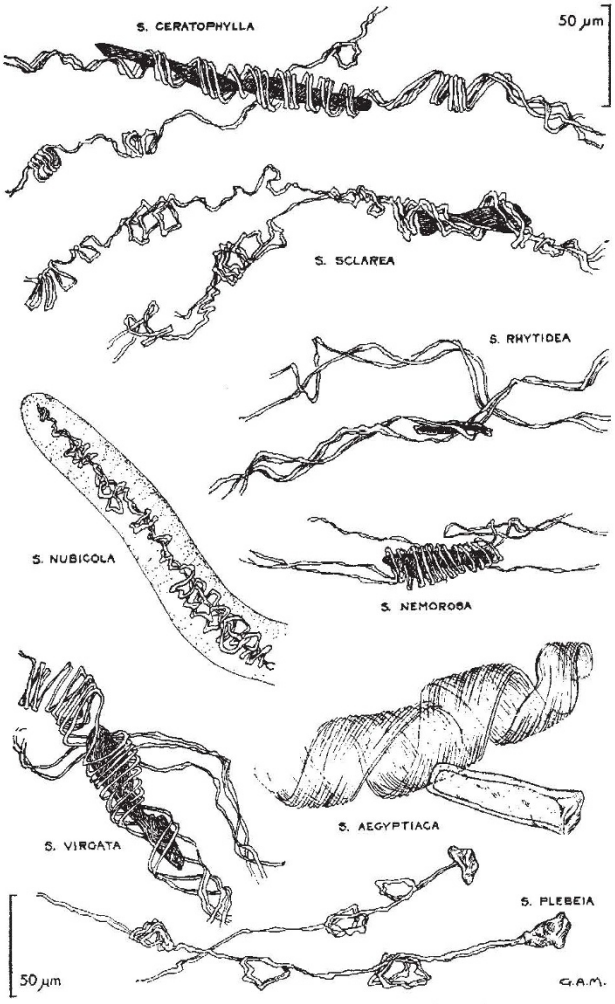
The powerful convulsant actions of bicuculline were first described almost forty years ago; this pharmacological property is to be expected of a substance that blocks central inhibitory processes. The drug is a phthalide-isoquinoline alkaloid, and studies of its chemical structure and the biological activity of structurally related alkaloids yield the added bonus of providing some suggestive evidence about the particular steric configuration of the GABA molecule which is recognized by GABA receptors in the brain.

The availability of this new antagonist drug provides clear pharmacological evidence that GABA is likely to be an inhibitory transmitter in the mammalian brain. With this tool, it should now be possible to map fairly rapidly the distribution of GABA-inhibitory synapses in the CNS, and to determine whether they are as numerous and widely distributed as the relatively high GABA content of the tissue would suggest.

BOTANY

More than an Amorphous Mass



These coils and threads have been found in the mucilage produced by nutlets of north-west Asian species of *Salvia* when they are wetted. Although I. C. Hedge, who described the structures (*Notes from the Royal Botanic Garden, Edinburgh*, XXX, No. 1; 1970), found that they varied from species to species, they do not seem to have much taxonomic value.

PROTEINS

Flourish of Factors

from our Molecular Biology Correspondent

A NOTABLE recent development is the discovery in the most diverse contexts of absolute requirements for cyclic AMP, that *bouquet garni* of modern biochemistry. If the conclusions of Kuwano and Schlessinger (*Proc. US Nat. Acad. Sci.*, **66**, 146; 1970) are to be believed, it is even involved in protein synthesis. Its implication in transcription in at least one system seems to have been established, and there have been indications of an effect on efficiency of translation. Kuwano and Schlessinger now find that it is capable of interacting with the G-factor of *E. coli*, an enzyme catalysing the translocation process on the ribosome, with hydrolysis of GTP. From filter assays it transpires that 3′ : 5′-cyclic AMP alone among a range of adenine derivatives binds to G-factor with a binding constant of about 10^5, but only in the presence of GTP. In a temperature-sensitive mutant, in which the G-factor activity is heat-labile, binding capacity for cyclic AMP also vanishes with increased temperature. Moreover, when the steroid antibiotic, fusidic acid, which operates by preventing translocation with inhibition of GTPase, is introduced the binding of cyclic AMP is reversed.

It thus seems clear that a stable ternary complex exists of G-factor, GTP and cyclic AMP. GDP, the product of the GTPase reaction, however, strongly inhibits the binding of the AMP. One must now be prepared to assume that all this is not fortuitous, but part of a greater design, which Kuwano and Schlessinger unfold in the following terms: GTP operating as an activator induces a conformational change in the G-factor, so as to enable it to bind cyclic AMP. The ternary complex then encounters the ribosome, already festooned with messenger RNA, peptidyl-tRNA at one site and aminoacyl-tRNA at the other. The GTP is hydrolysed, a peptide bond is formed and the new peptidyl-tRNA transferred to the other site. This is translocation. With GDP now present on the G-factor, the conformation reverts, and the cyclic AMP is released. Why, a strangled cry may well escape the reader's lips, postulate this new layer of complexity, when eight or nine soluble factors have already been reported, whose places in the cycle of protein synthesis are by no means all properly assigned? Kuwano and Schlessinger are ready with an answer: the GTPase activity, they believe, and have said in earlier papers, is also concerned in the activation of a ribosomal nuclease (ribonuclease V), which serves to break down the messenger RNA when it is no longer required. Translocation, with degradation of messenger, is seen as an alternative to the "productive" translocation that occurs in peptide synthesis. Whereas cyclic AMP does not diminish protein synthesis, it does inhibit the activation of the nuclease. It is suggested that the concentration of cyclic AMP governs the likelihood that the messenger will be translated, rather than degraded, and so determines ultimately the amount of protein produced. These are interesting cogitations, but are, as Kuwano and Schlessinger recognize, far from proven.

A new and different factor in *E. coli*, reported to cause the release of tRNA from the ribosome, is described by Ishitsura and Kaji (*ibid.*, 168). Whereas G-factor releases tRNA by way of translocation, the