planck Institute for experimental medicine, Göttingen from 1964. He then took up the post of Adjunct Professor at University of Göttingen, Dept. of chemistry from 1972-1997. He currently is an Emeritus Professor at the Max-Planck Institute for experimental medicine.
While at the University of Göttingen Professor Eckstein took several sabbaticals at University of Washington, Seattle, Dept. of Pharmacology with D. Storm(1980), Medical Res. Council, Laboratory of Molecular Biology, Cambridge, UK, with G. Winter (1987) and Hebrew University, Jerusalem, Dept. of Biol. Chemistry with H. Soreq (1998)

Professor Eckstein has received numerous awards, including (1972) Carl-Duisberg Gedächtnispreis of Gesellschaft Deutscher Chemiker; (1992) Alexander-von-Humboldt-Gay Lussac Award for French-German Scientific cooperation, (1997) Hans Krebs lecture, University of Sheffield, Dept. of Chemistry, (1997/98) Joels Foundation Visiting Professor, Hebrew University, (2000) Richard-Kuhn-Medaille of Gesellschaft Deutscher Chemiker, (2006) Honorary Ph. D. by the Hebrew University

Dr Adrian Ferré-D'Amaré, Fred Hutchinson Cancer Research Center, USA (Speaker)
Adrian R. Ferré-D'Amaré earned his Ph.D. at The Rockefeller University under the guidance of Prof. Stephen Burley. He carried out post-doctoral research in the laboratory of Prof. Jennifer Doudna at Yale University as a Jane Coffin Childs Fellow. In 1999, he joined the faculty of the Fred Hutchinson Cancer Research Center in Seattle, USA, where he is currently Full Member. He is also an Investigator of the Howard Hughes Medical Institute and an Affiliate Associate Professor of the Department of Biochemistry at the University of Washington. Past distinctions include the Eli Lilly & Co. Research Award of the American Society for

Microbiology (2004), and selection as a Distinguished Young Scholar in Medical Research by the W.M. Keck Foundation (2003-2008).

Dr Adrian Ferré-D'Amaré, Fred Hutchinson Cancer Research Center, USA (Speaker)
Adrian R. Ferré-D'Amaré earned his Ph.D. at The Rockefeller University under the guidance of Prof. Stephen Burley. He carried out post-doctoral research in the laboratory of Prof. Jennifer Doudna at Yale University as a Jane Coffin Childs Fellow. In 1999, he joined the faculty of the Fred Hutchinson Cancer Research Center in Seattle, USA, where he is currently Full Member. He is also an Investigator of the Howard Hughes Medical Institute and an Affiliate Associate Professor of the Department of Biochemistry at the University of Washington. Past distinctions include the Eli Lilly & Co. Research Award of the American Society for Microbiology (2004), and selection as a Distinguished Young Scholar in Medical Research by the W.M. Keck Foundation (2003-2008).

Dr Martin Hanczyc, University of Southern Denmark, Denmark (Speaker)
Martin Hanczyc is an Associate Professor at the Institute of Physics and Chemistry and the center for Fundamental Living Technology (FLinT) in Denmark. He is also an Honorary Senior Lecturer at the Bartlett School of Architecture, University College London. He received a bachelor's degree in Biology from Pennsylvania State University, a doctorate in Genetics from Yale University and was a postdoctorate fellow under Jack Szostak at Harvard University. He has published in the area of protocells, complex systems, evolution and the origin of life in various journals including JACS and Science. He is developing novel synthetic chemical systems based on the properties of living systems. These synthetic systems are termed 'protocells' as they are model systems of primitive living cells and chemical examples of 'artificial' life.

Professor David Lilley FRS, University of Dundee, UK (Organiser, Chair and Speaker)
A chemist by training, David Lilley has worked in the field of nucleic acid structure and function his entire career. He first solved the structure of the four-way (Holliday) junction in DNA, and subsequently studied its dynamics (most recently using single-molecule methods) and interactions with proteins. In the past 15 years he has worked on structure and function in RNA, with a special interest in ribozyme structure and mechanism. He has also made significant contributions to methodology of nucleic acid structure, especially fluorescence resonance energy transfer both in ensembles and single molecules.

Dr Robert Pascal, University of Montpellier, France (Speaker)
Born in 1952, he graduated in physical-organic chemistry and then undertook a PhD thesis on improvements of Strecker synthesis by catalytic pathways defended in 1980, which marked the beginning of a long-term interest for the prebiotic chemistries of amino acids and peptides. His main fields of interest comprise organic reactivity of amino acid derivatives, peptide and peptide materials chemistries, intramolecular reactivity and its connexion with the explanation of enzyme efficiency, and, lastly, prebiotic chemistry with a special interest for early biochemical processes. Appointed by the CNRS in 1978, he is presently Senior Scientist and leader of the DSBC (Complex Biomolecular Systems Dynamics) team of the Max Mousseron Institute of Biomolecules (IBMM) in Montpellier.

Professor Joseph Piccirilli, University of Chicago, USA (Speaker)
Currently, Piccirilli is Associate Professor in the Department of Biochemistry and Molecular Biology and in the Department of Chemistry at The University of Chicago. Professor Piccirilli earned his Ph.D. in 1989 from Harvard University, working as a graduate student on the construction of unnatural base pairs in Steven Benner's laboratory first at Harvard and then at ETH Zurich as a Harvard Travelling Scholar. From Zurich, Piccirilli moved to Boulder, Colorado to work on the catalytic mechanisms of RNA catalysis in the laboratory of Thomas Cech. In 1993, Professor Piccirilli moved to the University of Chicago to begin his independent career as an assistant professor. He was promoted to Associate Professor with tenure in 2001. His research interests encompass nucleic acid chemistry, RNA catalysis, structure and function of noncoding RNA, the origin of life, and RNA-protein interactions.

Dr Venki Ramakrishnan, Medical Research Council, UK (Chair)
Venki Ramakrishnan has had a longstanding interest in ribosome structure and function. In 2000, his laboratory determined the atomic structure of the 30S ribosomal subunit and its complexes with ligands and antibiotics. This work has led to insights into how the ribosome "reads" the genetic code, as well as into various aspects of antibiotic function. In the last few years, Ramakrishan's lab has published high-resolution structures of functional complexes of the entire ribosome during decoding, peptidyl transfer, translocation and termination. Since 1999, he has been on the scientific staff of the MRC Laboratory of Molecular Biology in Cambridge.

Dr Marina Rodnina, Max Planck Institute for Biophysical Chemistry, Germany (Speaker)
Marina Rodnina received the master's degree in Biology and Genetics from the University of Kiev (Ukraine) and the PhD in Molecular Biology from the Institute of Molecular Biology and Genetics of the Ukrainian Academy of Sciences in Kiev. She has been a full professor at the University of Witten, Germany. Since 2008, she has served as Director of the Department of Physical Biochemistry at the Max Planck Institute for Biophysical Chemistry, Goettingen, Germany. Her research focuses on the mechanisms of ribosome function, translational GTPases, and fidelity of gene expression. Her group pioneered the use of kinetic and fluorescence methods in conjunction with quantitative biochemistry to solve the mechanisms of translation.

Professor Paul Schimmel, The Skaggs Institute for Chemical Biology, The Scripps Research Institute, USA (Speaker)
Paul Schimmel is Ernest and Jean Hahn Professor of Molecular Biology and Chemistry at The Scripps Research Institute. Prior to joining The Scripps, he was John D. and Catherine T. MacArthur Professor of Biochemistry and Biophysics at MIT (Massachusetts Institute of Technology). Author or coauthor of more than 450 scientific publications, he is also coauthor of a widely used 3-volume textbook on biophysical chemistry. His research interests have focused on aminoacyl tRNA synthetases as interpreters of the genetic information. He is an elected member of the American Academy of Arts and Science, the US National Academy of Sciences, the American Philosophical Society, and the Institute of Medicine. Among other achievements, Schimmel's laboratory discovered a universal mechanism for correcting errors in the interpretation of genetic information, and went on to show how this mechanism is essential for maintaining cellular homeostasis and for preventing serious pathologies and disease.

Professor Norm Sleep, Yale University, USA (Speaker)
I studied the effects of mantle plumes on the base of the lithosphere. Buoyant plume material flows laterally with this lithosphere forming an up-side down drainage pattern. For example, the flow of plume material from beneath East Antarctica may cause volcanism along the Ross Sea Coast. I have also investigated the long-term stability of cratonal lithosphere. This material needs to be both more viscous and less dense than ordinary mantle to have persisted over the last 2-3 billion years. Dynamics is relevant to the habitability of the Earth. For example, tectonic forces, erosion, and deposition all tend to produce continental surfaces near sea level. The Earth has the right amount of water for this to happen. Hydrogen from serpentinization is lush a pre-biotic and early biotic environment on active rocky planets. The productivity, however, is order of magnitude less than modern photosynthesis. Angela Hessler constrained the atmospheric temperature to less than 50°C at 3.2 billion years ago from the behavior of quartz during weathering. In collaboration with student Paul Hagin and Mark Zoback, I applied rate and state friction formalism to compaction of sand. I am continuing by applying the results to the strengthening of faults while they are at rest and the origin of dialatancy.

Professor Scott Strobel, Yale University, USA (Speaker)
Scott Strobel (http://www.yale.edu/strobel/) is the Henry Ford II Professor of Molecular Biophysics and Biochemistry at Yale University and a Professor of the Howard Hughes Medical Institute. He completed his graduate studies with Peter Dervan at Caltech and performed postdoctoral research with Thomas Cech at University of Colorado at Boulder. He joined the Yale faculty in 1995 and served as Department Chair for the past three years. Scott's work focuses on RNA catalysis in systems ranging from group I intron splicing to the peptidyl transferase center of the ribosome. He also studies the structural basis of riboswitch function. In 2008 he received the Schering Plough Research Institute award from the American Society of Biochemistry and Molecular Biology for his work on RNA catalysis. He served as co-organizer of the RNA Society meeting in 2003 and the 2006 Nucleic Acids Gordon Conference. He serves on the editorial board of *RNA*.

Professor Hiroaki Suga, The University of Tokyo, Japan (Speaker)
Hiroaki Suga was born in Okayama City, Japan in 1963. He received his B. Eng. and M. Eng. from Okayama University and Ph. D. in Chemistry from the Massachusetts Institute of Technology in 1994. After three years of post-doctoral work in Massachusetts General Hospital, he was appointed as a tenure-track Assistant Professor in the Department of Chemistry in the State University of New York at Buffalo to carry his independent research group. In 2002, he obtained his tenure and became Associate Professor. In 2003, he moved to the Research Centre for Advanced Science and Technology in the University of Tokyo as Associate Professor, and soon after he was promoted to Full Professor. In 2010, he changed his affiliation to the Department of Chemistry, Graduate School of Science.

Professor John Sutherland, MRC Laboratory of Molecular Biology, Cambridge, UK (Organiser, Chair and Speaker)
John Sutherland studied chemistry at the University of Oxford under the tutelage of Peter Atkins and Gordon Lowe, and then spent a spell as a Kennedy Scholar at Harvard with Jeremy Knowles. Upon return to the UK, he carried out his doctoral work with Jack Baldwin at Oxford, and then stayed in Oxford first as a Junior Research Fellow and then as a University Lecturer in Organic Chemistry. In 1998 he took a chair in Biological Chemistry at Manchester, and in 2010 moved to the MRC Laboratory of Molecular Biology in Cambridge as a Group Leader. He is interested in chemistry associated with the origin of life, and in evolution. His research group has made contributions in the area of prebiotic nucleotide synthesis and RNA chemistry which resulted in him being awarded the Max Tishler Prize Lectureship at Harvard in 2009.

Professor Jack Szostak, Massachusetts General Hospital/Harvard Medical School, UK (Speaker)
Dr. Szostak is an Investigator of the Howard Hughes Medical Institute, Professor of Genetics at Harvard Medical School, and the Alex Rich Distinguished Investigator in the Dept. of Molecular Biology and the Center for Computational and Integrative Biology at Massachusetts General Hospital. Dr. Szostak is a member of the National Academy of Sciences, and a Fellow of the New York Academy of Sciences, the American Academy of Arts and Sciences, and the American Association for the Advancement of Science.

Dr. Szostak's early research was on the genetics and biochemistry of DNA recombination, which led to the double-strand-break repair model for meiotic recombination. At the same time Dr. Szostak made fundamental contributions to our understanding of telomere structure and function, and the role of telomere maintenance in preventing cellular senescence. For this work Dr. Szostak shared, with Drs. Elizabeth Blackburn and Carol Greider, the 2006 Albert Lasker Basic Medical Research Award and the 2009 Nobel Prize in Physiology or Medicine.

In the 1990s Dr. Szostak and his colleagues developed in vitro selection as a tool for the isolation of rare functional RNA, DNA and protein molecules from large pools of random sequences. His laboratory has used in vitro selection and directed evolution to isolate and characterize numerous nucleic acid sequences with specific ligand binding and catalytic properties. For this work, Dr. Szostak was awarded, along with Dr.

Gerald Joyce, the 1994 National Academy of Sciences Award in Molecular Biology and the 1997 Sigrist Prize from the University of Bern. In 2000, Dr. Szostak was awarded the Medal of the Genetics Society of America, and in 2008 Dr. Szostak received the H.P. Heineken Prize in Biophysics and Biochemistry.

Dr. Szostak's current research interests are in the laboratory synthesis of self-replicating systems and the origin of life.

Dr Mike Yarus, University of Colorado, USA (Speaker)
Michael Yarus is Professor Emeritus in the Department of Molecular, Cellular and Developmental Biology of the University of Colorado, Boulder, CO, USA. He has studied the structure and function of tRNA, mRNA and rRNA in protein biosynthesis since the beginning of his career, first in modern translation, and then more recently, in simpler selected RNAs that might mimic progenitors of the modern mechanisms.

Professor Ada Yonath, Weizmann Institute of Science, Israel (Speaker)
Ada Yonath studied chemistry at the Hebrew University, earned a Ph.D. degree from Weizmann Institute of Science (WIS) and carried postdoctoral education at Carnegie-Melon university and MIT, USA. Currently she is a professor of structural biology at WIS, holds the Kimmel Professorial Chair, and directs the Kimmelman Centre for Biomolecular Structure and Assembly. In 1986-2004 she also headed a Max-Planck-Research Unit in Hamburg, Germany.

Among others, she is a member the US National Academy of Sciences; the Israel Academy of Sciences and Humanities; the American Academy for Art and Science and the European Molecular Biology Organization. She also holds honorary doctorates from Tel Aviv, Ben Gurion, Bar Ilan and Oxford Universities.
Her awards include the 1st European Crystallography Prize; the Israel Prize; The Paul Karrer Gold Medal; the Louisa Gross Horwitz Prize; the Paul Ehrlich Ludwig Darmstaedter Medal; the Wolf Prize; the UNESCO Award for Women in Science; the Albert Einstein World Award of Science; the Erice Prize for Peace and the Nobel Prize for Chemistry.

Upcoming Royal Society events

From bears' winter-sleep to advanced antibiotics
Professor Ada Yonath, Weizmann Institute of Science, Israel
6.30pm on 24 February 2011

To facilitate instant recovery of active life once bears wake up from their winter sleep, nature provides ingenious mechanism based on periodic packing of their ribosomes, the cellular machines that translate the genomic instructions into proteins.

This mechanism inspired crystallization of bacterial ribosomes, thus producing the samples which eventually yielded the stunning ribosomes' molecular structure. Owing to their fundamental role in life cycle, ribosomes are targeted by many antibiotics.

The structures of these antibiotics in complex with ribosomes revealed their modes of action, shed light on strategies used to differentiate ribosomes of the pathogens from those of patients, provided insights into mechanisms acquiring resistance to antibiotics, and elucidated structural bases for the design of more potent antibiotics.

Carbon storage: caught between a rock and climate change
2011 Bakerian prize lecture
Professor Herbert Huppert FRS
6.30pm on 24 March 2011

Since the formation of the Earth, the global mean surface temperature, carbon dioxide (CO_2) and methane content of the atmosphere have varied considerably. But over the past 150 years there have been dramatic increases in all three values. Professor Herbert Huppert, the Director of the Institute of Theoretical Geophysics at the University of Cambridge, will explore this rise and its probable significance, as well as one option that can potentially halt the rise in CO_2 - carbon storage.

This technology may combat the rise in greenhouse gases by storing CO_2 in vast porous geological formations. For the last fifteen years there has been considerable effort devoted to storing, or sequestering, some of the millions of tons of CO_2 resulting from the burning of fossil fuels which otherwise would have been emitted into the atmosphere. The first project, the Sleipner gas field off Norway's coast, has successfully stored approximately 15 million tons of CO_2 since 1996. This lecture will explore some of the physical, chemical and fluid dynamical processes in the storage of CO_2, as well as evaluate the risk of leakage back into the atmosphere.

Admission free – no ticket or advance booking required.
Doors open at 5.45pm and seats will be allocated on a first-come-first-served basis. More information available at royalsociety.org/events

These events will be broadcast live on the web at royalsociety.org/live and available to view on demand within 48 hours of delivery.
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