The unstoppable Maud Menten never really ceased her studies. Shown here (left) at a gathering in honor of her retirement from Pitt in 1950.

AFTER MAUD MENTEN, BUSTER BROWNS AND BIOCHEMISTRY WOULD NEVER SEEM THE SAME

BY REBECCA SKLOOT

SOME CALLED HER MISS MENTEN

Through the ice of winters and the balmy warmth of summers from 1918 to 1950, Maud Menten lurched through Shadyside and Oakland in her Model T Ford. After her jackrabbit starts, she would settle behind a wheel far taller and wider than she was, leaning slightly forward, wearing her Paris hats, blue dresses with stained-glass hues, and Buster Brown shoes. She never knew exactly which pedal to push when. *Oh heavens,* she would say, *now, is it the middle or right one to stop and the left one to go, or middle to go, left to stop?* She wasn't sure, so she would push them all. Folks said she made up with enthusiasm and quick starts what she lacked in driving skill, and they knew to stay out of her way. On the road it was for fear of losing their lives, but elsewhere, it was because they knew she was unstoppable. Driving her Model T was about the only thing Menten couldn't do. And if anyone tried to talk her out of anything—Arctic expeditions or mountain climbing or solving one of the most complex biochemical problems of the twentieth century—Menten, whose petite frame and sea-blue eyes projected only tenderness, would smile sweetly and keep right on doing it her way.

CORBIS

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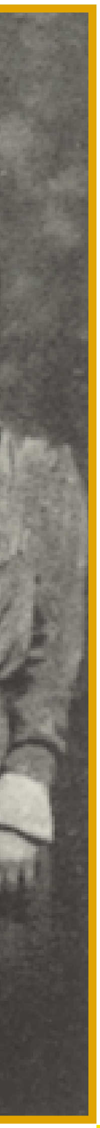
LEFT: Menten, c. 1918. ABOVE: Menten (front row center) with women in Pitt's 1932-33 chapter of Zeta Phi, the national women's medical "fraternity."

People probably tried to talk her out of boarding a ship alone and heading for Germany the year the *Titanic* sank; of course she went. She wanted to work with Leonor Michaelis, a well-known biochemist.

Menten, who eventually became a professor at the University of Pittsburgh School of Medicine and head of pathology at Children's Hospital of Pittsburgh, worked with Michaelis to demystify enzyme kinetics—the study of rates and mechanisms of enzymatic reactions. They developed a tool that would become pivotal in the history of biochemistry: the Michaelis-Menten Equation. The equation, which provides a mathematical means for determining the rate of an enzyme reaction, has been called the foundation of modern enzymology, and it is a standard for most subsequent enzyme-kinetic measurements. Moreover, the development of most drugs in this century would not have been possible without that understanding. When Michaelis and Menten published their work in 1913, little was known about enzymes, including their basic chemical nature.

Enzymes are protein catalysts that direct virtually all metabolic events in the body: events such as DNA and RNA synthesis, glucose production, and countless others. Enzymes speed up the rates of reactions while selectively channeling their substrates—the compounds they act on—into useful pathways to create metabolic products essential for normal bodily functioning. To make all of this possible, each enzyme has a specialized cleft on its surface, a pocket called the "active site," that binds to its substrate to form an enzyme-substrate complex. The rate at which this binding happens determines the rate and amount of the final product. Since the development of the Michaelis-Menten Equation, this is not the guessing game it once was. The equation is taught in every undergraduate biochemistry course (though in textbooks Menten's name is often misspelled "Menton"), and it's used exhaustively in most research laboratories.

Beyond her work on this famous equation, Menten wrote or cowrote about 100 research papers, many of which are historic contributions. She was a primary author of a study on radiobromide and cancer that happened to be the first monograph from what was then the Rockefeller Institute for Medical Research.



If a Nobel laureate was mentioned, she was likely to ask, *What has he done since?*

(Though if you call, they'll tell you they have never heard of her.) In addition, she uncovered the value of immunization for treating infectious diseases in animals.

More importantly, Menten is believed to be the first to study human hemoglobins using electrophoresis (an innovation widely credited to Linus Pauling, though her work on this predated his by many years).

And with Junge and Green, she discovered the azo-dye coupling reaction. This finding is credited as the first example of enzyme histochemistry.

She wasn't easy to please. If a Nobel laureate was mentioned, Menten was likely to ask, *What has he done since?* To a laboratory full of scientists who she thought needed to work harder, or in a new direction, she would let loose with a tirade, then fasten her hat firm as she stormed out the door, saying, *I've stirred them up, so now I can go.*

Menten was known for her 18-hour workdays, for delivering one-third of all daily pathology lectures as well as attending every lab session, and for being one of the most versatile scientists at Pitt.

She told colleagues that her interests revolved around pathology, oxidases, nucleic acids, tumor cells, surface tension, bacterial toxins, and pneumonia. Then there was her work with hormones, scarlet fever, and the sick youth she treated at Children's Hospital, who loved her soft eyes and motherly expressions. And that list says nothing of her clarinet, her paintings that hung uncredited for years in the halls of Pitt, eventually finding their way into art exhibitions. Nor does it touch on her passion for astronomy or languages (she spoke at least one Native American language as well as Russian, French, German, Italian, and no one's quite sure what else) or tea time, which she was known to observe with homemade scones and Scottish shortbread on Royal Crown Derby china.

Rain and wind lashed open coats and turned umbrellas inside out on July 11, 1979, at the University of Toronto, where, during the 11th International Congress of Biochemistry, a plaque was mounted in muddied cement with a short description of Menten's life and accomplishments. Her portrait now hangs at Pitt, where there are memorial lectures in her honor and a named chair, but those who knew her have commented that Menten's recognition came long past due.

Armed with four degrees–including an MD and a PhD—and several published papers, Menten joined the school's Department of Pathology in 1918 as an instructor. She retired in 1950 as full professor—a position to which she was promoted only in 1948. Then, as arthritis slowly incapacitated her, Menten, who was born in 1879 in Port Lambton, Canada, returned to her native soil, where she pursued oncology research at the British Columbia Medical Research Institute until her death in 1960. One of her collaborators noted, "She did not waste away. She used herself up."

To this day, Menten is little known. The famous paper she wrote with Michaelis, in which they describe their equation for the first time, refers to her only as "Miss Menten," according to published reports. Some called her simply "Michaelis's assistant." And for those who want to learn more about this mysterious woman, there is little to find. Most who knew Menten have gone, and few wrote down their thoughts and memories of her.

She was one of the first women to graduate from a Canadian medical school or practice biochemistry. She was one of the first full-time faculty members at the School of Medicine. Her work laid the groundwork for modern drug therapy and biochemistry. Yet if you ask folks about Maud Menten, about her life and her stories, you're almost guaranteed a one-word reply:

"Who?" ■

THIS TIME, E = AN ENZYME
THE RESULT—A NEW ERA FOR BIOCHEMISTRY

$$E + S \underset{K_{-1}}{\overset{K_1}{\rightleftarrows}} ES \xrightarrow{K_2} E + P$$

$$v = \frac{[S]\ V_{max}}{[S] + K_m}$$

Menten and Michaelis proposed this model (top), which shows that an enzymatic reaction takes place in two steps. First, the enzyme binds reversibly to its substrate, creating an enzyme-substrate (ES) complex. Second, this complex breaks down, forming the product (P) and regenerating the free enzyme (E).

The Michaelis-Menten equation illustrates that the velocity (V) of a reaction varies with the concentration of the substrate: v = initial velocity of the reaction, V_{max} = the reaction's maximal velocity, K_m = Michaelis constant, which indicates an enzyme's affinity for its substrate, and [S] = substrate concentration. —*RS*