A THEORETIC CONTROL APPROACH IN SIGNAL-CONTROLLED METABOLIC PATHWAYS

RAMESH GARIMELLA$^1$, UMA GARIMELLA$^2$, AND WEIJIU LIU$^1$

$^1$Department of Mathematics
$^2$Department of Biology
University of Central Arkansas
201 Donaghey Avenue, Conway, AR 72035, USA
(Communicated by Yang Kuang)

Abstract. Cells use a signal transduction mechanism to regulate certain metabolic pathways. In this paper, the regulatory mechanism is analyzed mathematically. For this analysis, a mathematical model for the pathways is first established using a system of differential equations. Then the linear stability, controllability, and observability of the system are investigated. We show that the linearized system is controllable and observable, and that the real parts of all eigenvalues of the linearized system are nonpositive using Routh’s stability criterion. Controllability and observability are structural properties of a dynamical system. Thus our results may explain why the metabolic pathways can be controlled and regulated. Finally observer-based and proportional output feedback controllers are designed to regulate the end product to its desired level. Applications to the regulation of blood glucose levels are discussed.

1. Introduction. Biochemical reactions occurring in cells can be grouped into metabolic pathways containing sequences of chemical reactions in which each reaction is catalyzed by specific enzymes, and the product of one reaction is the substrate for the next one. The compounds formed at each step are the metabolic intermediates (or metabolites) that lead ultimately to the formation of an end product. Figure 1 shows a generic metabolic pathway.

\[ P_1 \xrightarrow{E_1} P_2 \xrightarrow{E_2} \cdots \xrightarrow{E_n} P_n \xrightarrow{E_{n+1}} P_{n+1} \]

Figure 1. A generic metabolic pathway.

Cells are always in a homeostatic condition, and therefore the amount of product present or produced is always within certain range of concentrations. Homeostasis is maintained by metabolic regulation primarily by feedback inhibition. In feedback inhibition, the enzyme catalyzing the first committed step in a metabolic pathway is temporarily inactivated when the end product binds to allosteric sites of that enzyme. However there are other ways of regulating the metabolic pathways.

2000 Mathematics Subject Classification. 92C45, 92C40, 93D20, 34D05.

Key words and phrases. cell signaling, metabolic pathway, output feedback control, regulation.