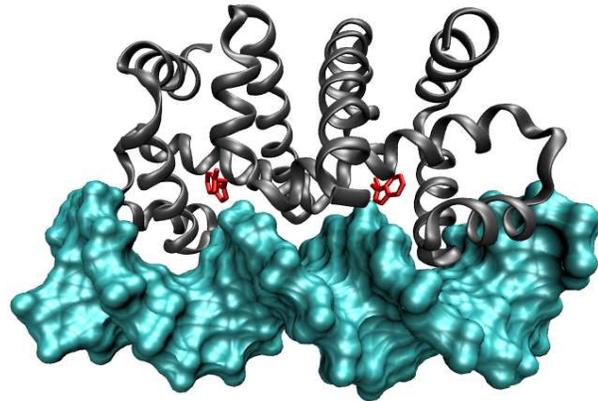


## Accurate Genetic Switch in *Escherichia coli*: Novel Mechanism of Regulation by Co-repressor

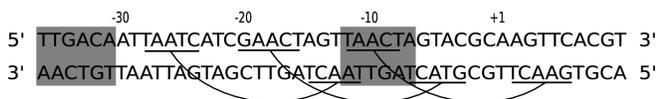
The *trp* operon regulation is a paradigm of gene regulation in bacteria. The repression is achieved by attachment of active *trp* repressor (grey) to operator and masking RNA polymerase recognition sequence. The *trp* repressor is a small (25 kD) protein consisting of two 107 amino acids chains. In order to become active, *trp* repressor binds in independent manner two molecules of co-repressor (tryptophan, marked in red).



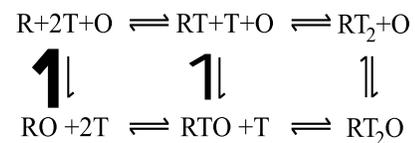
**Holo-repressor/operator complex**

We proposed a new model of repression, which greatly differs from previous mathematical models. One, two or three *trp* repressors can bind to the operator and repress the transcription. Moreover, reaction rates for detachment of repressors from the operator strongly depend on tryptophan concentration, since tryptophan can also bind to the repressor-operator complex and stabilize it. Therefore, the mean lifetime of the repressor-operator complex depends on concentration of the Trp. From the mathematical modeling and analysis of reaction rate and equilibrium constants emerges a high-quality, accurate and effective module of *trp* repression. This genetic switch responds accurately to fast consumption of tryptophan from the interior of a cell. It switches with minimal dispersion when the concentration of Trp drops below thousand molecules per cell and is very stable in case of high Trp concentration.

**A**



**B**



apo-repressor > semiholo-repressor > holo-repressor

A. The sequence of the *trp* operator-promoter region. The underlined bases are recognized by repressors. The numbers indicate positions relative to the first transcribed residue (+1). The recognition sequences for RNA polymerase are marked with gray boxes. B The proposed scheme of reactions for regulation of *trp* operon. R, T, O – repressor, tryptophan and operator, respectively. The decay rate constants decrease from apo to holo-repressor.

1. Tabaka M., Cybulski O. and Hołyst R. (2008) Accurate genetic switch in *Escherichia coli*: novel mechanism of regulation by co-repressor. *J. Mol. Biol.* (in press)