At a meeting of the FACULTY OF ARTS AND SCIENCES on December 6, 2022,
the following tribute to the life and service of the late Guido Guidotti
was spread upon the permanent records of the Faculty.

GUIDO GUIDOTTI

BORN: November 3, 1933
DIED: April 5, 2021

Guido Guidotti, a member of the Harvard faculty for 58 years, was an imaginative, rigorous, and innovative researcher who carried out pioneering scientific research into how proteins embedded in biological membranes perform their physiological functions in transport and signal processing. He was a giant in this field. More generally, he was a biochemist's biochemist. He was renowned as an inspiring and caring teacher of general biochemistry, hormones, and membranes—a role he continued until shortly before his death—and was a devoted mentor to junior faculty. Guidotti was a warm and gentle human being whose smile could light up a room. He supported an entire ecosystem of undergraduates and laboratory members long after they left Harvard. Guidotti was instrumental in fostering the then-new Department of Biochemistry and Molecular Biology. As department chair, he shepherded construction of the Sherman Fairchild Biochemistry Building. Later, he quietly guided the Ph.D. track in Engineering and Physical Biology (EPB), an early university effort at this interface.

Guido Guidotti was born on November 3, 1933, in Florence, Italy, but grew up in his beloved Naples. He was a brilliant student, despite the disruptions of World War II. He came to the U.S. as an American Field Service student in Decatur, Illinois, in 1950. After briefly returning to Naples, he went back to Decatur for college at Millikan University and then trained as a physician at Washington University, St. Louis. Being told that a career in medicine required him to do research, he went to Rockefeller University in 1958 as a Ph.D. student. He carried out seminal research on the peptide and subunit composition of hemoglobin with Lyman Craig. Guidotti originally intended to return to Washington University but instead chose an academic path. He arrived at Harvard as Assistant Professor in 1963, was tenured in 1969, and ultimately was named Higgins Professor of Biochemistry.

The trajectory of Guidotti's discoveries is the wandering, yet mysteriously coherent, path of a fearless scientist. Early continuation of his hemoglobin studies culminated in a general model for the basis of allostery. He then began research into membrane proteins, where little was known. A colleague relates: "I saw Guidotti give a plenary lecture at a meeting. He

started by drawing two parallel lines on the chalkboard [corresponding to the two sides of the membrane] and wrote 'inside' to the far left and 'outside' to the far right [denoting the inside and outside of the cell]. He commented that this summarized, to his knowledge, the state of understanding of how membrane proteins were structured in the membrane and how they functioned." Guidotti's ensuing research filled in his chalkboard drawing. By 1976 he could write: "Solutes are carried across eukaryotic plasma membranes by oligomeric glycoproteins which span the cell membrane and conduct transport by undergoing conformational changes." He identified and determined the topologies of the ion transporter that enables removal of carbon dioxide from tissues into the lungs, the Na+/K+ ATPase (which determines the electrical properties of neurons), and many others. He pioneered studies into insulin regulation of membrane protein activity. Finally, Guidotti's intuition culminated in his discovery that a protein called CD39 is an "ecto-ATPase," which sits in the cell membrane and hydrolyzes extracellular adenosine triphosphate to ensure appropriate extracellular concentrations of that and related compounds. When CD39 activity is perturbed, neurons in the brain do not recover after they fire, blood does not know when to clot, inflammatory responses in cancer and disease are compromised, veins and arteries calcify, and pain responses are perturbed. Guidotti's discovery lit up the research community. His findings set the stage for now-exploding therapeutic efforts that target CD39. Guidotti's later research also revealed a remarkable mechanism in which CD39 activity is governed by mechanical effects within the membrane.

Guidotti was a teacher in every aspect of his life. He was a paradigm of the true "Harvard professor." He taught 75 terms, often offering two or three courses per year. He taught his department's basic undergraduate biochemistry and physical chemistry courses for 35 years. Using his medical training, he linked biochemistry to medicine long before it became fashionable. Seeing a gap in the curriculum, he initiated an upper-level biochemistry course and taught 40 terms of upper-level courses in membranes and hormones. Students often took more than one course from him. Many of the thousands of undergraduates he taught went on to become doctors. He could never enter a Boston hospital without someone saying, "I took your biochemistry course." Finally, for ten years, he taught a Freshman Seminar titled "What Is Life," bestowing his decades of insight, knowledge, and perspective to students in their most formative years. Guidotti loved teaching, and he loved and cared for his students, often helping them with challenges outside the classroom. They returned that love with cards, letters, and presents, which filled his office. Accordingly, in 2000, he was awarded Harvard's Phi Beta Kappa Prize for Excellence in Teaching.

Above all, Guidotti was modest, humble, kind, generous, and enabling of everyone in his sphere. Scientific fame and credit were never the point. Famously, Guidotti would not put his name on his trainees' publications unless he had contributed experimentally, with his own hands, until forced to do so by funding organizations. He was an accomplished soccer player and bicyclist and had extensive knowledge of art, music, and books. He was insightful, wise, and foresighted in all aspects of his life.

Guido Guidotti died at home on April 5, 2021. His spirit and influence live on in the beloved members of his family, who always came first in his life: his brother, Mario, and Mario's wife Ludi Borello; their daughter, Alice, and her two children, Gaia and Fabio; his son, Guido Jr., Guido Jr's wife, Anna Yoo, and their son, Nicholas Yoo Guidotti (the sunshine of Guido's later life); and Nancy Kleckner, his soulmate, wife, and Harvard colleague for 40 years. The "community of Guido" will always cherish his spirit and his love as they now must somehow manage without him.

Respectfully submitted,

Daniel Kahne
Samuel Kunes
Richard Losick
Matthew Meselson
Nancy Kleckner, Chair

For more information on Guidotti's life and scholarship, see "Guido Guidotti - A Life" by Nancy Kleckner at https://nrs.harvard.edu/URN-3:HUL.INSTREPOS:37368811, "Guido Guidotti (1933 – 2021)" by Steven Clarke at https://www.asbmb.org/asbmb-today/people/031622/guido-guidotti-1933-2021-1, and "A membrane ATPase without transporter activity: Guido Guidotti's laboratory and the search for CD39" by Laurel Oldach at https://www.jbc.org/article/S0021-9258(22)00447-1/fulltext.