ABSTRACT In cellular regulatory networks, genetic ac- tivity is controlled by molecular signals that determine when and how often a given gene is transcribed. Implications of this noisy pattern of gene expression for cellular regulation include: (i) the switching delay for genetically coupled links, hence the time for the cell to execute cascaded functions, can vary widely across isogenic cells in a population; (iIn these links, for appropriate combinations of input signals, transcripts are initiated and the protein product ac- cumulates when production exceeds degradation; the increas- ing protein concentration simply broadcasts the information that the promoter is "on." The message is "received" or detected by the concentration-dependent response at the protein signal's site(s) of action, stimulating a response at each site in accord with that site's chemical behavior. (Herein the term "stochastic" is used in the statistical sense of resulting from a random process.) We formalize and quantify this notion of randomness in genetic regulatory mechanisms by explicitly characterizing the statistics of the random processes implicit in the chemical reactions (4). We have analyzed the chemical reactions con- trolling transcript initiation and translation termination in a single such "genetically coupled" link as a precursor to modeling networks constructed from many such links. (We use the term "protein signal" to mean the regulatory protein concen- tration in its effective form at its site of action.) In this paper we examine the properties of a single geneti- cally coupled link as a precursor to modeling networks con- structed from many such links. In all organisms, networks of coupled biochemical reactions and feedback signals organize developmental pathways, me- tabolism, and progression through the cell cycle. Specifically, we ask what determines the time required for protein concentration to grow to effective signaling levels after a promoter is activated and how statistical variations in this time can affect observed cellular phenomena across a cell population. By analogy to electrical circuits, we will refer to this time interval between the switching on of the first promoter and activation or repression of the second promoter as a "switching delay." There is also a switching delay of a different magnitude for the inverse functions when the controlling promoter is switched off. Then, as a concrete illustration of switching delays over a genetically coupled link, we simulate a representative link using parameters characteristic of links in bacterial regulatory networks. In biochem- ical regulatory networks, the time intervals between successive events are determined by the inevitable delays while signal molecule concentrations either accumulate or decline. Sim- ulation of the processes of gene expression shows that proteins are produced from an activated promoter in short bursts of variable numbers of proteins that occur at random time intervals. There are numerous unexplained examples of phenotypic variations in isogenic populations of both pro- karyotic and eukaryotic cells that may be the result of these stochastic gene expression mechanisms. The time delay in genetically coupled links (Fig. Copyright ?Fig.