Transcription factor binding energy vs. biological function

M. DJORDJEVIC, E. GROTEWOLD, The Ohio State University — Transcription factors (TFs) are proteins that bind to DNA and regulate expression of genes. Identification of transcription factor binding sites within the regulatory segments of genomic DNA is an important step towards understanding of gene regulatory networks. Recent theoretical advances that we developed [1,2], allow us to infer TF-DNA interaction parameters from in-vitro selection experiments [3]. We use more than 6000 binding sequences [3], assembled under controlled conditions, to obtain protein-DNA interaction parameters for a mammalian TF with up to now unprecedented accuracy. Can one accurately identify biologically functional TF binding sites (i.e. the binding sites that regulate gene expression), even with the best possible protein-DNA interaction parameters? To address this issue we i) compare our prediction of protein binding with gene expression data, ii) use evolutionary comparison between related mammalian genomes. Our results strongly suggest that in a genome there exists a large number of randomly occurring high energy binding sites that are not biologically functional. [1] M Djordjevic, submitted to Biomol. Eng. [2] M. Djordjevic and A. M. Sengupta, Phys. Biol. 3: 13, 2006. [3] E. Roulet et al., Nature Biotech. 20: 831, 2002.

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