SESSION 19. Biological Control Systems III

19-4. Continuous Servo Control System for the Study and Improvement of Homeostatic Blood Sugar Level Control

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THE ANALYSIS OF THE CONTROL of blood sugar level in the living organism presents a challenging problem. The challenge is on many different levels. From the point of view of the control engineer, the biologic control of serum glucose level is a highly remarkable achievement.

The glucose level is regulated with a high gain system allowing little steady state deviation. Transiently, the system responds with highly favorable characteristics. This is all the more remarkable since the capacity of pool space of the glucose pool in the body fluids represents only one or two hours supply.

From the point of view of the physiologist, glucose level regulation is an exceedingly complex process involving many different structures and functions of the organism. Besides the liver and the pancreas, the central nervous system, especially the hypothalamus, the pituitary, adrenal and thyroid glands, the kidney and the digestive system as well as the musculature are involved. It would seem improbable, therefore, that a sufficient number of factors could be kept constant in order to study the remaining ones with any degree of confidence.

It might be supposed that the need for high gain regulation is to reduce transient disturbances and not in order to keep the blood glucose sugar level in steady state at a precisely regulated value, since departure of 10 or 20% from this value has not resulted in any noticeable impairment of functioning. The steady state accuracy of this regulating system appears to be of the order of 2 or 3% which is a value considerably in excess of the tolerable limits of even the structure most sensitive to glucose concentration fluctuations, namely, the brain.

The application of control system theory to this system makes it appear that the system is analyzable as a multiloop system with the pancreas being a primary comparator, sensing blood sugar level and releasing chemicals such as insulin at a rate which is a function of the blood sugar level sensed. A secondary loop sensor is the hypothalamus which in turn controls endocrine activity and modifies the action of the pancreas. The function of the liver appears to be not as a sensing element but as a storage and control element which is responsive to the outputs of the pancreas, and to the adrenal hormones in response to exercise commands. The amount of glycogen stored in the liver represents about 20 times the amount of glucose stored in the body fluids and thus is enough for about one day's supply. The rate of utilization of blood glucose is regulated by the thyroid hormones as well as by adrenal hormones, the former increasing, the latter decreasing the rate of utilization.

The blood sugar level thus represents a delicate balance between the glucose introduced by the liver and from the digestive tract and its utilization by the peripheral tissues. That this delicate balance is maintained so closely is a truly remarkable feat especially when one considers the impossibility of using negative chemical concentration in the control of such a system.

In order to study this system by control system techniques, the dynamic responses in the resting state to disturbances are observed. In the resting state and within limited physiologic levels of blood sugar concentration, changes in the adrenal hormones do not become an appreciable factor. It is well known that in the resting condition the adrenal hormones become a major influence on the utilization of glucose only at a dangerously low blood sugar level. By introducing small quantities of glucose and of insulin intravenously, the transient responses of the regulatory system can be observed by the use of an autoanalyzer which continuously measures blood sugar level with a transportation lag of 6 minutes. The output of this analyzer in turn is made to drive a variable speed pump so that the rate of administration of glucose or of insulin is regulated directly by the blood sugar level itself. In this way a secondary loop is added to the biologic control system which makes it possible to alter its regulatory function. Through introducing desired dynamic characteristics in this auxilliary regulatory loop, by inserting a small electric analog computer, one can modify the regulatory characteristics and also attempt to improve regulation in cases of natural malfunctioning. The possible application of such a regulatory loop to diabetes is discussed.

The importance of external feedback loops for the study of organic chemical regulation or "chemostats" is stressed. In addition to stimulation by step, impulse and sinusoidal inputs, such loops help in the evaluation of the dynamic characteristics and structure of the control system under study.