addition, new proteins were recognized as regulated by FlhD/FlhC in the category that relates to anaerobic respiration. We interpret this as an indication that pattern mining is a useful tool for the analysis of complex microarray and network data.

The second biological question that was asked was what functional categories of proteins (indicated by their HMM) are involved in the regulation of ABC transporter genes. A search was performed for patterns containing 'ABC'. After selecting a pattern involving 'ABC', the hmm.abc_tran domain appears in the 'Descriptor' column labeled (1). HMMs of proteins that regulate ABC transporter genes were taken from the 'Descriptor' column, labeled (0). The genes encoding these regulators were taken from the 'Gene 0' column. The specific ABC transporter genes that are regulated by this regulator were taken from the 'Gene 1' column. These regulations are summarized in Table 2 and correspond to the Pattern Information page.

Proteins regulating ABC transporters were grouped into functional categories again, based upon their properties (HMM). Two-component systems each consist of a histidine kinase (hmm.hiska) and a response regulator (hmm.response_reg) (for a review, please, see [41]). RcsCDB is a rare case of a three-component system, where the first component (RcsC) contains both functional domains [42]. In the cases of RcsCDB, EnvZ/OmpR, and TorS/TorR, histidine kinases and response regulators have been identified as regulators of ABC transporter genes (Table 2). In the cases of PhoR/PhoB, NarX/NarL, NarQ/NarP, and NtrB/NtrC (synonym GlnG that was identified as a regulator of ABC transporter genes by its hth_8 domain), only the response regulator was found to regulate ABC transporter genes. Overall, the contribution of two-component systems to the regulation of ABC transporters seems to be large. Considering the small degree of overlap between the regulated genes, it seems like many two-component systems are specific for a certain set of ABC transporter genes.

An example of how BISON can be used to create hypotheses that can be further examined experimentally is given as an extension of the above study and involves the second functional categories of proteins that regulate ABC transporter genes, DNA binding proteins: ModE (hmm.hth_1) is a known repressor of the *modA* operon that encodes a molybdate specific transporter [43] and the *ccmA* operon that encodes a haem transport system [44]. While early studies with the *ccmA* operon showed that transcription was induced during anaerobic growth, regulation by known regulators of anaerobic respiration (FNR, ArcB/ArcA) could not be detected [44]. With this study, we found a regulation of *ccmA* by NarX/NarL and NarQ/NarP (Table 2). Both these two-component systems are global regulators during anaerobic growth in the presence of nitrate [45]. This leads to the hypothesis that regulation of

Table 2: Regulators that affect the expression levels of ABC transporter genes

Regulator gene[1]	HMM of the regulator[2]	Regulated genes[3]	HMM of regulated proteins[4]
Two-component systems			
torS	response_reg	*fepC*	abc_tran
phoB	response_reg	*ugpC, pstB, phnL, phnK, phnC*	abc_tran
narL	response_reg	*cydC, cydD, ccmA*	abc_tran
narP	response_reg	*ccmA*	abc_tran
rcsB	response_reg	*tauB, fepC, ycjV, nikD, nikE, malK*	abc_tran
torR	hiska	*fepC*	abc_tran
rcsC	hiska, response_reg	*tauB, fepC, ycjV, nikD, nikE, malK*	abc_tran
ompR	response_reg	*yehX, cysA, proV, ugpC, dppD*	abc_tran
envZ	hiska	*yehX, cysA, proV, ugpC, dppD*	abc_tran
glnG	hth_8	*glnQ, potG, dppF, dppD, hisP, yhdZ*	abc_tran
DNA binding proteins			
modE	hth_1	*modC, ccmA*	abc_tran
cysB	hth_1	*tauB, cysA*	abc_tran
cbl	hth_1	*tauB*	abc_tran
oxyR	hth_1	*sufC*	abc_tran

[1]Genes encoding regulators that affect the expression levels of ABC transporter genes are taken from the 'Gene 0' column on the navigation page.
[2]HMMs for the regulators are taken from the 'Descriptors' column on the navigation page. HMMs are indicative of the functional categories of regulators (bold subheadings) that affect the expression levels of ABC transporters.
[3]Genes encoding ABC transporters that are affected by the regulators in column 2 are taken from the 'Gene 1' column on the navigation page.
[4]HMMs for the regulated proteins are taken from the 'Descriptors' column on the navigation page. HMMs are indicative of ABC transporters.