

A Model of the Signal Transduction Process under a Delay

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Received 18 October 2016; Accepted (in revised version) 30 May 2017.

Abstract. The signal transduction pathway is the important process of communication of the cells. It is the dynamical interaction between the ligand-receptor complexes and an inhibitor protein in second messenger synthesis. The signaling molecules are detected and bounded by receptors, typically G-Protein receptors, across the cell membrane and that in turns alerts intracellular molecules to stimulate a response or a desired consequence in the target cells. In this research, we consider a model of the signal transduction process consisting of a system of three differential equations which involve the dynamic interaction between an inhibitor protein and the ligand-receptor complexes in the second messenger synthesis. We will incorporate a delay τ in the time needed before the signal amplification process can take effect on the production of the ligand-receptor complex. We investigate persistence and stability of the system. It is shown that the system allows positive solutions and the positive equilibrium is locally asymptotically stable under suitable conditions on the system parameters.

AMS subject classifications: 34D05, 34D20

Key words: Signal transduction pathway, locally asymptotically stable, persistence, ligand-receptor, delay.

1. Introduction

Signal transduction process has been a focus of attention of many researchers. As mentioned in [1, 5], the living organism is composed of cells. To conduct of life, the cells need to interact with each other by releasing a signal molecule of a cell and acts on another cell to produce a change in cell function for example growth, metabolism, catabolism, and so on. All cells are highly responsive to specific chemicals in their external environment. The way of communication of cells is represented by a signaling pathway.

Even though, the functions of cell signaling is to control and maintain normal physiological balance within the body, when the cell senses and responds correctly by signal

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transmittance, this can lead to proper development, repairing, and so on, otherwise if it loss the controllable of signaling pathway, this can be a key factor in the generation of disorders such as cancer or many serious diseases, see in [1, 2, 10].

Signal transduction is the mediation of molecular signals from extracellular to intracellular of the cells. The molecular circuits are detection, amplification and diverse integration of external signals to generate responses.

By considering a mechanism for detecting and responding specifically to external signals of cells. One of the more complex strategies for running the signal process concerns a three-stage G protein coupled enzyme cascade, represented in [5, 9]. The process starts from the G protein, which consists of 3 subunits: α , β , and γ subunits. It is activated by a specialized membrane receptor's interaction with a particular ligand. After that, the receptor is activated and turns on the heterotrimeric G protein, by causing the G protein to convert GDP (guanosine diphosphate) to GTP (guanosine triphosphate). The GTP-bound α -subunit is then separated from β and γ subunits and either or both regulates the effector unit (the adenylate cyclase or AC), whose activity produces secondary messengers such as cyclic adenosine monophosphate (cAMP). The G protein is transient and is terminated by the GTPase activity of the α -subunits. GTPase converts bound GTP to GDP, and finally the protein is inactivated.

In the work of C. Rattanakul et al. [8], based on previous research works [3, 4, 6, 7, 9], they obtained a model for the signal transduction path way consisting of a system of two differential equations which governs the interaction between an inhibitor protein and the ligand-receptor complexes. Their model assumes that cAMP equilibrates very rapidly which reduces their model to a two dimensional one. We do not make such assumptions, making our model more accurate.

Then, as in [8], we will be able to write the following steps for the reference model.

Let S be the amount of α -subunits of G protein in the inactive state and S^* be that in the active state. S and S^* can be switched to the other by the activating and inhibiting agents, which are denoted A and I , respectively. These agents are stimulated by the external signal, which binds to the cell receptors on the cell membrane. The dynamics of the activator density A and inhibitor density I are shown in the following equations

$$\frac{dA}{dt} = -k_{-a}A + k_aR, \quad (1.1)$$

$$\frac{dI}{dt} = -k_{-i}I + k_iA, \quad (1.2)$$

where $R(t)$ is the membrane surface density of the ligand bound receptors. The first terms on the right of equations (1.1) and (1.2) are the corresponding removal rates, and the second terms are the corresponding rates of production.

By using the dynamics of mass action, the equations for S^* is

$$\frac{dS^*}{dt} = -k_{-s}IS^* + k_sAS, \quad (1.3)$$

where the first term on the right is the removal rate and the second term is the activation rate.