

Molecular Networks

WS 11/12

PLDE and qualitative abstraction

Exercise 1 Based on the following excerpt from a paper dealing with starvation stress response in *E. Coli* construct a simple PLDE model comprising two components, representing Fis/fis and the rrn operons. Do a phase space analysis for a phase space partition derived from pertinent nullclines and threshold planes, and calculate the qualitative state transition graph for your PLDE model for the partition derived from only the threshold planes.

The control of the expression of stable RNAs by the global regulator Fis is an example of gene expression regulation by a transcriptional activator. During exponential phase, when the demand for protein synthesis is high, promoters of the seven rrn operons account for more than 60% of the cellular transcription products (Bremer and Dennis, 1996). The high activity of these promoters has been related to their stimulation by the protein Fis (Appleman et al., 1998, Nilsson et al., 1992, Zhang and Bremer, 1996 and Zhang et al., 2002). In particular, the protein activates transcription by binding to regulatory sites and stabilizing the interaction between RNA polymerase and ribosomal promoters in a cooperative manner (Aiyar et al., 2002, Bokal et al., 1995, Hirvonen et al., 2001, Paul et al., 2004, Schneider et al., 2003 and Zhi et al., 2003). Below a certain threshold concentration of Fis, the stable RNA genes are poorly expressed, whereas above this threshold their expression reaches its maximum level.

In E. coli, the production of stable RNAs varies in proportion to the growth rate, to match the cell's changing demand for protein synthesis. Most of this regulation is achieved at the level of transcription of the seven rrn operons (Dennis et al., 2004, Murray et al., 2003, Murray and Gourse, 2004, Paul et al., 2004 and Schneider et al., 2003). Stable RNAs are produced from two promoters, P1 and P2. The activity of the former is stimulated by the protein Fis, which allows rapid bacterial growth (Appleman et al., 1998, Nilsson et al., 1992, Zhang and Bremer, 1996, Zhang and Bremer, 1996 and Zhang et al., 2002). On the contrary, rrnP2 is considered a house-keeping promoter, because it is much less responsive (Schneider et al., 2003) and no Fis-dependent regulation has been demonstrated.

In addition to activating rrn production, Fis has been shown to repress its own expression, by binding to the promoter region of the gene (Ball et al., 1992, Ninnemann et al., 1992 and Pratt et al., 1997). As in the previous example, the activity plot of fis is a sigmoidal curve. However, expression of this gene is now a decreasing function of the Fis concentration. Moreover, the curve is shifted to a higher concentration range, which reflects the fact that Fis binds more weakly to its own promoter region than to that of rrn.