

By combining **naturally occurring genetic components** in unique ways, it has become possible to **artificially engineer genetic networks** that possess sophisticated functional capabilities.

Transcriptional control operates at the level of **mRNA synthesis** through the use of **inducible transcriptional activators** and **repressors** that are capable of binding naturally occurring or specifically engineered **promoters**. **Prokaryotic gene control systems** generally use inducible repressors and activators drawn from well-documented **genetic operons** such as the lac operon of *Escherichia coli*. **Bacterial response regulators** also form the basis of synthetic **eukaryotic** gene regulation systems, although given transcriptional differences they require adaptation.

In considering the **design** of a synthetic genetic network for a **biological application** it is useful to imagine what kind of **functions** one might wish to create. Some applications may benefit from a **mechanism** that ensures a network produces a **consistent** and **stable response**. For other applications, one may require a system that produces **more than one discrete expression state**.

To produce a **unified** and **consistent outcome** a biological process must be **capable of withstanding** a certain degree of **variation** and **difference**. A key development in our understanding of how stability is maintained was through the discovery of **autoregulatory feedback loops** in which proteins, directly or indirectly, influence their own production. An **autofeedback mechanism** can either be **negative**, in which a protein **inhibits** its own production, or **positive**, in which a protein **stimulates** its own production.

The **expression output** of many cell-based regulatory networks is often a **logic** response generated by one or more **input signals**. Their **output** is either **ON** or **OFF** across a wide range of inducer concentrations, except for a small concentration window where transitions between the two states occur. By utilizing several **compatible heterologous gene control systems**, it has been possible to design a range of **eukaryotic logic circuits** that follow strict **Boolean logic** in their integration of two input signals.

To **detect** weak transcriptional responses that, despite being difficult to detect *in vivo*, are often involved in **regulatory functions** where only **trace amounts** of a gene product are required. In typical transcriptional studies aimed at **determining** the **conditions** under which a **promoter** is activated, a **reporter gene** is placed **downstream** of the promoter and assayed under varying conditions. However, where the promoter **response is weak** it is often **not possible** to discern any kind of activity. By placing a **repressor cascade downstream** of the promoter it was possible to **amplify** an otherwise undetectable promoter response.

The key requirements for a **band-detection network** (responding to an inducer within a given concentration range) are the design of modular components that enable the detection of a **low-threshold**, a **high threshold**, and a way of **integrating the two thresholds**.

The **pulse-generating network** produces output when a **threshold** concentration is reached, and then through a **feedforward mechanism** shuts down reporter expression regardless of whether the concentration continues to rise or fall. Like the **band-detection network** the **pulse-generating network** provides important insights into how pulse-generating behavior could occur in **natural systems**.