solution was allowed to stand at 37° C it was inactivated, but not irreversibly: activity could be restored with ATP, phosphocreatine or theophylline in the presence of Mg^{2+}. They found that cyclic AMP decreased the level of the active enzyme. They conclude that inactivation is the formation of an alternative, inactive, form of the enzyme and that restoration of activity represents the conversion back to the active form.

Earlier work by E. G. Krebs's group and also by Chelala and Torres indicated that muscle phosphorylase *b* kinase is activated by ATP–Mg^{2+} and cyclic AMP; muscle phosphorylase *a* phosphatase is now shown to be activated by ATP and phosphocreatine and inactivated by cyclic AMP. Combining these findings it is evident that cyclic AMP must be the key substance that coordinates the two enzyme systems responsible for the level of active phosphorylase.

PROTEIN SYNTHESIS

More about Initiation

from our Cell Biology Correspondent

SEVERAL enzymes, the initiation factors, are required for starting protein synthesis *in vitro* in *E. coli* extracts. That much is indisputable, but precisely what the factors do is still disputed, as two papers in this issue of *Nature* (pages 944 and 947) prove. By column chromatography Hershey, Dewey and Thach (944) have obtained the f-1 initiation factor more than 90 per cent pure, and a second factor, f-2, 30 per cent pure. These two factors are believed to be associated with native 30*S* ribosomes but not with 70*S* or 50*S* ribosomes or 30*S* ribosomes obtained by splitting the 70*S* particle *in vitro*. The current idea is that the factors catalyse the formation of the initiation complex between a 30*S* ribosome, *m*RNA, f-1 and f-2 factors, GTP and f-met-*t*RNA_f, and are then released at some later stage in the formation of the 70*S* ribosome or chain elongation. Using ^3H-labelled f-1, Hershey *et al.* find that this factor binds only *in vitro* in an initiation complex when all the other components are present. The factor f-1 does not bind to 30*S* ribosomes in the absence, for example, of *m*RNA or f-2.

When 50*S* ribosomes are added to the initiation complex to form 70*S* ribosomes all the f-met-*t*RNA_f sediments with the 70*S* ribosomes, but the f-1 factor is absent from both the 70*S* and 30*S* regions of a gradient. Clearly, addition of 50*S* ribosomes causes the release of f-1 from the complex. When an analogue of GTP, GMP–PCP, which is not hydrolysed, is used instead of GTP, f-1 is still released when 70*S* ribosomes are formed. This indicates that although GTP seems to be essential for binding of f-1, hydrolysis of GTP is not essential for the release of f-1. The other factor, f-2, on the other hand, has a GTPase activity and so is probably released only after hydrolysis of GTP, in which it presumably plays a part. This suggestion has yet to be tested, but if it proves to be correct it means that the two factors go through similar but separate attachment and release cycles, f-1 being released before and f-2 after GTP hydrolysis.

Unlike the experiments of Hershey *et al.* which support current dogma, Mangiarotti's work (page 947 of this issue) leads to the unorthodox suggestion that at least two of the so-called initiation factors are involved in chain termination rather than chain initiation. Mangiarotti talks about initiation factors A and B, not f-1 and f-2, which illustrates one of the troubles of chain initiation literature, which is bedevilled with different names for the same factors. Factor A at least, however, is believed, by its discoverer, to be identical with f-1 (*Nature*, **219**, 1016; 1968).

Mangiarotti suggests that the reason why 70*S* ribosomes and 30*S* ribosomes, obtained by splitting 70*S* ribosomes *in vitro*, require the factors for chain initiation is simply that the factors are lost during isolation, especially during centrifugation in sucrose gradients. In other words, the systems such as that which Hershey *et al.* have used are artefacts. What is the evidence? Mangiarotti has used the RNA of bacteriophage R17 as messenger and tested the capacity of variously prepared ribosomes to synthesize protein or to liberate factors A and B on washing. If 70*S* ribosomes are not washed or sedimented through sucrose before the tests, they can synthesize protein as well as ribosomes containing native 30*S* subunits, and when washed the 70*S* ribosomes yield factors A and B. But 70*S* ribosomes sedimented in sucrose are dependent on added factors for protein synthesis and do not yield factors when washed.

Mangiarotti makes an ingenious suggestion to explain what the two factors may be doing, and why they apparently function during initiation in systems like those of Hershey *et al.* He suggests that they are involved in chain termination and help to free the peptidyl site of ribosome, a necessary precondition for initiation because the f-met-*t*RNA_f binds to the peptidyl site of the 30*S* ribosomes. Because 70*S* ribosomes, and the 30*S* subunits derived from them, are likely to have peptidyl *t*RNAs at this site, factors A and B would be needed to free the site in order to observe initiation *in vitro*.

Whatever the role of the various initiation factors, it now seems clear that the exchange of ribosomal subunits and cyclic dissociation and reassociation of 30*S* and 50*S* ribosome subunits during successive rounds of protein synthesis is a universal process. Adapting the methods which have been used to show this in *E. coli*, Kaempfer (page 950 of this issue) has shown such exchange in the eukaryote yeast cytoplasm. Demonstration of the universality of this process is consoling, not least because the search for f-met-*t*RNA_f or some equivalent initiator in eukaryotes has so far proved fruitless.

GEOLOGY

Pre-Cambrian Cataclysm

THE occurrence of a world-wide cataclysm about 1,300 million years ago has been inferred by Dr Norman Herz from the distribution and dating of anorthosite massifs (*Science*, **164**, 944; 1969). Could the cataclysm have been the capture of the Moon by the Earth?

Anorthosites are formed at high pressures and temperatures that exist only in the lower crust or upper mantle; they commonly occur as massifs in association with igneous or metamorphic rocks. There are more than fifty anorthosite massifs in Canada and the United States and a similar number elsewhere in the world. Dr Herz is apparently the first to notice that when the anorthosite massifs are plotted on a map of the world as it looked before the present phase of