John Howard Northrop

On July 5, 1981, John Howard Northrop will reach the venerable age of four score and ten. He is active and well for a man of his age but a bit unhappy that his diminished eyesight makes him no longer the skeet supermarksman he once was.

The Editors of The Journal of General Physiology and some of Dr. Northrop's friends wish to use this occasion to express their gratitude for his 62-year-long association with the Journal. That association began in 1919, when he published an article in its first volume (1). He joined the editorial board in 1924 and he continues as an Honorary Editor. We also wish to review briefly for the new generation of investigators some of Dr. Northrop's studies which established concepts now taken for granted. (A more complete review of his work was given in the Journal in 1962 [2]).

Immediately after receiving his doctorate in Chemistry from Columbia University in 1915, Northrop joined the staff of Jacques Loeb at The Rockefeller Institute for Medical Research. Dr. Loeb was not only a brilliant experimentalist, he was also a keen observer and he liked what he saw in his new associate. Northrop and Loeb enjoyed a happy and productive association until the latter's death in 1924. Soon afterward, Dr. Northrop was made a Member of the Institute.

Although he made a number of experimental excursions into a variety of biological phenomena, which led to significant conclusions, Northrop's best-known contributions were the establishment of the chemical nature of enzymes and his obtaining evidence that bacteriophage contains nucleic acid. He also developed the phase rule solubility method for evaluating protein purity.

The nature of enzymes was very much in doubt during the first quarter of this century when several European authorities described them as adsorption complexes between small organic structures and larger, ill defined "carriers." Northrop had become thoroughly familiar with the proteases pepsin and trypsin through his many studies of their kinetic properties. He then turned his attention to their isolation. James B. Sumner of Cornell University had just isolated a crystalline protein with high urease activity, but his evidence that the enzymatic property was linked inseparably to that protein was not strong. When Northrop isolated the crystalline protein pepsin, he deliberately selected a variety of procedures which might have been expected to separate the enzymic activity from the protein if the European model had been correct. When these procedures yielded no separation of the activity from the protein and no change in activity per unit of protein, Northrop was forced to conclude that the two properties were probably inseparable. Working with his highly competent associate, Dr. Moses Kunitz, Northrop found that similar procedures failed to separate the enzymatic activity from the crystalline protein trypsin. Kunitz then went on to find the same for crystalline chymotrypsin,

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ribonuclease, and deoxyribonuclease. This evidence convinced the most skeptical investigators of the proteinous nature of enzymes. Nothing has altered that conclusion in the succeeding years. Northrop's interest in the nature of viruses began in the early 1920s. He followed the early studies of bacteriophage and worked briefly with potato X virus and had planned to work with tobacco mosaic virus. These subcellular self-replicating units fascinated Northrop, who returned to the study of bacteriophage in 1935 after his work on pepsin was complete. He purified a quantity of staphylococcus phage and fractionated it using some procedures that he had developed for enzymes. These purified

PRINCETON, 1939. (*Left to right*) Mortimer L. Anson, Roger M. Herriott, John H. Northrop, Victor Desreux, Moses Kunitz.

fractions of phage proved to have a phosphorus content of five percent and an absorption spectrum of a nucleoprotein. This finding provided some of the earliest evidence that nucleic acid is an essential component of a virus.

During World War II, Northrop's activity was directed into a different field, but afterward he returned to bacteriophage. He was puzzled by the nature of lysogenic bacteria, especially by their induction by mutagenic agents.

In 1951, Northrop (3) made a prophetic suggestion about the nature of bacteriophage. He noted that perhaps "The nucleic acid may be the essential, autocatalytic part of the [phage] molecule, as in the case of the transforming

principle of the pneumococcus, and the protein may be necessary only to allow entrance to the host cell."

Honors were bestowed on Dr. Northrop by many universities, academies, societies, and other institutions. In 1946, he shared the Nobel Prize in Chemistry with James B. Sumner and Wendell M. Stanley.

"Big Jack," as he is known to some of his friends, has retired to the dry climate of Arizona. Those of us who received inspiration and guidance from him wish to express our eternal gratitude to him and, together with his many other friends, wish him continued good health and many happy birthdays.

Roger M. Herriott

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