Conceptual model of E. coli transcriptional machinery

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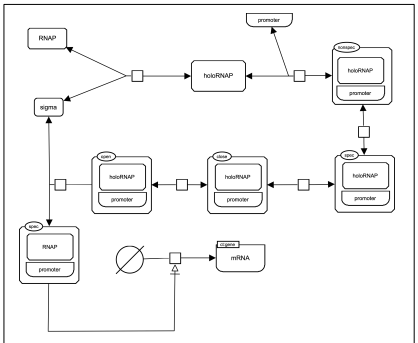
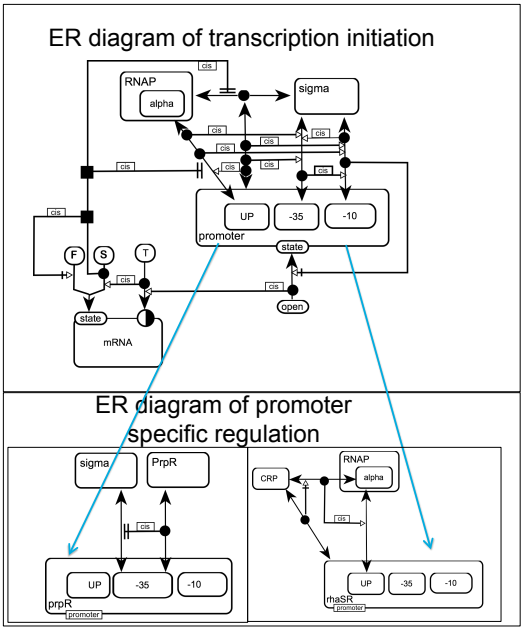


PD diagram of transcription initiation

Background

At the moment one type of analysis of transcription regulatory networks (TRNs) in prokaryotes is topological analysis of graph structure of possible regulatory interaction links (see for example [1]). That type of analysis takes into account possibility links that designate the fact that one gene product in some conditions can modulate transcription of the other. The benefit of such approach is that it is allow analyzing TRN at the whole cell level. At the same type it is known that at least some responses are regulated by abundance of elements of transcription machinery [2-3].

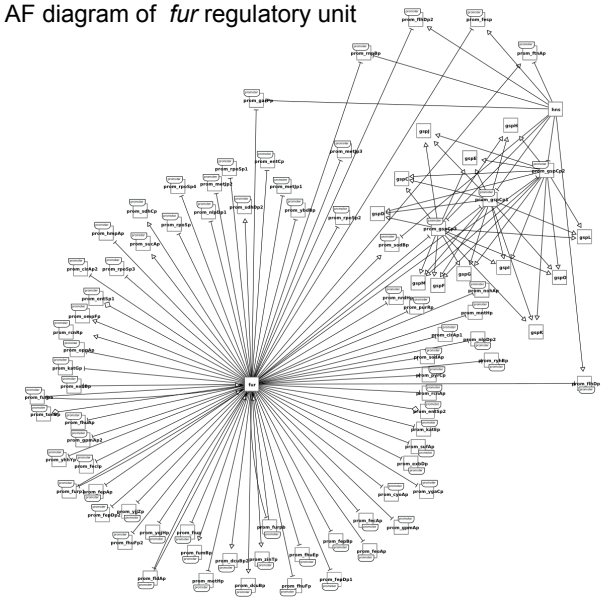


Results

To develop more quantitative model of whole cell transcription network we need to reorganise information available to us to make it suitable for model design and analysis. We will use SBGN family of visual modelling languages [4] to perform this task. The regulation of prokaryotic transcription combine two important features, which makes it interesting and difficult to model. First, interaction of RNA-polymerase with promoter always follow strict scenario, which is known for quite a while [5] and is shown as PD diagram. At the same time every promoter has its own set of regulators to control rate of promoter utilisation. We also need to take into account that in many cases promoter is regulated by some of its products. So to describe whole cell regulatory network we need to take into account both promoter regulation specificity and network of mutual regulation. We will achieve this with combining all three languages of SBGN.

Activity flow (AF) diagram is used to outline global structure of regulatory network. Small exception of in, depicting regulatory network around fur protein is shown here. That network differ from standard gene networks is that we have separate 'class' of entities to represent promoter and we took operon structure of the E.coli genome into consideration so one promoter regulate transcription of several genes [6]. AF diagram allow to trace regulatory interactions in the network and guide development of model for specific subsystem.

To collect, present and analyse details of regulation of individual promoter we are using Entity Relationship (ER) language. The benefit of ER language is decontextualisation of interactions that allow us build our model from parts like a LEGO. First we have created the ER version of generic promoter, to do this we have to use little tric here: we have introduced generic entities "Promoter" and "Sigma" to represent average promoter and unspecified sigma-factor used by RNAP. Now using thus 'generic' diagram as template we can draw detail of individual promoter regulation. We are using UoI element of SBGN language to link specific biological element, like prpR promoter, to generic "Promoter" entity on the basic diagram. It a similar way we are using UoI to mark promoter activities on AF diagram.



Summary

We have developed conceptual model of whole cell E. coli TRN with SBGN ER, SBGN PD and SBGN AF languages. We are building of our model as hierarchy of ER diagrams, where next level provide more detailed presentation of some model from previous level. We are using Unit of Information elements to organise ER diagrams into hierarchy an provide semantic links diagrams of different languages. That model is the first step towards incorporation of some quantitative information into whole cell TRN modeling.

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