*[T]here is no conflict between causality and teleonomy.*

*(Ernst Mayr, 1961)*

Rational explanations of natural phenomena are based on scientific laws linking cause and effect. The application of a force on a body changes its momentum. A temperature gradient creates flow of energy down the gradient. Such laws form the basis not only of explanations of past events but also of predictions of future events. Thus, Newton's laws would allow us to predict how long or how much energy it will take to translocate an object, Fourier's law of heat conduction can be used to predict the time to cool a hot object and so on. Similarly, predicting the evolving composition of a chemically reacting mixture (say at constant temperature and pressure) can be accomplished by the application of mass balances with chemical kinetics, which specifies reaction rate as a function of concentrations of reacting species, and the use of stoichiometric laws. That the success of this scientific methodology with describing the behavior of inanimate systems, could also apply to living systems is but a natural extension of thought. Indeed, numerous instances can be cited of success in this direction. Thus in modeling metabolism, theories based on steady state for intracellular metabolites have had their measure of success in relating experimental measurements of uptake of substrate to intracellular metabolic activity. While this success is owed to the use of physicochemical laws, some predictive attributes have been rendered by infusing a concept of "efficiency" into the process; an example is the concept of maximizing biomass yield adopted by what is popularly known as Flux Balance Analysis (FBA) (Orth et al., 2010).

If in the metabolic scenario just portrayed above, we had sought to *predict* the uptake rate of substrate by specifying its concentration in the cells' environment, the challenge is greatly intensified as uptake of substrate depends upon how it is dispensed by *regulatory* processes among different pathway options. Metabolism is subject to regulation through selective syntheses of enzymes and control of their activities. For example, diauxic growth observed first by Monod (1942), consists in the preferred use of glucose from mixtures with other substrates such as lactose, xylose, arabinose, etc. The *lac operon* is a control site on the DNA for the metabolism of lactose which is turned off in the absence of lactose or in the presence of a more readily available energy source. The *lac operon* comprises two kinds of genes, repressor and functional genes. The repressor genes prevent lactose metabolism by derailing transcription. When lactose is present and is to be metabolized, the functional genes provide for the synthesis of

the enzyme (beta-galactosidase) needed to break lactose down. These molecular processes can indeed be modeled using the methodology for analyzing chemical reactions. However, the preference shown for a readily available energy source such as glucose against metabolizing lactose has a rationale that is more attractive for a different kind of theory, one that bears the stamp of past experience; viz., using glucose was better in some sense than metabolizing lactose. Insofar as our focus is on currently existing species, it would seem natural to profess that their strategic behavior is inspired by the goal of survival. A theory based on such goal-directedness could circumvent the need for describing how it is actually accomplished. In other words, we could dispense with describing the molecular processes of gene regulation governing the synthesis of the glucose enzyme and preventing the synthesis of the lactose enzyme. Furthermore, other regulatory processes yet to be unearthed could be subsumed by the theory, thus providing for a comprehensive accounting of metabolic regulation.

The quote at the beginning of this chapter relates to the issue of how goal-directedness could adorn a theory that must be rationally based on cause and effect. While teleology (a doctrine that espouses goal-centered activity) has been an inseparable aspect of explaining biological phenomena, its use has not been without mixed emotions. On one hand, it seemed to resist the spirit of explanations based on cause and effect, and on the other, it possessed an enlightening quality. For example, to express bacterial preference for glucose against lactose as a more efficient strategy sounds more interesting than a tortuous description of the events involved bereft of the suggested motive! Mayr (1961) points out that the disrepute of teleology has come about from its historical association with evolutionary progression to superior forms. Rather evolution is to be viewed as a cause-and-effect phenomenon, the cause being random changes and the effect being survival in a competitive environment. Goal-directed behavior can be understood as the consequence of a coded program such as that on the DNA and thus be eminently a causality based phenomenon. Pittendrigh (1958) has aptly suggested the use of the term "teleonomy" as a means to sever its implication from that of its maligned predecessor, teleology.

Biological systems may thus be appropriately viewed as *cybernetic* systems to reflect the foregoing approach to their investigation. The concept of cybernetics is believed to have originated with Plato and has had a history of development until Norbert Wiener (1948) provided it with a rigorous mathematical structure. Wiener defined cybernetics as the science of "control and communication in the animal and machine." To the extent cybernetics refers to the art of steering a system toward a goal, the modeling of microbial metabolism portrayed in this book is an example of the cybernetic approach. However, the development here is not in strict conformity with the classical methodological organization of cybernetics.