WASHINGTON, June 19 — Dr. Donald S. Fredrickson announced today his resignation as director of the National Institutes of Health, the Federal agency that has given the United States a dominant position in biomedical research.

Dr. Fredrickson's resignation for "personal reasons" was initially disclosed to about 350 employees at the end of a morning meeting on the agency's compound in suburban Bethesda, Md. The widely respected 55-year-old expert on blood fats said that the agency seemed "as exhilarating and worthwhile as in the summer of 1953 when I arrived."

He added: "The last six years, however, have been spent in the relentless company of the administrative burdens of the director. It is time to shed them for a while, lest I forget completely how to be a scientist and a physician."

Dr. Fredrickson then read his letter of resignation to President Reagan, asking to be allowed to leave the agency on July 1. A second letter to Richard S. Schweiker, Secretary of Health and Human Services, said, "I take this step with great ambivalence, for N.I.H. is in the very marrow of my bones."

Not a Political Decision
In a telephone interview later, Dr. Fredrickson denied that he was leaving because of unhappiness with Reagan Administration health policies and appointments.

"This is by no means a political decision," said Dr. Fredrickson. He said Mr. Schweiker had asked him to remain in charge of the National Institutes of Health. However, he said, "after six years in such a job, you wonder whether you'll retain the freshness and keen reflexes to do this kind of complex work."

What sparked his decision, he said, was the realization that several major jobs at the agency were opening, including the directorships of two of the 11 institutes that occupy the campus-like compound.

"I had to assure them I'd be here, and I couldn't," said Dr. Fredrickson.

With a budget of about $2.4 billion, the agency supports thousands of medical and biological research projects, both on their home grounds and at universities across the nation. The aim of the agency, with about 12,000 employees, is the support of biomedical research into the causes, prevention and cure of illness.

Dr. Fredrickson's resignation started his colleagues. "It was a real surprise," said one agency employee who attended this morning's meeting. "It was short, sweet and sort of stunning."

Mr. Schweiker, in a "Dear Don" letter, expressed "profound regret" at Dr. Fredrickson's resignation. He said that under Dr. Fredrickson's direction, "the N.I.H. has faithfully and effectively pursued the mission of transferring medi-