

 COMMENTARY

Impact synthesis of the RNA bases

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Any discussion related to how life began on this planet inevitably invokes the question as to the origin of bio-organic molecules, a field called prebiotic chemistry (1). How did organic compounds come to populate the early Earth? Before 1953, this question itself was not widely considered within the realm of experimental science. However, since the pioneering results of the Miller–Urey experiment that produced amino acids from electrical discharges passing through simple gases (2), the field of prebiotic chemistry has been extremely prodigious in demonstrating abiotic syntheses for multitudes of organic compounds. However, it became apparent that prebiotic chemistry was faced with a more challenging question. How did the biomolecules of life get selected out of such complex, prebiotic mixtures?

Particular significance has been placed on understanding the selection of the nucleobases adenine (A), cytosine (C), guanine (G), and uracil (U), given their role in the RNA world hypothesis (3). The hypothesis is a premise that life may have emerged with genetic and enzymatic function based exclusively on RNA (4). Some research has pointed to the possibility that selection criteria may have relied on nucleobases that were able to persist the longest in the prebiotic environment. Others have considered the possibility that early RNA life used a wide range of nucleobases, and over time unique selection pressures emerged that favored the extant bases. In terms of using a synthetic origin or availability argument, it has been found that varying conditions are needed to demonstrate the production of all of the RNA bases. Invoking multiple stage and multiple environmental scenarios for the selective prebiotic synthesis of the nucleobases seems extremely unlikely. What would be intriguing would be the demonstration that all of the RNA bases are selectively produced under the same conditions, and that those conditions might be considered plausible to prebiotic chemistry and the early Earth environment. This is what Ferus et al. set out to do in their most recent contribution, and they begin with a simple organic compound called formamide (Fig. 1) (5).

Formamide appears to be widespread in the universe. Astronomers have recently reported its presence in our solar system found within the atmospheres of comets (6), and since the 1970s, formamide has been detected in multiple regions in the interstellar medium (7). The known chemistry and ubiquity of formamide has made it an attractive primordial feedstock compound for the production of many prebiotic molecules (8). Experiments on the prebiotic synthesis of nucleobases using formamide have

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been an active area of research (9–11), but some disheartening observations were routinely made. At best, only three of the four RNA bases have been observed in a single experiment. The missing base typically was guanine. However, when the prebiotic synthesis of guanine could be demonstrated, it would be at the exclusion of other bases, often a pyrimidine, such as cytosine or uracil. However, these studies were important because they demonstrated that formamide could be a common feedstock for each RNA base. What remained was the task of finding plausible conditions that could access all of the bases in one experiment (8).

In a previous publication, Ferus et al. had calculated that if formamide were exposed to much higher energies it would be able to access reaction pathways that produce the nucleobase products (12). Thus, a central model in their current work (5) is the subjection of formamide to experiments that simulate the energy output resulting from an extraterrestrial impact. Simulated impact or shock synthesis of organic compounds has remained a plausible model for the production

of organic compounds needed for prebiotic chemistry and the origin of life (13, 14). A tantalizing argument for this scenario lies with the coincidence of estimates for when life might have originated (4.4–3.5 billion y ago) and the Late Heavy Bombardment (4.0–3.8 billion y ago), a period when the early Earth received a pronounced increase in the impact rate of asteroidal and cometary material (15).

Ferus et al. (5) follow the aftermath of the simulated impact, which causes the breakdown of formamide into a variety of simple gases and radical intermediates (see Fig. 1). The authors show how the formation of these radicals, mainly CN• and H•, combine with formamide to increase the molecular complexity of the mixture leading to stable and previously studied chemical intermediates. In combination with their previous work, Ferus et al. detail how the radicals CN•, H•, and NH₂•, continue to drive the chemistry to produce the purines and pyrimidines (12, 16). A unifying outcome, and of particular interest to prebiotic chemistry, is Ferus et al.'s (5) demonstration that 2, 3-diaminomaleonitrile (DAMN) is a common precursor to all of the RNA bases under these conditions. DAMN has long been known to be a key chemical precursor to the purine nucleobases (1, 9–11), but this is the first report that DAMN has been implicated in the synthesis of pyrimidines. The generation of the CN• radical from the breakdown of formamide and its subsequent reactions has been calculated to be the explanation for how DAMN can access both reaction pathways of pyrimidines and purines.

The prebiotic synthesis of nucleobases helps address only one of a long list of questions. The origin-of-life community also needs convincing reports to demonstrate how the bases could have realistically accumulated in the early Earth environment. How prebiotic organics escaped degradation by the widespread occurrence of water on the early Earth is an example of such a question. In the late 1990s, Stanley Miller and co-workers investigated the hydrolytic stabilities of nucleobases at high temperatures to

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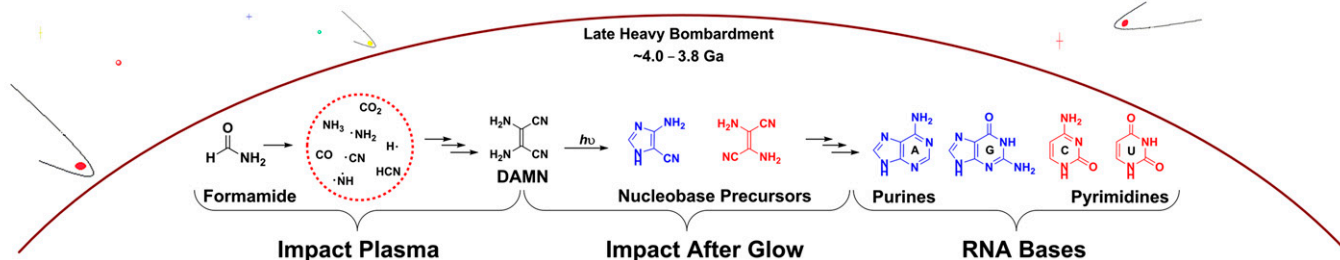


Fig. 1. The RNA nucleobases can be produced when formamide is subjected to a high-energy density event that simulates an extraterrestrial impact on the early Earth.

crudely approximate bolide impacts on large bodies of water or oceanic hydrothermal vents (17). The extremely fast degradation rates on a geological time scale led Miller to conclude that none of the RNA bases could have persisted in a prebiotic environment, nor could they be a part of the first genetic material. However, Ferus et al. (5) demonstrate a possible solution to this problem.

Of all of the RNA bases, cytosine is particularly notorious for its hydrolytic instability (18); it can be easily transformed into uracil through a hydrolysis reaction called deamination. This problem was observed by Ferus et al. (5) because they could not detect cytosine in their formamide-only experiments. Although their mechanistic model predicted the formation of cytosine as a precursor to uracil, the deamination reaction likely prevented the observation of cytosine under those conditions. However, when the authors conducted the impact simulation experiments in the presence of a clay mineral cytosine was detected, and in much higher abundance than uracil. Ferus et al. go on to show how using a negative control, the likely role of the clay is the adsorption of cytosine to the mineral surface (19), which limited its hydrolytic degradation. The use of minerals to catalyze reactions of formamide is well documented (8),

but the preservation of a labile nucleobase under these highly energetic conditions may provide a scenario for the prebiotic accumulation of cytosine.

In recent years the use of formamide as a reagent and solvent has garnered many proponents in the origin-of-life research community (8, 20). The work by Ferus et al. (5)

provides an intriguing example for how the chemistry of formamide is being used to address some of the underlying problems that have persisted in the field.

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- Orgel LE (2004) Prebiotic chemistry and the origin of the RNA world. *Crit Rev Biochem Mol Biol* 39(2):99–123.
- Bada JL, Lazcano A (2003) Perceptions of science. Prebiotic soup—Revisiting the Miller experiment. *Science* 300(5620):745–746.
- Rios AC, Tor Y (2013) On the origin of the canonical nucleobases: An assessment of selection pressures across chemical and early biological evolution. *Isr J Chem* 53(6-7):469–483.
- Robertson MP, Joyce GF (2012) The origins of the RNA world. *Cold Spring Harb Perspect Biol* 4(5):a003608.
- Ferus M, et al. (2014) High-energy chemistry of formamide: A unified mechanism of nucleobase formation. *Proc Natl Acad Sci USA* 112:657–662.
- Biver N, et al. (2014) Complex organic molecules in comets C/2012 F6 (Lemmon) and C/2013 R1 (Lovejoy): Detection of ethylene glycol and formamide. *Astron Astrophys* 566:L5.
- Adande GR, Woolf NJ, Ziurys LM (2013) Observations of interstellar formamide: Availability of a prebiotic precursor in the galactic habitable zone. *Astrobiology* 13(5):439–453.
- Saladino R, Crestini C, Pino S, Costanzo G, Di Mauro E (2012) Formamide and the origin of life. *Phys Life Rev* 9(1):84–104.
- Saladino R, Crestini C, Cicciello F, Costanzo G, Di Mauro E (2007) Formamide chemistry and the origin of informational polymers. *Chem Biodivers* 4(4):694–720.
- Barks HL, et al. (2010) Guanine, adenine, and hypoxanthine production in UV-irradiated formamide solutions: Relaxation of the requirements for prebiotic purine nucleobase formation. *ChemBioChem* 11(9):1240–1243.
- Hudson JS, et al. (2012) A unified mechanism for abiotic adenine and purine synthesis in formamide. *Angew Chem Int Ed Engl* 51(21):5134–5137.
- Ferus M, et al. (2014) High-energy chemistry of formamide: A simpler way for nucleobase formation. *J Phys Chem A* 118(4):719–736.
- Chyba C, Sagan C (1992) Endogenous production, exogenous delivery and impact-shock synthesis of organic molecules: An inventory for the origins of life. *Nature* 355(6356):125–132.
- Martins Z, Price MC, Goldman N, Sephton MA, Burchell MJ (2013) Shock synthesis of amino acids from impacting cometary and icy planet surface analogues. *Nat Geosci* 6(12):1045–1049.
- Gomes R, Levison HF, Tsiganis K, Morbidelli A (2005) Origin of the cataclysmic Late Heavy Bombardment period of the terrestrial planets. *Nature* 435(7041):466–469.
- Ferus M, et al. (2012) On the road from formamide ices to nucleobases: IR-spectroscopic observation of a direct reaction between cyano radicals and formamide in a high-energy impact event. *J Am Chem Soc* 134(51):20788–20796.
- Levy M, Miller SL (1998) The stability of the RNA bases: Implications for the origin of life. *Proc Natl Acad Sci USA* 95(14):7933–7938.
- Shapiro R (1999) Prebiotic cytosine synthesis: A critical analysis and implications for the origin of life. *Proc Natl Acad Sci USA* 96(8):4396–4401.
- Cleaves HJ, et al. (2012) Mineral-organic interfacial processes: Potential roles in the origins of life. *Chem Soc Rev* 41(16):5502–5525.
- Benner SA, Kim H-J, Carrigan MA (2012) Asphalt, water, and the prebiotic synthesis of ribose, ribonucleosides, and RNA. *Acc Chem Res* 45(12):2025–2034.