**Research Statement, David Shub**

**Origin, evolution and function of self-splicing introns**

Until recently, it had been thought that RNA splicing occurs only in eukaryotes. We now know that genes encoding tRNAs in a variety of bacteria and mRNAs of viruses infecting *E. coli* and *B. subtilis* contain introns that are removed at the RNA level. The splicing event is autocatalytic, not requiring participation of proteins of other RNAs. These introns resemble the well-studied intron ribozyme of *Tetrahymena*, in both structure and splicing mechanism.

Our work is proceeding in two directions:

**Origins and evolution**

Hypotheses have been advanced that (1) give catalytic RNA a central role in life's origin (the RNA world) and (2) propose that the structure of contemporary proteins is the result of extensive recombination between introns (exon shuffling). Absence of introns from eubacteria presented a serious drawback to these attractive ideas. Our analysis of the distribution and molecular evolution of bacterial introns will help to resolve whether introns were already present in the common ancestor of all living things.

**Intron function**

If introns are indeed ancient, bacteria must have lost most of their introns. We assume that introns must provide a useful function in the rare cases where they have been retained. Through in vitro mutagenesis and DNA cloning, we are able to introduce intron-less copies of genes into bacteria. Insight into the role of intron splicing is obtained by observing differences in gene function and regulation. Genetic analysis of intron structure is used to determine the parameters required for activity of an RNA enzyme.