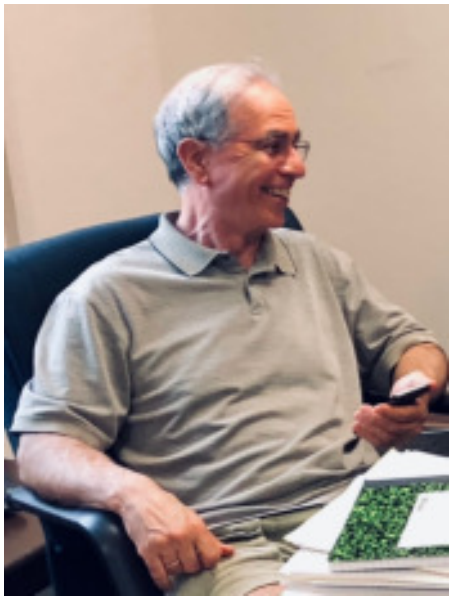
Neocles B. Leontis
(1955 – 2020)



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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 Ohio State University in 1977, where he had majored in chemistry, and in 1986, he obtained a Ph.D. from Yale University in biophysical chemistry. 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 resonances, 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 the 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 non-canonical base pairs (Romby et al. 1988) and proposals had been advanced for what those pairing 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 23 sRNA 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 with 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 out-reach was deeply ingrained in Neocles' spirit and drive. At the University, he was a passionate teacher, explaining patiently 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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