

# The ascent of molecules

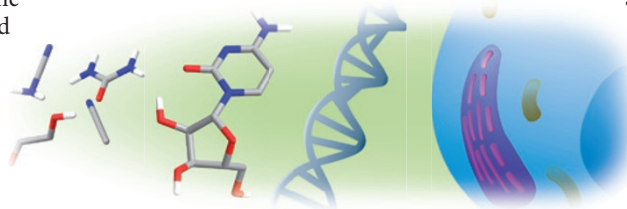
A collection of articles in this issue focuses on the chemical origin of life — how simple molecules present on the early Earth could have evolved into the complex dynamic biochemistry that we know today.

In 2010, while pondering the question of why chemistry often gets a rough ride in the mainstream media, this journal suggested<sup>1</sup> that “chemistry lacks the easily articulated grand challenges associated with physics or biology”. Nevertheless, the following year, designated by the United Nations as the International Year of Chemistry, provided the perfect opportunity to try and crystallize exactly what the ‘big problems’ associated within chemistry are. Philip Ball put the question “How did life begin?” at the top of a list of ten unsolved mysteries<sup>2</sup> that, he said, were “some of the most profound scientific questions” that “pertain to the science of atoms and molecules” — that is, chemistry.

The classic experiment relating to the chemical origins of life, describing the formation of amino acids when an electric discharge was passed through mixtures of methane, ammonia, water and hydrogen — now widely known as the Miller–Urey experiment — was reported<sup>3</sup> by Stanley Miller in *Science* in 1953. So, although this is not a new area of research, it is certainly one that has seen a recent resurgence of interest<sup>4</sup>. Many different aspects of chemistry<sup>5</sup> are brought together in this interdisciplinary field that encompasses topics such as the prebiotic synthesis of nucleosides and nucleotides, the assembly of these small building blocks into information-containing polymers (DNA and RNA), the origin of homochirality, the formation of protocells — and whether this occurred before or after the formation of the basic molecules of life (DNA, RNA and proteins). One might also pose the question of whether these events even occurred on the early Earth, or whether these molecules may have been transported here from elsewhere, perhaps on a meteorite like the one that crashed into the Earth in Murchison, Australia in September 1969.

Two Articles in this issue focus on one small (but important) part of this huge puzzle: the selective ligation of ribonucleotides to form exclusively the 3',5'-linked RNA chains — rather than a mixture of 2',5' and 3',5' connections — that are found in contemporary biology. An Article from John Sutherland and co-workers<sup>7</sup> continues in the theme of their 2009 Letter<sup>8</sup> to *Nature*, which, in describing

a prebiotically plausible synthesis of the pyrimidine nucleotides, highlighted the importance of systems chemistry in understanding the prebiotic world. In their latest work, the Sutherland group show that similar systems-chemistry approaches can explain this important regioselectivity problem. A combination of prebiotically plausible reactants effects a site-selective reaction that results in acylation of the 2'-hydroxyl group and thus promotes ligation in the desired 3',5'-fashion.



The other Article, from Jack Szostak and co-workers, takes a complementary approach<sup>9</sup>. By examining the activity of RNA molecules containing a mixture of 2',5' and 3',5' linkages, they show that a mixture of isomers may not have been a problem for the evolution of RNA. Indeed, they provocatively suggest that the formation of these isomers may even have been beneficial, because their presence renders the backbone of polynucleotides irregular, which in turn weakens the binding between strands in duplexes. This could facilitate the separation of RNA strands (a necessary step for replication) in the absence — or before the existence — of enzymes.

The ability of RNA to act as both a catalyst and as a store of genetic information is at the heart of the RNA-world hypothesis, in which RNA fulfilled both of these roles in early life before being replaced by the contemporary trio of DNA, RNA and proteins. In an accompanying News & Views article, Armando Hernandez and Joseph Piccirilli note the importance of demonstrating, in a laboratory, non-enzymatic copying of RNA as evidence for such an RNA world. They explain how the formation of mixed linkages in the RNA backbone has been a problem in achieving this goal, and comment that “together, these two studies make it a little easier to visualize the emergence of the RNA world from prebiotic chemistry”.

These articles describing and discussing research on this topic are complemented by an interview with Matthew Powner, now based at University College London. Powner worked with both the Sutherland and Szostak research groups, as a PhD student and a postdoctoral researcher, respectively, and is a co-author of both Articles that appear in this issue. In the interview, Powner describes how he sees the two pieces of work fitting together as part of “a colossal chemical jigsaw”, and also discusses his own nascent independent research career.

Powner's passion for this subject is evident from the answers, not least when he gives reasons for why this topic should be funded. We asked him this question because, in these straightened economic times, a case often needs to be made (particularly to funders) for why a given piece of research demonstrates an obvious long-term societal (usually monetary) benefit. Powner points to our fundamental thirst for knowledge and compares the funding of this field to that of the Large Hadron Collider. The unanticipated benefits of such blue-sky research are frequently cited as the best reason for it to be supported. It seems reasonable to suggest that such benefits may be likely to arise from interdisciplinary topics, such as the origin of life, because understanding them requires the collaboration of researchers from so many different specialties. In attempting to answer questions as fundamental as “where do we come from?”, the chemical origins of life is also surely a topic that can — if explained correctly — get the general public interested in chemistry in a positive way. And you can't put a price on that. □

## References

1. *Nature Chem.* **2**, 599 (2010).
2. Ball, P. *Sci. Am.* **305**, 48–53 (2011).
3. Miller, S. L. *Science* **117**, 528–529 (1953).
4. Ricardo, A. & Szostak, J. W. *Sci. Am.* **301**, 54–61 (2009).
5. Lynn, D., Burrows, C., Goodwin, J. & Mehta, A. *Acc. Chem. Res.* **45**, 2023–2024 (2012).
6. Kvenvolden, K. *et al. Proc. Natl Acad. Sci. USA* **69**, 809–811 (1972).
7. Bowler, E. R. *et al. Nature Chem.* **5**, 383–389 (2013).
8. Powner, M. W., Gerland, B. & Sutherland, J. D. *Nature* **459**, 239–242 (2009).
9. Engelhart, A. E., Powner, M. W. & Szostak, J. W. *Nature Chem.* **5**, 390–394 (2013).
10. Hernández, A. R. & Piccirilli, J. A. *Nature Chem.* **5**, 360–362 (2013).