is depleted by several orders of magnitude compared with other volatile elements. There are apparently only three possible explanations for this missing sulphur. The first is that it was never present in significant quantities in the material that accreted to form the Earth. This is unlikely. The various types of meteorite show no preferential depletion of sulphur, and therefore there seems little reason why the Earth as a whole should do so. The second possibility, of course, is Ringwood's high temperature event which would remove the sulphur initially present in the Earth. Again this is unlikely because it is difficult to visualize a high temperature process which would remove sulphur but not the other volatile elements.

The only other possibility seems to be that much of the sulphur originally present in the crust and mantle has segregated into the core. The evidence for this is not, however, merely the lack of evidence for the other two possibilities. Laboratory experiments carried out under pressures of up to 60 kbar show that of all the iron-rich melts, including iron itself, the Fe-FeS eutectic has the lowest melting point. This means that in any situation in which there is a temperature differentiation (such as the formation of the Earth's core), and assuming that the Fe-FeS preference holds at higher pressures, a sulphur-rich iron melt will be the first liquid formed. This would then sink into the core because of its low viscosity and high density.

ENZYMES

Sophisticated Nucleases

from our Molecular Biology Correspondent

A RECENT and riveting newspaper report referred to the enzymes in washing powders as "minute organisms", and imputed to them all but sentient qualities. Such thoroughgoing vitalism might with more justification be provoked by enzymes of more highly developed intelligence than subtilisin. Some quite awe-inspiring examples have recently come to light among the more specialized nucleases. Smith and Wilcox (*J. Mol. Biol.*, **51**, 379; 1970) describe the purification of a restriction enzyme from the bacterium *Haemophilus influenzae*. The function of this molecule is to recognize and attack a foreign DNA that enters the cell, while avoiding suicide through damage to its own DNA. Such an enzyme has previously been studied in *E. coli*, and in both species it breaks down the alien DNA into large pieces. In the assay, it causes a rapid drop in viscosity of the DNA, but without release of nucleotides, so that it must be an endonuclease. It requires magnesium, but no ATP or S-adenosylmethionine, which are co-factors of the *E. coli* enzyme. It operates only on native two stranded DNA, and the failure of polynucleotide kinase to introduce a (labelled) phosphoryl end-group into the fragments, except after treatment with alkaline phosphatase, shows that the nuclease cuts between the 3'-hydroxyl and the 5'-phosphoryl group.

The enzyme makes no single stranded nicks and evidently recognizes only one site in every 1,000 or so base pairs, for this is the limiting size of the product. On the assumption of random sequence, any unique run of six nucleotides would appear once in 1,024 pairs: this then seems a likely length for the recognition site. In the admirable paper that follows, Kelly and Smith (*ibid.*, 393) determine the substrate site

sequence. ^{32}P -labelled T7 phage DNA was exposed to the restriction enzyme, the 5'-phosphoryl end-groups were removed with phosphatase, and the resulting ends rephosphorylated by ^{32}P -ATP and kinase. The DNA was then digested to oligomers with pancreatic deoxyribonuclease and treated with venom exonuclease to give 5'-nucleotides from their ends. The ^{32}P label appeared in AMP and GMP, so that the break evidently occurs at a purine. Terminal dinucleotides were prepared from deoxyribonuclease digests using Lehman's exonuclease I, which stops at the dimer stage. Two ^{32}P -containing dimers were found, both containing ^{32}P -AMP, one of which released A on treatment with venom enzyme, the other G. Thus the large fragments all ended in pPupA. The sequence was extended by fractionation of a digest by ion-exchange according to length, and two ^{32}P -trimers were again obtained. At the tetramer stage there were six products, so that the specificity evidently peters out at this point. The uniqueness of the labelled trimers indicates that the same sequence, namely, (5')pPupApC(3'), is present in either strand at the break. Leaving no stone unturned, Kelly and Smith then show that the restriction enzyme makes clean double stranded breaks, and not close-lying single stranded breaks. Using micrococcal nuclease to degrade in the opposite direction from the venom enzyme, they show that the sequence from the 3'-end of the break is also unique, and complementary to the other. Thus the enzyme indeed recognizes a six nucleotide sequence, distributed on either side of the chopping site.

The symmetry of the sequence about the break is, as Kelly and Smith point out, not unreasonable, for if the enzyme is to break both strands at once, it must itself possess two active sites, related by a two-fold axis. (Such a situation has indeed been recognized in Bernardi's spleen deoxyribonuclease.) Kelly and Smith conjecture that there may be separate recognition and (less discerning) nucleolytic subunits, which cut at A or G. The molecular weight is about 70,000. One supposes that, as in *E. coli*, the indigenous DNA is modified—by methylation, for example—to render its own substrate sites resistant.

Another interesting enzyme is the nuclease V, which Schlessinger and his colleagues find to be associated with the *E. coli* ribosome. They have now shown (Kuwano *et al.*, *ibid.*, 75) that it is an exonuclease, which degrades poly U, for example, from the 5'-end. Moreover, they report (*Science*, **168**, 1225; 1970) that after—and only after—mild thermal degradation, which makes RNA species such as ribosomal and phage RNA effective as messengers, the enzyme will degrade these too.

A remarkable nuclease, which is highly specific for the RNA strand in two stranded DNA-RNA hybrids, has been discovered by Hausen and Stein (*Europ. J. Biochem.*, **14**, 278; 1970), and dubbed ribonuclease H. The thermal melting of the hybrids can be followed by the disappearance of the ribonuclease H activity, and the precisely coincident onset of pancreatic ribonuclease activity, as the single strands become available. The specificity of the enzyme is most graphically shown by the complete invulnerability of a two stranded poly rU:poly rA complex, compared with the rapid digestion of poly U in a poly rU:poly dA duplex: the deoxy strand remains untouched. What the possession of this mysterious enzyme profits the cell it is hard to guess.