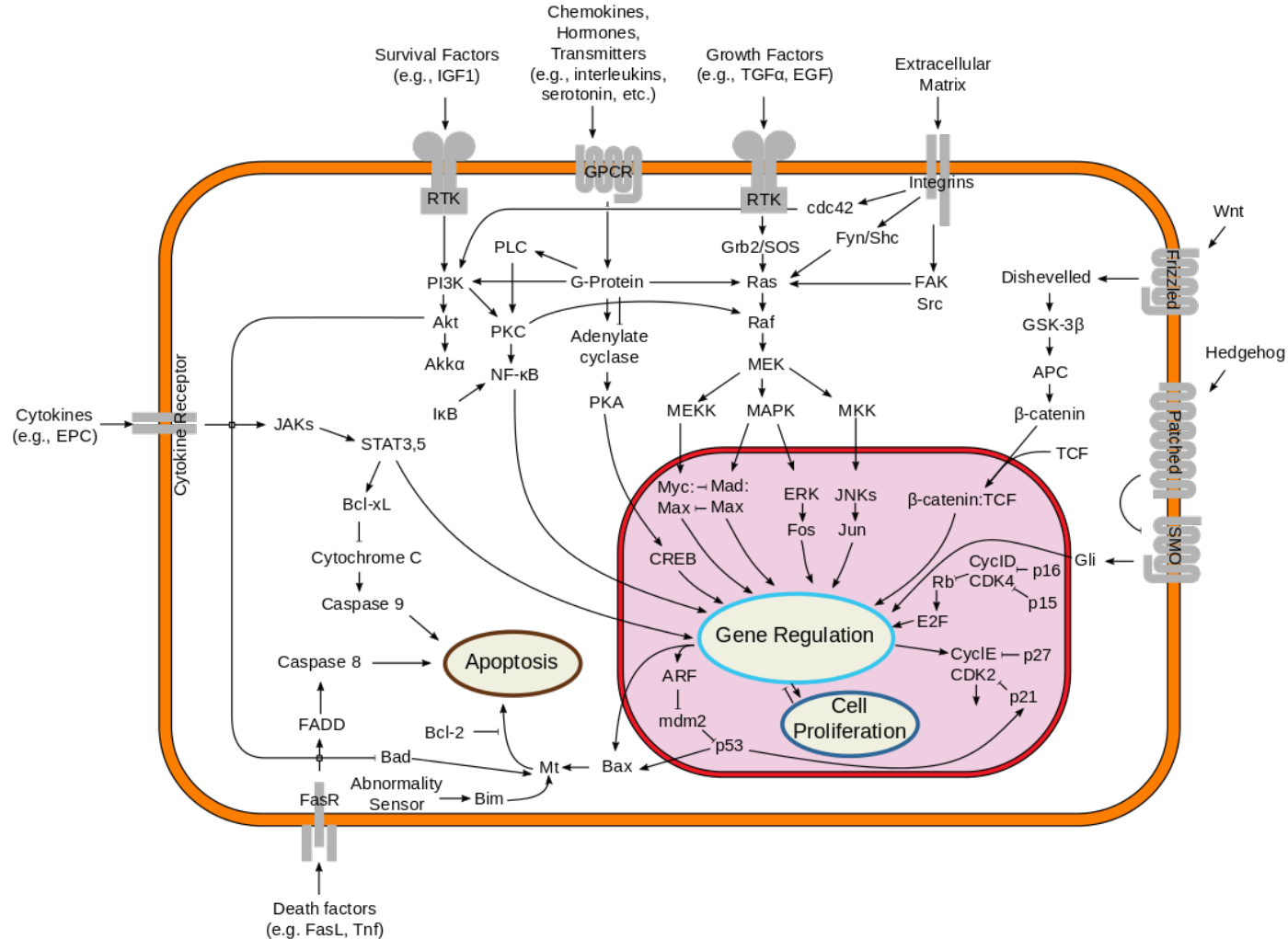
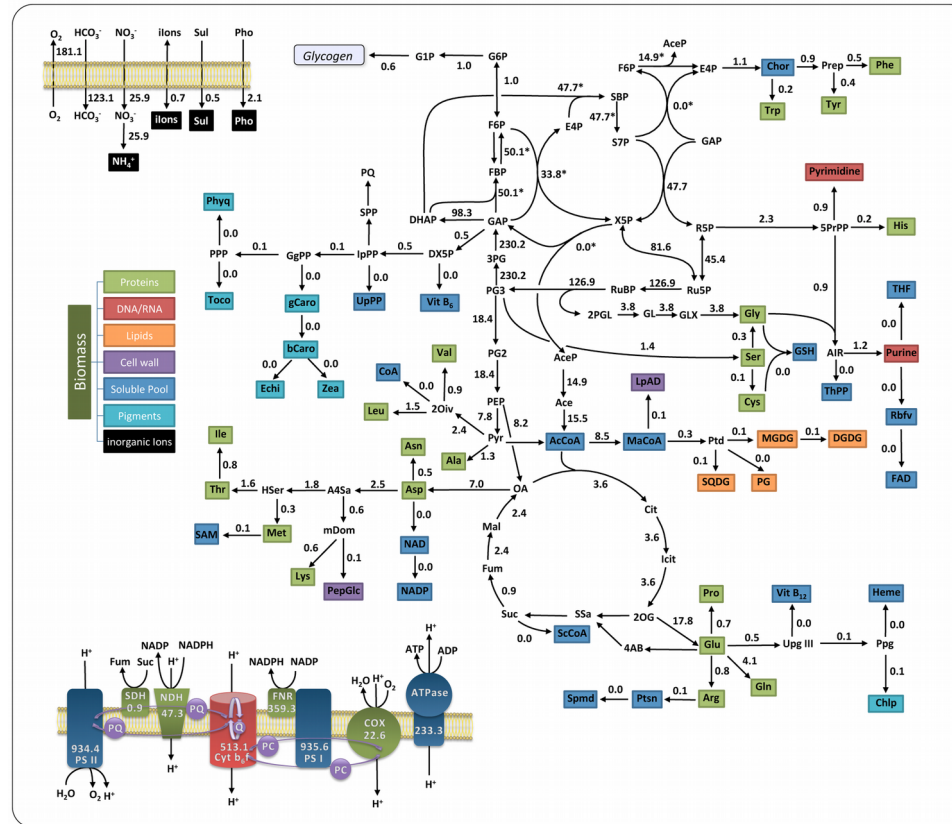


Application: signal transduction



Application: metabolism



Flux Balance Analysis of Cyanobacterial Metabolism: The Metabolic Network of *Synechocystis sp. PCC 6803*
Henning Knoop et al

Length and time scales

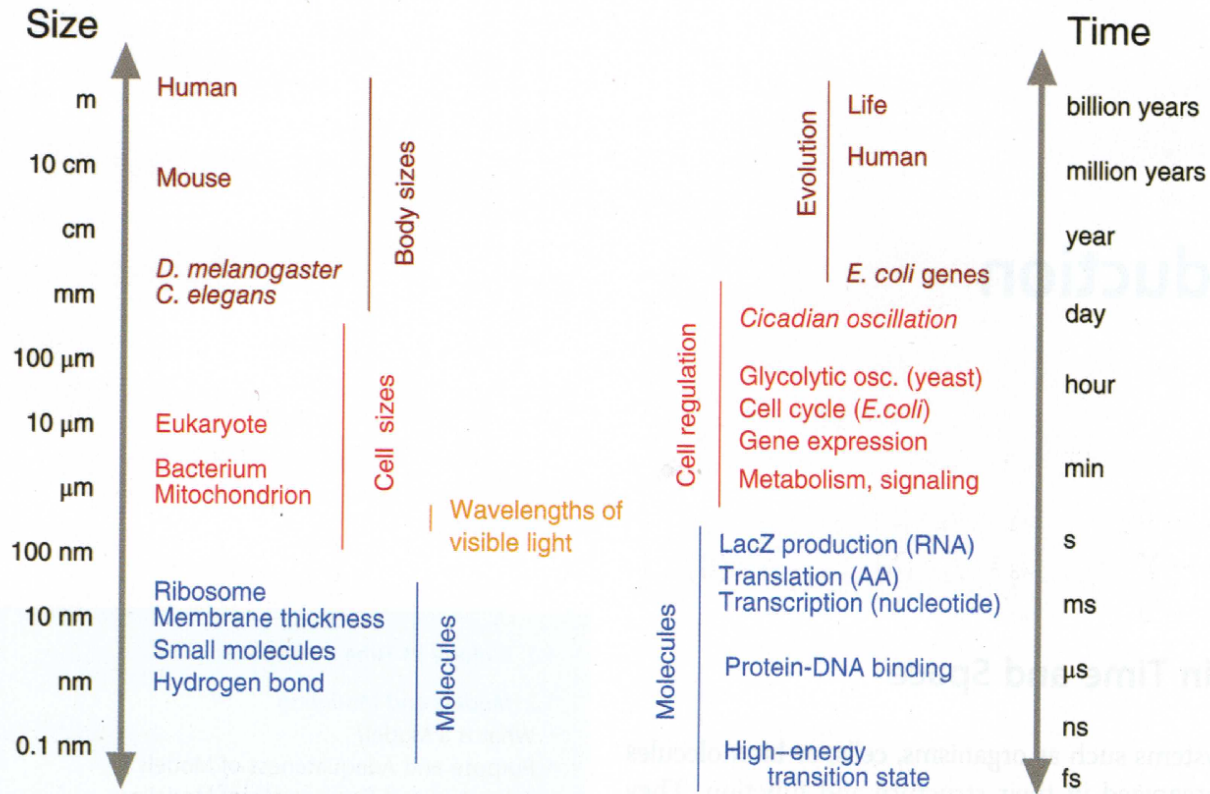


Figure 1.1 Length and time scales in biology. (Data from the BioNumbers database at bionumbers.hms.harvard.edu.)

Abstraction steps in modeling

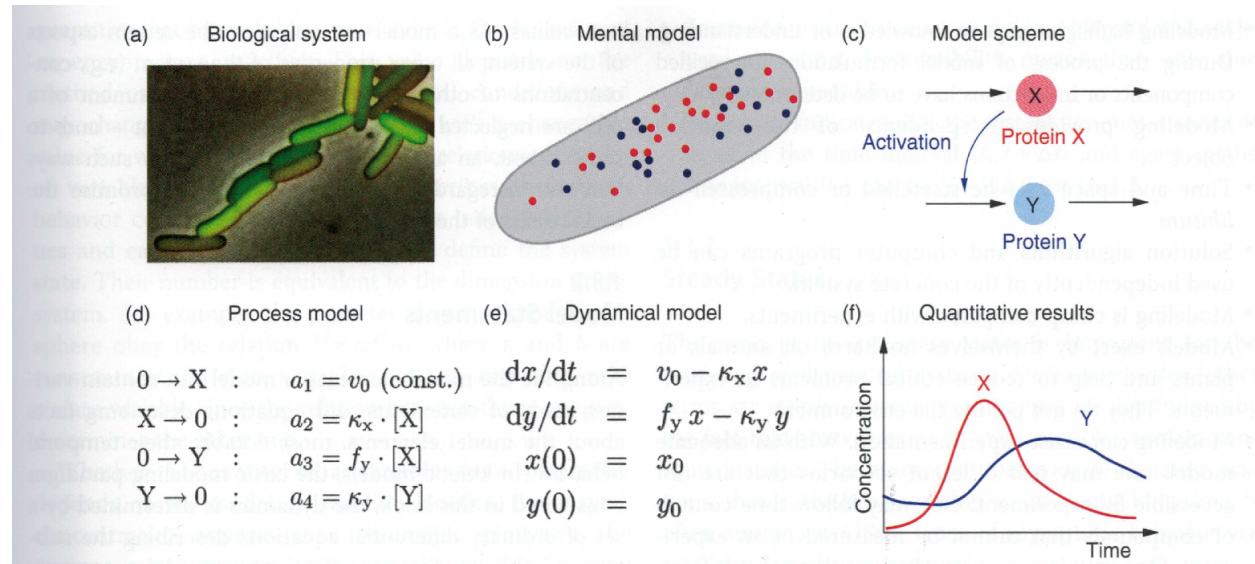


Figure 1.2 Typical abstraction steps in mathematical modeling. (a) *E. coli* bacteria produce thousands of different proteins. If a specific protein type is labeled with a fluorescent marker, cells glow under the microscope according to the concentration of this marker. (Courtesy of M. Elowitz.) (b) In a simplified mental model, we assume that cells contain two enzymes of interest, X (red) and Y (blue), and that the molecules (dots) can freely diffuse within the cell. All other substances are disregarded for the sake of simplicity. (c) The interactions between the two protein types can be drawn in a wiring scheme: each protein can be produced or degraded (black arrows). In addition, we assume that proteins of type X can increase the production of protein Y. (d) All individual processes to be considered are listed together with their rates a (occurrence per time). The mathematical expressions for the rates are based on a simplified picture of the actual chemical processes. (e) The list of processes can be translated into different sorts of dynamic models, in this case, deterministic rate equations for the protein concentrations x and y . (f) By solving the model equations, predictions for the time-dependent concentrations can be obtained. If the predictions do not agree with experimental data, this indicates that the model is wrong or too much simplified. In both cases, the model has to be refined.

Linear chain

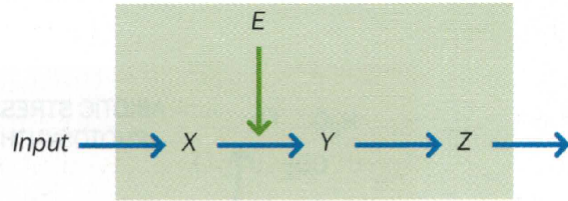


Figure 1.8 The human brain handles linear chains of causes and events very well. In this simple pathway, an external input is converted sequentially into X, Y, and Z, which leaves the system. The conversion of X into Y is catalyzed by an enzyme E. It is easy to imagine that any increase in *Input* will cause the levels of X, Y, and Z to rise.

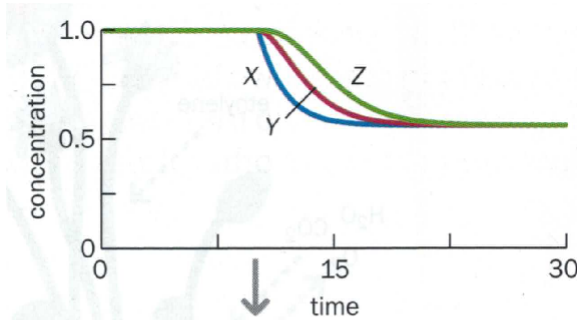


Figure 1.9 Simulations with the system in (1.1) confirm our intuition: X, Y, and Z reflect changes in *Input*. For instance, reducing *Input* in (1.1) to 75% at time 10 (arrow) leads to permanent decreases in X, Y, and Z.

Linear chain with feedback

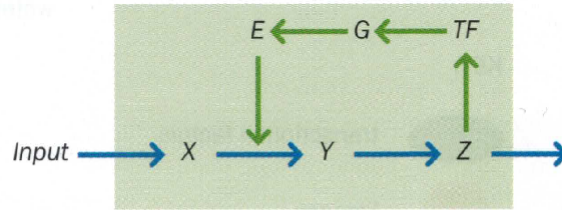


Figure 1.10 Even simple systems may not allow us to make reliable predictions regarding their responses to stimuli.

Here, the linear pathway from Figure 1.8 is embedded into a functional loop consisting of a transcription factor TF and a gene G that codes for enzyme E . As described in the text, the responses to changes in *Input* are no longer obvious.

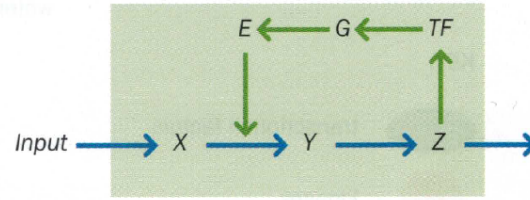
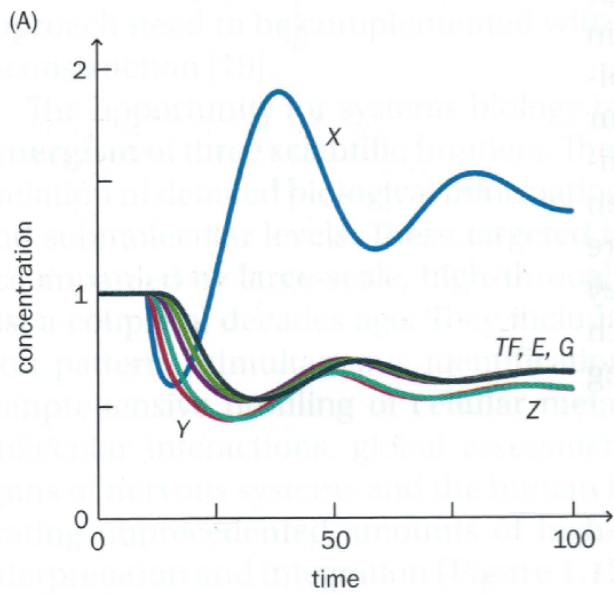


Figure 1.10 Even simple systems may not allow us to make reliable predictions regarding their responses to stimuli. Here, the linear pathway from Figure 1.8 is embedded into a functional loop consisting of a transcription factor *TF* and a gene *G* that codes for enzyme *E*. As described in the text, the responses to changes in *Input* are no longer obvious.

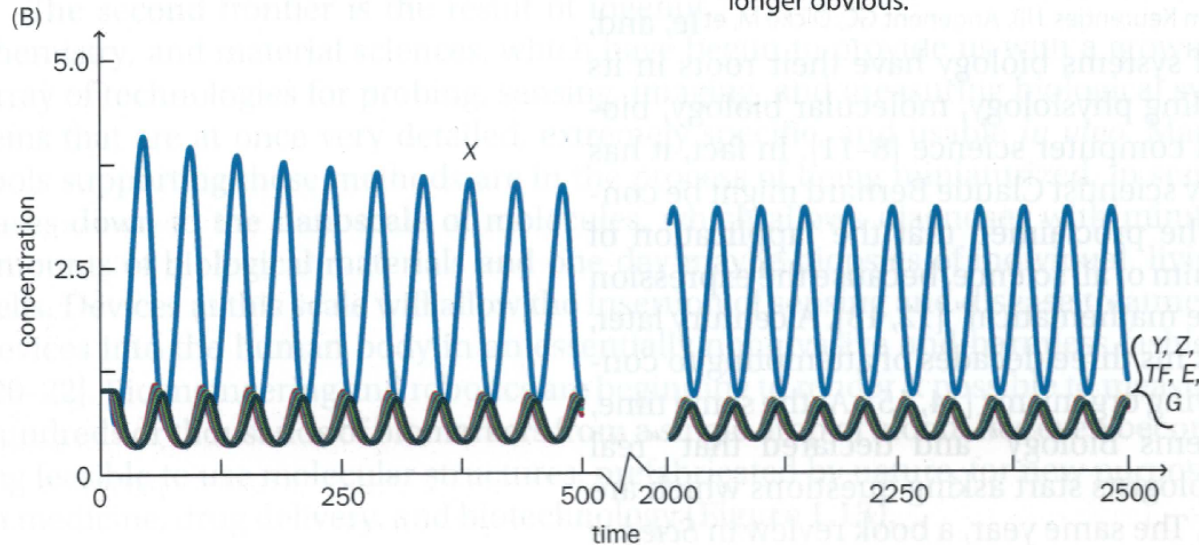


Figure 1.11 Simulation results demonstrate that the looped system in Figure 1.10 may exhibit drastically different responses. If the effect of *Z* on *TF* is very small, the response is essentially like that in Figure 1.9 (results not shown). (A) If the effect of *Z* on *TF* is relatively small, the functional feedback loop causes the system to go through damped oscillations before assuming a new stable state. (B) For stronger effects of *Z* on *TF*, the system response is a persistent oscillation.