screws, and his beautifully made apparatus provided with fine adjustment for helix angle and knife and cutter feed still exists.

The most significant development in the control of machine tools this century is hydraulic control. The idea of controlling a machine tool hydraulically had been put forward in the United States in 1893 by C. M. Conradson, but no great advances were made until the work of the Oilgear Company in the mid 1920s. The advantages gained over mechanical control were flexibility, infinitely variable speed, avoidance of shock on reversal of motion and constant pressure on the cutting tool. Hydraulic control also led to the application of servo mechanisms to machine tool control. Watt's steam engine centrifugal governor is the earliest example of this. Techniques of servo control have been applied to the most advanced system of machine tool control—numerical control. This permits continuous path machining and works straight from the dimensions and curves specified by the designer. The value of numerically controlled machine tools is in batch production: indeed, numerical control was conceived as a means of simplifying medium and small run production such as that encountered in the aircraft industry. This research was carried out over a period of five years starting in July 1949 at the Servomechanisms Laboratory of the Massachusetts Institute of Technology by Professor Gordon S. Brown and twenty-six co-workers.

Hyperbaric Oxygen

from our Microbiology Correspondent

MUCH has been written on the subject of oxygen toxicity since the classic studies of Bert in the 1870s, and many micro-organisms are now known to be affected adversely by increased oxygen concentrations. Aerobic bacteria can frequently tolerate partial pressures of oxygen of up to 2–10 atmospheres, but raising the hydrostatic pressure drastically increases their sensitivity to oxygen. The growth of aerobic bacteria is little inhibited at pressures of 50–100 atmospheres provided that the medium contains normal levels of oxygen, that is, less than 10 μg/ml. At higher pressures, however, the lag phase and generation time are prolonged and the maximum population is depressed. Furthermore, with the exception of barophilic species, increasing the pressure to 400–600 atmospheres inhibits growth, and extended compression often sterilizes the culture. ZoBell and Hittle (*Canad. J. Microbiol.*, **13**, 1311; 1967) have found that hyperbaric oxygen concentrations (35–105 μg/ml.) are similarly lethal at pressures as low as 4 atmospheres. Even barophilic marine bacteria such as *Pseudomonas perfectomarinus*, which will grow at pressures of more than 600 atmospheres if the medium is low in oxygen, are susceptible to hyperbaric oxygen at a pressure of 5 atmospheres. ZoBell and Hittle reiterate that a disturbed redox balance, oxidation of thiol or disulphide enzymes and an accumulation of toxic oxidation products are among the factors contributing to hyperbaric oxygen toxicity.

Recent work with euglenoid algae has defined more precisely some of the repercussions of hyperbaric oxygen on metabolism. Bégin-Heick and Blum (*Biochem. J.*, **105**, 813; 1967) discovered that cell division in *Astasia longa* was inhibited when culture aeration with air + carbon dioxide (95 : 5) was replaced by an oxygen + carbon dioxide (95 : 5) mixture. Growth was resumed at the normal rate after re-gassing with air + carbon dioxide and both the initial inhibition and the post-oxygen recovery occurred very rapidly. In this system the toxic effect of oxygen is obvious even at atmospheric pressure. Assay of mitochondrial enzymes showed that succinate–cytochrome *C* oxidoreductase, NADH–cytochrome *C* oxidoreductase, succinate dehydrogenase and the succinate oxidase system had greatly reduced activities compared with preparations from cells grown in air + carbon dioxide. The oxygen effect can be related, therefore, to a mitochondrial lesion, and the 75 per cent fall in succinate dehydrogenase activity is entirely responsible for the reduced activities of the succinate–cytochrome *C* oxidoreductase and the succinate oxidase system. The fact that NADH–cytochrome *C* oxidoreductase is also inhibited by oxygen is indicative of a second site of action in the electron transport chain.

Blum and Bégin-Heick (*Biochem. J.*, **105**, 821; 1967) have made the interesting observation that the closely related *Euglena gracilis* var. *bacillaris* is only sensitive to hyperbaric oxygen when grown in a low-phosphate (20 μM) medium with ethanol as the carbon source. *Euglena* under these conditions showed a decreased rate of respiration and an inability to resume growth when phosphate was replenished. This oxygen toxicity was far less marked when the alga was grown on glucose. Like *Astasia*, oxygen sensitized *Euglena* also had decreased activities of succinate- and NADH–cytochrome *C* oxidoreductases and succinate dehydrogenase when compared with cells grown in a high-phosphate (20 mM) medium. Although the differentiating action of hyperbaric oxygen plus low phosphate on cells grown with ethanol and glucose may reflect different sensitivities of endogenous and exogenous oxidative pathways, the mechanism of the sensitizing effect of low-phosphate as such still has to be resolved.

Proteins and Ligands

from our Molecular Biology Correspondent

THE study of the behaviour of ligands has been a promising approach to the difficult problem of observing and interpreting localized conformational changes in proteins, associated, for example, with enzyme activity. Ligands may in some cases compete directly with a substrate at an active site, or they may stabilize one conformational state of the protein with respect to others for which they have lower affinities.

An interesting example of the latter phenomenon comes from Markus *et al.* (*J. Biol. Chem.*, **242**, 4402; 1967), who have studied the binding of anionic dyes to serum albumin—a protein chiefly noted for its propensity to bind an extraordinary variety of small molecules of different kinds. The albumin with and without these ligands was then used as a substrate for five different proteolytic enzymes, and in all cases the bound ligand was found to inhibit digestion. From the stoichiometry of the binding, it appears that only two dye molecules need to be attached to produce the full effect. There are also appreciable changes in the distribution of the products of limited proteolysis. The most attractive explanation is that the protein exists in a state of equilibrium between two or more

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