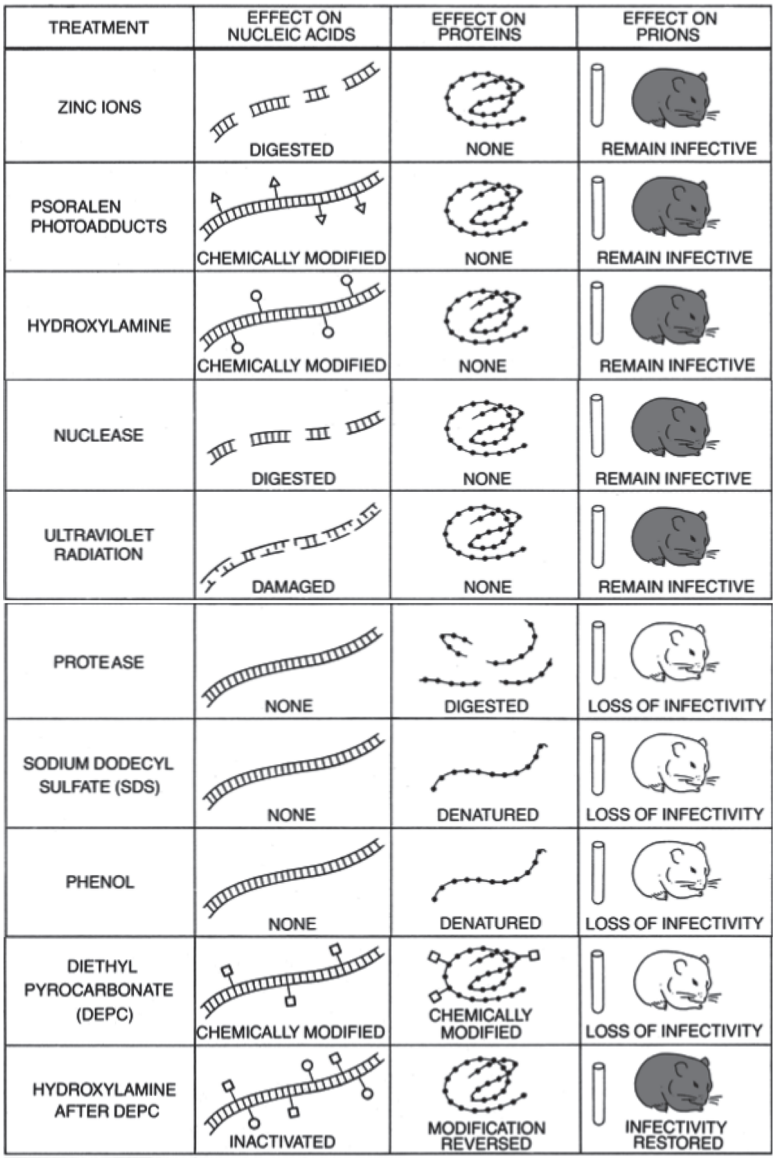
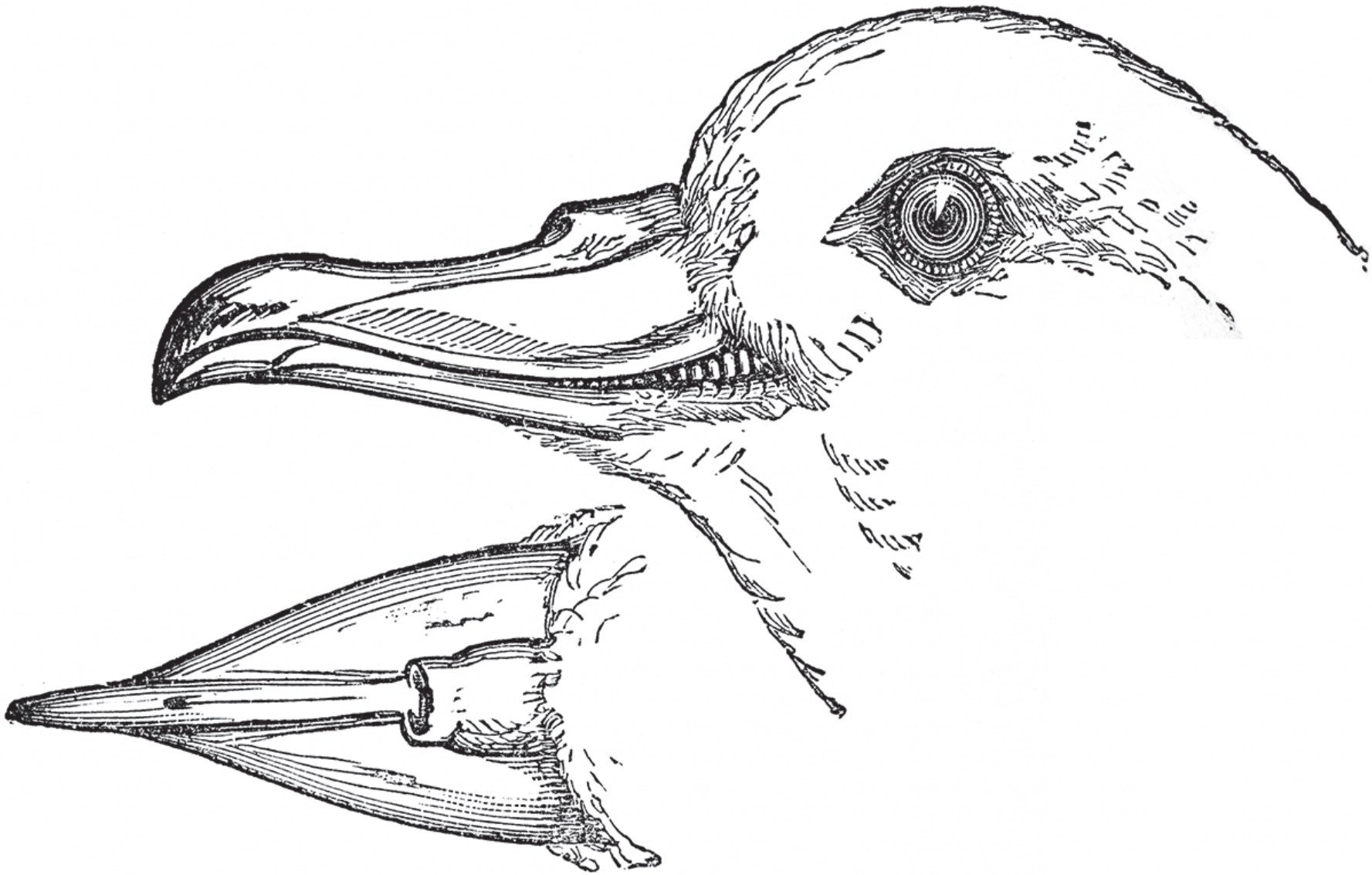
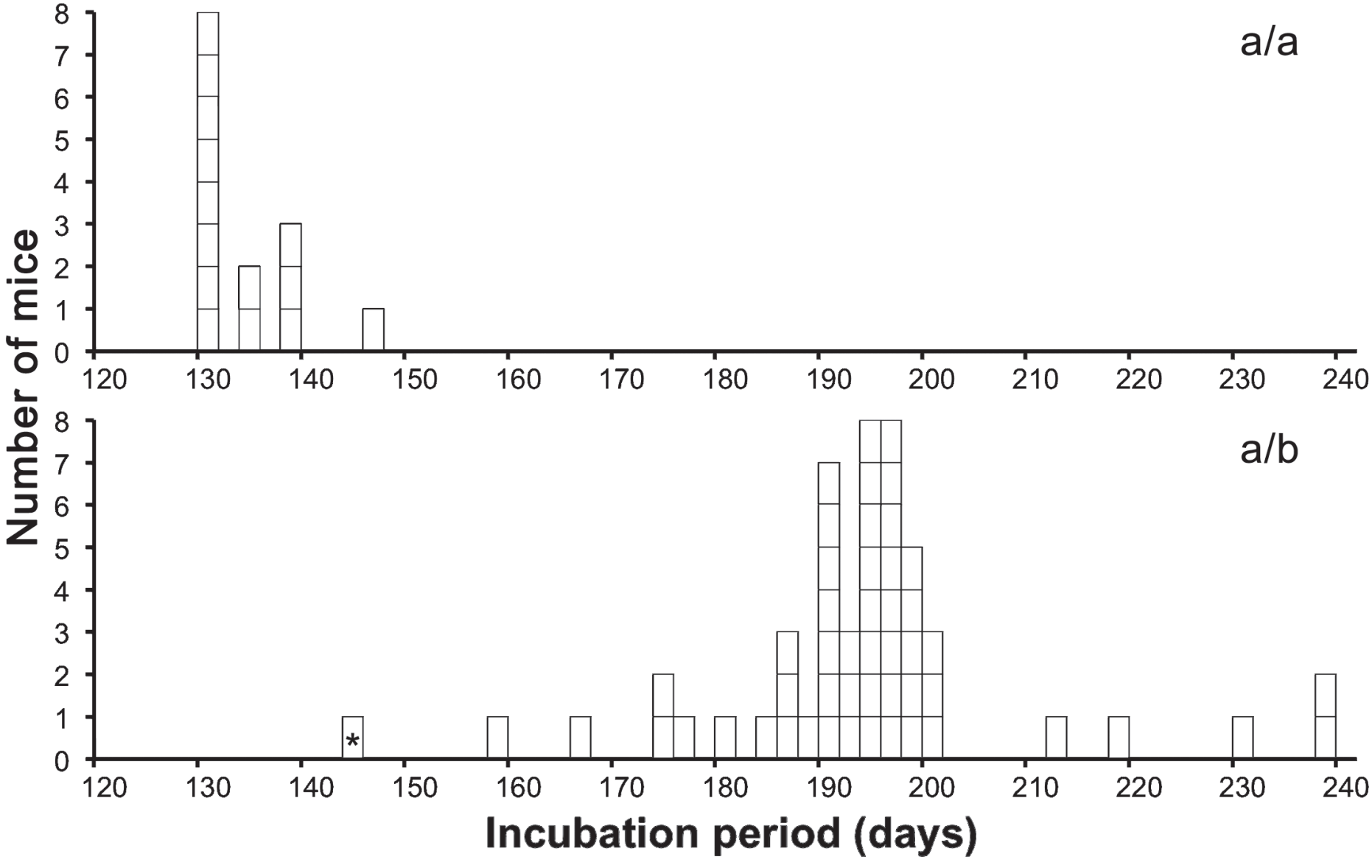


Figure 13 Preparations enriched for the scrapie infectivity were resistant to inactivation by procedures that selectively altered nucleic acids but susceptible to those that modified proteins. Enzymes called nucleases degrade DNA and RNA, slicing them up into their constituent bases; some, called DNases, chew up only DNA, while others, called RNases, degrade RNA, and yet others degrade both. Six procedures that modified only proteins inactivated the purified scrapie agent. When diethylpyrocarbonate (DEPC) was added to our purified preparations, the scrapie agent was inactivated. DEPC modifies both proteins and nucleic acids, so this experiment, by itself, was unhelpful; however, DEPC could be removed from proteins—but not from nucleic acids—by another chemical, hydroxylamine. Equally important, in the absence of DEPC modification, hydroxylamine reacts with nucleic acids but not with proteins.



PRION VITTATUS. (After Buller.)

Figure 15 To my horror, there it was: a marine petrel found in the Southern Ocean pronounced PRY-on, with a long I. The birds are named for their serrated, or sawtooth, beaks (the Greek word priwn means "saw").


a/a
a/b
Number of mice
Incubation period (days)
0
1
2
3
4
5
6
7
8
120
130
140
150
160
170
180
190
200
210
220
230
240
*

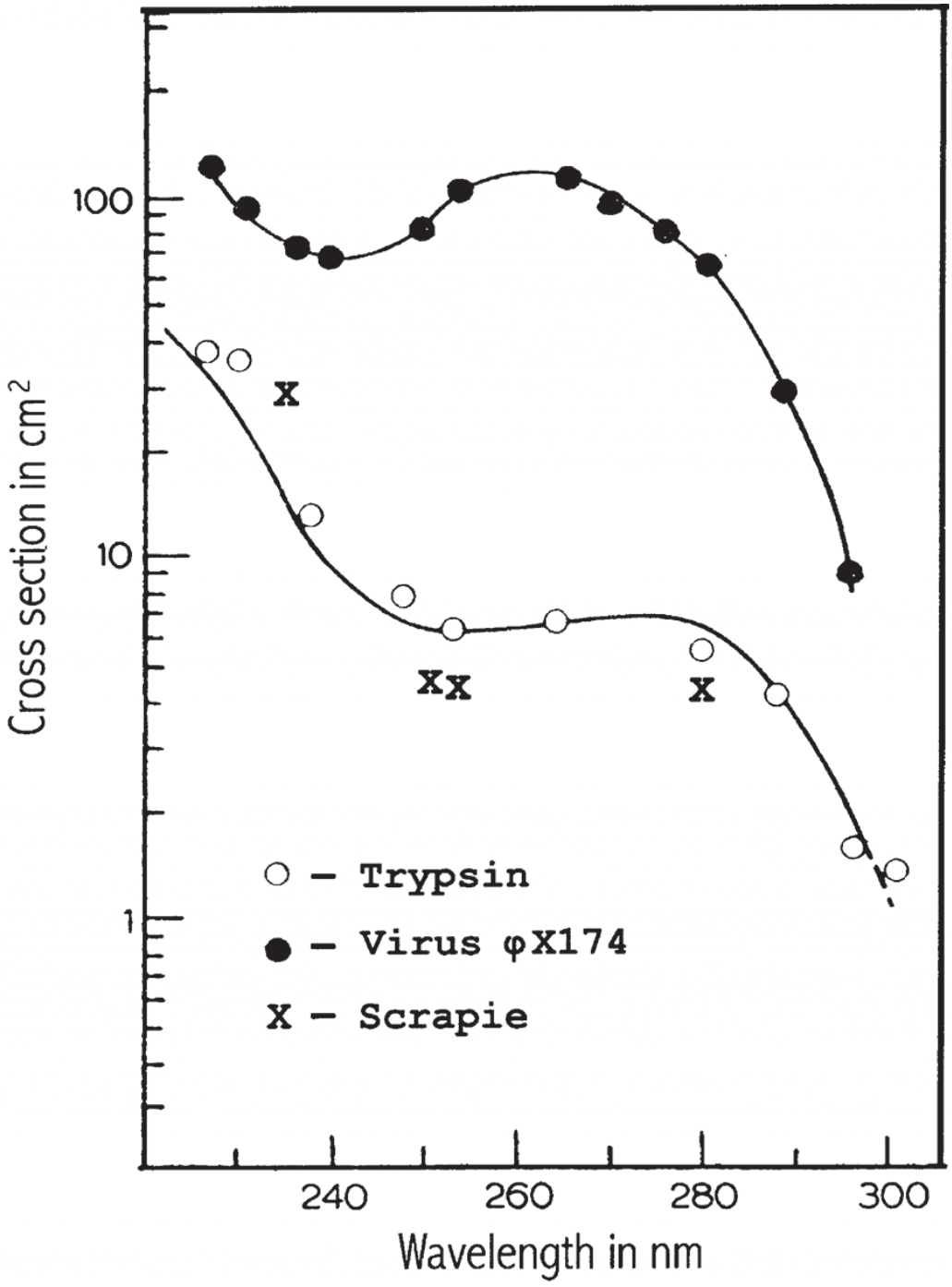


Figure 31 During a visit to the Brookhaven National Laboratory on Long Island, Richard Setlow showed me a startling piece of data he had published in 1957: a graph delineating different inactivation spectra for two proteins—the enzymes aldolase and trypsin—using various wavelengths of UV light. Then he showed me that the data for the scrapie agent reported in 1970 by Tikvah Alper and Raymond Latarjet: their data points (×) fell precisely on the trypsin curve.

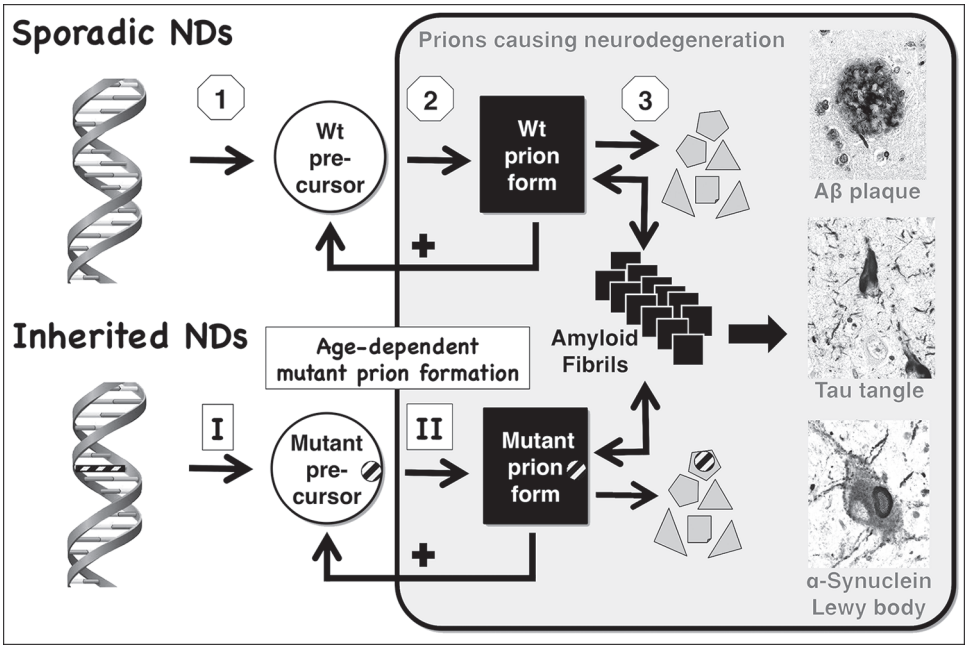


Figure 33 Neurodegeneration caused by prions. Sporadic NDs: In sporadic neurodegenerative diseases (NDs), wild-type (wt) prions multiply through self-propagating cycles of posttranslational modification where the precursor protein (top circle) is converted into the prion form (top square), which generally is high in β-sheet content. The small polygons represent proteolytic cleavage products that are generated during the clearance of prions. Depending on the protein, the fibrils coalesce into Aβ amyloid plaques in Alzheimer's disease, neurofibrillary tangles in Alzheimer's disease or the frontotemporal dementias, or Lewy bodies in Parkinson's disease or Lewy body dementia. Drug targets for the development of therapeutics (octagons): (1) lowering precursor protein, (2) inhibiting prion formation, and (3) enhancing prion clearance. Inherited NDs: Late-onset heritable neurodegeneration argues for two discrete events: the first event (arrow I) is the synthesis of mutant precursor protein (bottom circle), and the second event is the age-dependent formation (arrow II) of mutant prions (bottom square). The bar with diagonal lines in the DNA helix represents mutation of a base pair within an exon, and the small circles with diagonal lines signify the corresponding amino acid substitution.

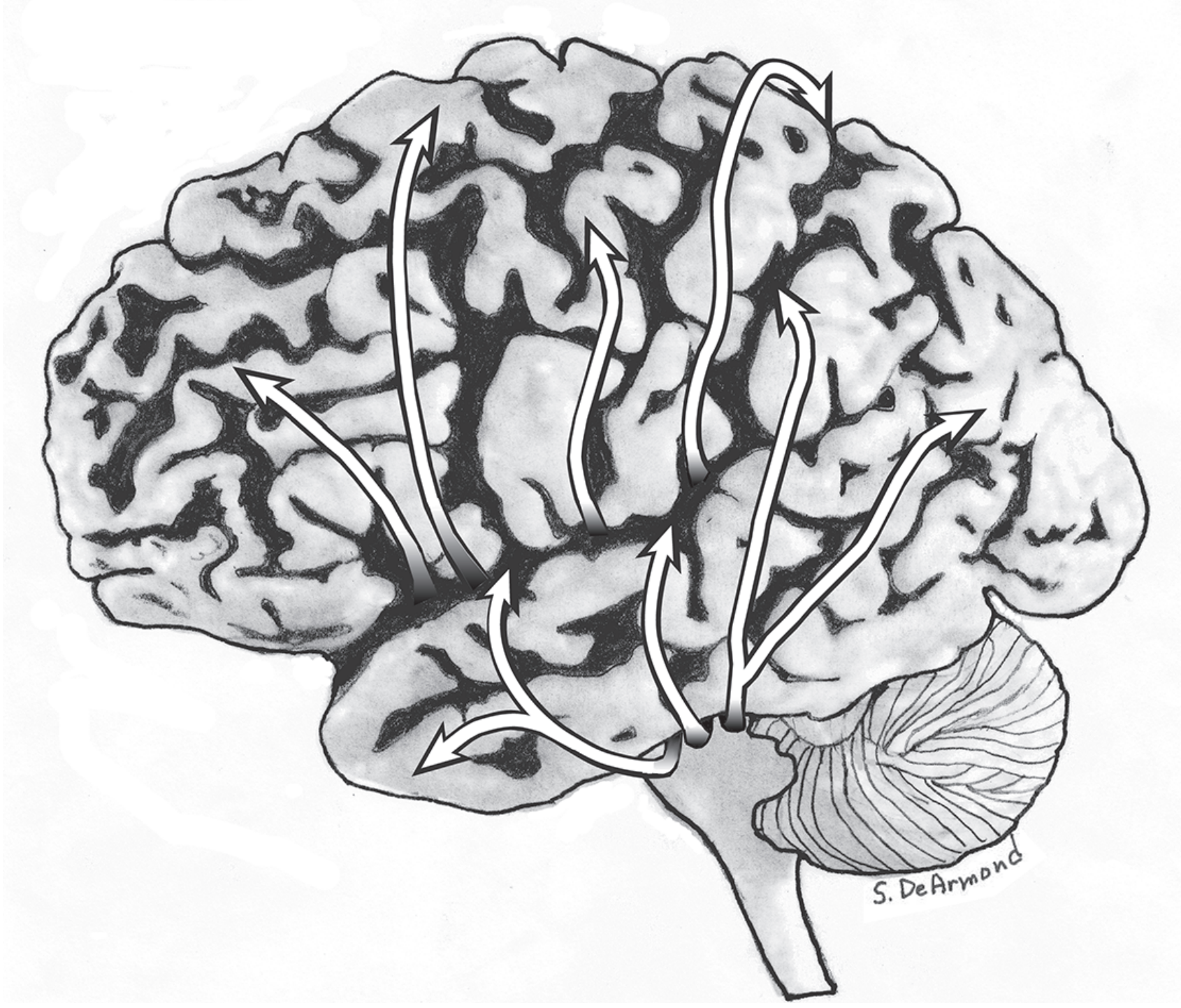


Figure 34　Spread of Aβ plaques and neurofibrillary tangles in the brains of patients with Alzheimer's disease.