# De novo RNA circuits in living cells

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## Abstract

We propose a general methodology based on biophysical principles to automatically design RNA components with complex features previously only found in transcription factors: non-linearity, feedback, signal transduction, multimeric riboregulation, "switchable" RNA cascades and anti-termination RNA switches. Furthermore, we are able to engineer regulatory RNAs able to self-circularize after undergoing a maturation step. Our RNAs are different to any known non-coding sequence and their predicted behavior is validated in *E. coli* at the population and single-cell levels. The RNA networks can also be used to regulate target genes in any living system where CRISPR is known to work. We also show that we can sense the transcript levels of a target gene *in vivo*, which could later be used to determine the cell-cycle phase or the tissue in eukaryotic cells. Our RNAs can form complex interaction networks to provide novel synthetic gene networks working in prokaryotic that could be extended to eukaryotic systems.

**Keywords:** De novo design, computational design, RNA, gene circuits

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