Structural Chemistry (2021) 32:9–10
https://doi.org/10.1007/s11224-020-01653-2

ORIGINAL RESEARCH

Paradigms and paradoxes: decoding the "genetic code"

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Received: 11 September 2020 / Accepted: 22 September 2020 / Published online: 1 October 2020

Abstract

We propose to keep the term "genetic code" to describe the nucleotide sequence in DNA and RNA and use the term "genetic cipher" to describe the key for decoding the genetic codes of DNA and RNA into the amino acid sequences of proteins.

Keywords Genetic code · Genetic cipher · Nucleic acids · Proteins · Francis Crick

In this Note, we propose to delineate the double use of the term "genetic code," which since its inception has been used to describe two central, but fundamentally different, concepts, in molecular biology. We propose the term "genetic code" be limited to describing the nucleotide sequence in DNA and RNA genomes, which encode for all proteins and RNA molecules that make life possible for all organisms in nature. This definition is consistent with the definition of codon, a sequence of three nucleotides which together form a unit of genetic code in a DNA or RNA molecule. We further propose that the term "genetic cipher" be used to describe the key or algorithm for decoding the numerous genetic codes into the amino acid sequences of proteins. This proposal is consistent with the notion of Francis Crick, who referred to the decoding algorithm as the translation rule and thought that the proper term for this would be the "genetic cipher." According to Crick, "I did not know this at the time, which was fortunate because 'genetic code' sounds a lot more intriguing than 'genetic cipher'" [1]. The former term was accepted and has continued to be used by molecular biologists and all others to describe how nucleotide sequences are translated into amino acid sequences.

Dedicated to the memory of Francis Crick

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Francis Crick described the "genetic code" as "the key to molecular biology, because it shows how the two great polymer languages, the nucleic acid language and the protein language, are linked together" [2]. However, the term genetic code is properly used to describe the nucleotide sequences in DNA/RNA; hence there are a very large number of genetic codes (plural) in nature. The other (improper) use of the term genetic code (singular) is a misnomer, which has been used to describe the rule (algorithm) for translating the language of genetic codes (DNA and RNA nucleotides) into the language (amino acids) of proteins. This latter improper use of the term genetic code has introduced confusion and the need for meticulous explanation each time it is used. For example, on February 8, 2004, a few months before Crick died, one of us (Hargittai) visited him and in our conversation with him, we discussed the question, who was the first to raise the issue of the genetic code? This is how this part of the conversation began: "Let us start with defining what the genetic code is, so that we all agree what it is we are talking about. The genetic code is the means by which information is transmitted from the bases of the nucleic acids to the amino acids of the proteins" [3]. Thus, the need to define what was meant by the genetic code pointed to the clumsiness and confusion originating from the double meaning of the term. Incidentally, Crick agreed that the history of the initiative to search for this key or algorithm needed clarification. According to Crick, he had discussed it in presentations only but never recorded it in any publication, and even his lecture notes relating to this topic had been lost.

In conclusion, the purpose of this note is to clearly define and delineate the terms *genetic code* and *genetic cipher* to promote clear communication about these two critical, but fundamentally different, concepts in molecular biology. It would have been better had Crick insisted on this separation of the terms. It would have happened a lot earlier and it would

have been a lot easier for him to get it accepted. Still, it should be done because these crucial terms are to remain with us indefinitely. Changing the term "The Genetic Code" to "The Genetic Cipher" would both accurately describe its true biological function and make the definition of "genetic code" consistent with the presence and biological function of numerous genetic codes within all genomes in nature.

Funding Open access funding provided by Budapest University of Technology and Economics.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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