Table S1: Evolutionary models for gene regulatory sequence (S), gene expression (E) and using phylogenetic information (P).

Model	Components			Applications	Species
MAFIA[1]	Р	S	-	Evolution of binding sites	Drosophila
EMMA[2]	Р*	S	-	CRM alignment and prediction	Drosophila
Kimono[3]	-	S	E	Clustering of promoter and expression	Simulation
MODEM[4]	-	S	E	Identifying target genes of a transcription factor	Yeast
REDUCE[5]	-	S	E	Motif prediction	Yeast
DCA[6]	Р	-	E	Identifying conserved and diverged co- expression patterns	Yeasts
SCSC[7]	P*	-	Е	Identifying conserved and diverged co- expression patterns	Mammals
Khaitovich[8]	Р	-	E	Neutral evolution of gene expression	Primates
Xie [this paper]	Р	S	E	Evolution of gene regulatory networks	Yeasts, Mammals

^{*} Only applied to two species.

- 1. Majoros WH, Ohler U (2010) Modeling the Evolution of Regulatory Elements by Simultaneous Detection and Alignment with Phylogenetic Pair HMMs. PLoS Comput Biol 6: e1001037.
- 2. He X, Ling X, Sinha S (2009) Alignment and Prediction of <italic>cis</italic>-Regulatory Modules Based on a Probabilistic Model of Evolution. PLoS Comput Biol 5: e1000299.
- 3. Holmes I, Bruno W (2000) Finding regulatory elements using joint likelihoods for sequence and expression profile data. Proc Int Conf Intell Syst Mol Biol 8: 202-210.
- 4. Wang W, Cherry JM, Botstein D, Li H (2002) A systematic approach to reconstructing transcription networks in Saccharomycescerevisiae. Proceedings of the National Academy of Sciences of the United States of America 99: 16893-16898.
- 5. Bussemaker HJ, Li H, Siggia ED (2001) Regulatory element detection using correlation with expression. Nat Genet 27: 167-174.
- 6. Ihmels J, Bergmann S, Berman J, Barkai N (2005) Comparative gene expression analysis by differential clustering approach: application to the Candida albicans transcription program. PLoS genetics 1: e39.
- 7. Cai J, Xie D, Fan Z, Chipperfield H, Marden J, et al. (2010) Modeling Co-Expression across Species for Complex Traits: Insights to the Difference of Human and Mouse Embryonic Stem Cells. PLoS Comput Biol 6: e1000707.
- 8. Khaitovich P, Paabo S, Weiss G (2005) Toward a Neutral Evolutionary Model of Gene Expression. Genetics 170: 929-939.