Neocles B. Leontis (1955–2020)

On December 8th, 2020, Neocles B. Leontis died in a car crash not far from his hometown of Bowling Green, Ohio. At the time of his death, Neocles was Professor of Chemistry at Bowling Green State University and a member of the Bowling Green City Council. Born in Midland, Michigan, he grew up in Columbus, Ohio. He graduated from The Ohio State University in 1977, where he majored in chemistry, and in 1986 he obtained a PhD in biophysical chemistry from Yale University. He joined the faculty of Bowling Green State University in 1987.

Neocles had an insatiable appetite for knowledge and a wide intellectual curiosity. He was an avid reader and his lectures often addressed philosophical, sociological, or political issues, as well as science. His scientific research and teachings were focused on nucleic acids, especially RNA.

Neocles' first encounter with RNA occurred in the early 1980s, when he was a graduate student in Peter Moore's laboratory at Yale. There he used NMR to study a ~60 nt RNA called "fragment 1" that was obtained from 5S rRNA by limited RNase A digestion. It includes helices I, IV, V, and loop E of 5S rRNA, and binds ribosomal protein bL25. It was an attractive target because it and the oligonucleotides of which it is composed were easy to prepare in tens of milligram quantities—no small consideration in the pre-T7 RNA polymerase era—and being smaller than a tRNA, it was more tractable spectroscopically. The initial objectives were to assign its downfield, imino proton reso-

nances, which would help define its secondary structure, and then to measure imino proton exchange rates, which would yield insights into its dynamics. He was the first to use imino proton exchange rates to measure the breathing rates of base pairs in 5S rRNA and show how they are affected by bL25 binding and magnesium ion concentration (Leontis and Moore 1986).

Although experience with tRNA had shown that RNAs contain non-Watson–Crick base pairs, in the 1980s, their importance for RNA folding and architecture was still not fully grasped. In secondary structure diagrams, non-Watson–Crick juxtapositions were often shown as bubbles, e.g., loop E, and the nucleotides involved were thought to be unpaired and dynamic. Using chemical and enzymatic probing, Romby and coworkers had demonstrated that many of the loops in 5S rRNA include noncanonical base pairs (Romby et al. 1988), and proposals had been advanced for what those pairings might be (Westhof et al. 1989). However, it was only several years later that the secondary structure of loop E was determined crystallographically (Correll et al. 1997), and shortly thereafter it was demonstrated that the sarcin-ricin loop of 23S rRNA contains a closely related motif (Correll et al. 1998).

In 1997–1998, Neocles and his family came to Strasbourg for a sabbatical year and began a collaboration with E.W. that continued for the rest of his life. While on sabbatical, Neocles applied sequence conservations and the new structural knowledge alluded to above to detect loop E motifs in other RNAs, of which there are many (Leontis and Westhof 1998).

The quest for a fuller understanding of the architecture of RNA became Neocles' guiding star. In 2001, a nomenclature describing all types of base pairs between all base combinations where the name uniquely represents the interaction type was suggested (Leontis and Westhof 2001). Neocles was also a pioneer in RNA nanotechnology (Jaeger and Leontis 2000), and with his colleagues at Bowling Green State University, developed many tools and websites for searching and analyzing RNA structures (Sarver et al. 2008; Zirbel et al. 2009; Petrov et al. 2013), culminating in a method to directly map novel RNA sequences to known 3D modules such as the Loop E (Zirbel et al. 2015). He set up the RNA Ontology Consortium, an effort intended to gather consensus around RNA structure among mathematicians, bioinformaticians, biophysicists, and structural biologists (Hoehndorf et al. 2011).

It is important to remember that science is a human activity, embedded in human society, and outreach was deeply ingrained in Neocles' spirit and drive. At the university, he was a passionate teacher, explaining patiently

In memoriam

complicated chemical or biophysical concepts and constantly inventing teaching games. Neocles was an inspiring advisor and mentor for many graduate students and also supported the research of many undergraduates. He always showed compassion and was attentive to students' needs and their living conditions. He chaired the BGSU Faculty Senate in 2003 and was a program officer at NSF (2009–2012). For many years, he stood up for environmental and social justice issues at many meetings and demonstrations. His interest in these larger issues led him to enter local politics, and in 2019 he was elected to the Bowling Green City Council, where he successfully advocated for affordable housing, especially for students and young families, as well as better recycling schemes and safer streets for cyclists and pedestrians. Neocles bridged the gap between science and policy, underscoring the importance of scientists actively participating in all levels of government. His compassionate energy and knowledge will be missed more than ever, as the present pandemic demonstrates a critical need for those willing to offer patient and simple explanations of the biological world to which we belong.

His untimely and brutal death is a loss to the local community around his university and town, as well as to all of us RNA scientists around the world that use the concepts and tools he pushed so hard to develop and improve.

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REFERENCES

- Correll CC, Freeborn B, Moore PB, Steitz TA. 1997. Metals, motifs, and recognition in the crystal structure of a 5S rRNA domain. *Cell* **91**: 705–712. doi:10.1016/S0092-8674(00)80457-2
- Correll CC, Munishkin A, Chan YL, Ren Z, Wool IG, Steitz TA. 1998. Crystal structure of the ribosomal RNA domain essential for binding elongation factors. *Proc Natl Acad Sci* **95**: 13436–13441. doi:10.1073/pnas.95.23.13436
- Hoehndorf R, Batchelor C, Bittner T, Dumontier M, Eilbeck K, Knight R, Mungall CJ, Richardson JS, Stombaugh J, Westhof E, et al. 2011. The RNA Ontology (RNAO): an ontology for integrating RNA sequence and structure data. *Appl Ontol* **6**: 53–89. doi:10.3233/AO-2011-0082
- Jaeger L, Leontis NB. 2000. Tecto-RNA: one-dimensional self-assembly through tertiary interactions. *Angew Chem Int Ed Engl* **39**: 2521–2524. doi:10.1002/1521-3773(20000717)39:14<2521::AID-ANIE2521>3.0.CO;2-P
- Leontis NB, Moore PB. 1986. Imino proton exchange in the 5S RNA of *Escherichia coli* and its complex with protein L25 at 490 MHz. *Biochemistry* **25**: 5736–5744. doi:10.1021/bi00367a058
- Leontis NB, Westhof E. 1998. A common motif organizes the structure of multi-helix loops in 16 S and 23 S ribosomal RNAs. *J Mol Biol* **283**: 571–583. doi:10.1006/jmbi.1998.2106
- Leontis NB, Westhof E. 2001. Geometric nomenclature and classification of RNA base pairs. *RNA* **7**: 499–512. doi:10.1017/S1355838201002515
- Petrov AI, Zirbel CL, Leontis NB. 2013. Automated classification of RNA 3D motifs and the RNA 3D Motif Atlas. *RNA* **19**: 1327–1340. doi:10.1261/ma.039438.113
- Romby P, Westhof E, Toukifimpa R, Mache R, Ebel JP, Ehresmann C, Ehresmann B. 1988. Higher order structure of chloroplastic 5S ribosomal RNA from spinach. *Biochemistry* **27**: 4721–4730. doi:10.1021/bi00413a021
- Sarver M, Zirbel CL, Stombaugh J, Mokdad A, Leontis NB. 2008. FR3D: finding local and composite recurrent structural motifs in RNA 3D structures. *J Math Biol* **56**: 215–252. doi:10.1007/s00285-007-0110-x
- Westhof E, Romby P, Romaniuk PJ, Ebel JP, Ehresmann C, Ehresmann B. 1989. Computer modeling from solution data of spinach chloroplast and of *Xenopus laevis* somatic and oocyte 5S rRNAs. *J Mol Biol* **207**: 417–431. doi:10.1016/0022-2836(89)90264-7
- Zirbel CL, Sponer JE, Sponer J, Stombaugh J, Leontis NB. 2009. Classification and energetics of the base-phosphate interactions in RNA. *Nucleic Acids Res* **37**: 4898–4918. doi:10.1093/nar/gkp468
- Zirbel CL, Roll J, Sweeney BA, Petrov AI, Pirrung M, Leontis NB. 2015. Identifying novel sequence variants of RNA 3D motifs. *Nucleic Acids Res* **43**: 7504–7520. doi:10.1093/nar/gkv651

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