The role of incoherent microRNA-mediated feedforward loops in noise buffering

Osella M[1,2], Bosia C[1,2], Corà D[2,3], Caselle M[1,2]

Motivation

MicroRNAs are endogenous non coding RNAs that play important gene regulatory roles in animals and plants by pairing to the messenger RNAs of protein-coding genes to direct their post-transcriptional repression. Transcriptional and miRNA regulations are interlinked in a complex network in which the microRNA-mediated feed forward loop seems to be a motif (an overrepresented regulatory circuit). Since the common lore is that network motifs were selected by evolution to perform elementary regulatory tasks, one of the aims of nowadays systems biology is to understand motif functions. In this view, we focus on the incoherent version of miRNA-mediated feedforward loops to demonstrate their potential role in noise buffering.

Methods

The modelling strategy of the circuits in analysis is based on detailed master equations, taking into account the essential features of transcription, translation, degradation and interactions between genes. The analytical results are then checked through Gillespie simulations.

Results

We show that the incoherent microRNA-mediated feedforward loop couples a fine-tuning of target protein level with noise buffering. In particular it confers robustness to the target gene expression with respect to fluctuations in upstream factors. Moreover our model predicts that the optimal attenuation of fluctuations coincides with modest repression of the target gene expression. This feature is coherent with a fine-tuning function and in agreement with experimental observations of the actual impact of a wide class of microRNAs on the protein output of their targets.

Contact e-mail

mosella@to.infn.it

[1] Dipartimento di Fisica Teorica and INFN University of Torino, Torino [2] Center for Complex Systems in Molecular Biology and Medicine, University of Torino,Torino [3] Systems Biology Lab, Institute for Cancer Research and Treatment (IRCC), Università di Torino, Torino