**Signal transduction**: the process by which cells sense signals, integrate them, and execute a response. These responses typically require rewiring of the molecular networks inside the cell, e.g. by way of gene expression alterations.
Prokaryotic signaling: two-component signaling networks (bacteria can have tens of such systems)

Signal(-s)

1. Autophosphorylation by sensor

2. Phosphotransfer from active sensor to inactive response regulator

3. Dephosphorylation of active response regulator by inactive sensor

Sensor protein, often membrane embedded

Response regulator protein, often a transcription factor

(Inorganic) phosphate molecule

Gene regulation

Note that:
ATP equals ADP bound to P
**Different levels of detail**

**Signal(-s)**

1. ATP → ADP
2. ATP → ADP
3. ATP → ADP

**Gene regulation**

Stimulates reaction 3

**More realistic scheme**
(still a simplification because sensor and regulator are dimers)

**S** - Sensor protein
**R** - Response regulator; transcription factor
**L** - Signal

**L=signal**

**Detailed mechanistic description with all molecular events**

**Qualitative process description**
Eukaryotic signaling: much more complicated

Overview of entire process

Autophosphorylation of intracellular receptor domain upon signal binding

Example of a cascade of signaling events
Eukaryotic signaling: very complicated

Figure 2
A comprehensive map of the mTOR signaling network. This map was created with CellDesigner version 4.0.1. A total number of 777 reactions and 964 species were included. The SBML and PDF files of the mTOR map are available from the Supplementary information. The map can be best viewed in the PDF format (see Supplementary Figure S3). All of the species, proteins, reactions and cellular compartments included in the map are listed in the SBML file when opened by CellDesigner (http://celldesigner.org/). All of the unique proteins were listed in Supplementary Table S1. A cartoon view of the map (bottom right) depicting different functional modules was drawn to facilitate the exploration of the map. Symbols adopted to build the map are illustrated in the legend. This image is also available as a high resolution pdf.

The mTOR map
E Caron et al
Molecular Systems Biology 2010 & 2010 EMBO and Macmillan Publishers Limited

Wednesday, October 3, 12
Upstream regulators of mTORC1 signaling. Species, proteins, reactions and cellular compartments involved in mTORC1 signaling were extracted from the comprehensive mTOR map and illustrated using the process diagram language. Green and red reactions indicate activation and inhibition of mTORC1, respectively. Size and color of each component are configurable. Symbols are similar to those used in the legend of the Figure 2. The SBML and PDF files (see Supplementary Figure S4) of mTORC1 signaling are available from the Supplementary information.

The mTOR map
E Caron et al & 2010 EMBO and Macmillan Publishers Limited

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Eukaryotic signaling: very complicated
Signal flow, sensors, control systems are found everywhere in engineering: in biology we find them very hard to study. Why?
Systems biology: some common principles of signal transduction mechanisms

Covalent-modification induced conformational changes of proteins and dynamic equilibrium between conformation states. Other proteins can typically bind to only one of the conformations.

Enzyme-catalyzed covalent modification and demodification of signaling proteins

Input-output characteristics of signaling network and identification of output-input sensitivity and input thresholds: some signaling systems are sensitive some not; some have large input dynamic range and some not